PROGRAM FOR WEDNESDAY, JUNE 22ND

14:00-17:00 Session 1A: EvMed Directors Meeting

LOCATION: Junior Ballroom D at the Durham Convention Center

14:00-17:00 Session 1B: EvMed Students Meeting

LOCATION: Junior Ballroom D at the Durham Convention Center

18:00-20:00 Session : Opening Reception

LOCATION: Grand Ballroom Lobby at the Durham Convention Center

PROGRAM FOR THURSDAY, JUNE 23RD

07:00-08:00 Session: Continental Breakfast

LOCATION: Grand Ballroom Lobby

08:00-09:00 Session 2: Plenary Speaker: Helen Ball

CHAIR: *Charles Nunn* LOCATION: Grand Ballroom I

08:00 *Helen Ball*

Changing UK guidance and practice around maternal-infant sleep—did an evolutionary perspective help?

SPEAKER: *Helen Ball*

ABSTRACT. Anthropologists at Durham University's Parent-Infant Sleep Lab combine behavioural, physiological and ethnographic methods in their studies of maternal-infant sleep ecology. The outcomes of these studies have helped to change UK public health recommendations and hospital practices. This talk will explore whether an evolutionary perspective contributed to translating this research into policy and practice.

09:00-10:00 Session 3A: Sleep

CHAIR: *Katie Hinde* LOCATION: Grand Ballroom I

09:00 *David Samson*, *Melissa Manus* and *Charles Nunn*

Sleep duration, quality and timing in a non-electric population in Madagascar

SPEAKER: unknown

ABSTRACT. Sleep patterns are heavily impacted by technology and behavioral choices in developed countries, including through use of artificial lighting. However, little is known about sleep in "traditional" small-scale societies that lack access to electricity. Thus, we lack understanding of the extent of mismatch between our current sleep patterns and those of our ancestors. We characterized sleep in a rural community without electricity in Madagascar, and compared results to patterns of sleep found in great apes and in Western populations. Ten females and 13 males volunteered to wear actigraphic watches for up to 21 days per individual (329 nights total). Sleep onset averaged 19:21 hours (SD=3.38). Awake times were also early compared to developed countries (5:44), and showed less variation (SD=0.53), with individuals averaging 9.4 hours in bed. Of these hours, only 6.5 involved sleep. Sleep efficiency in the Malagasy population (70.7%) was grossly comparable to

orangutans (73.0%), but lower when compared to Western populations (88.8%). Wake after sleep onset (2.1 hours) was more than double typical values in developed countries. A linear mixed effects model revealed that older individuals slept longer ($\beta = 0.31$, $z = 2.82$, $p = 0.004$), and farmers slept less than non-farmers ($\beta = -0.41$, $z = 3.22$, $p = 0.001$) and had more fragmented sleep. Thus, traditional human populations exhibit shorter duration and greater flexibility of sleep expression than humans in developed countries, and shorter but equally efficient sleep when compared to great apes.

09:15 *Virginia J. Vitzthum*, *Jonathan Thornburg* and *Hilde Spielvogel*

Sleep patterns in breastfeeding women in a non-industrialized natural fertility population: Is there mother-infant conflict?

SPEAKER: unknown

ABSTRACT. Throughout human evolutionary history until the recent advent of effective contraception, virtually all women spent a majority of their reproductive years breastfeeding a succession of infants. Breastfeeding was typically on-demand and frequent, a pattern facilitated by close proximity, including co-sleeping, of a mother and her nursling. In contrast, in contemporary industrialized nations, women usually have fewer pregnancies, breastfeed less and forgo co-sleeping. In these populations, significant disruptions in the quality and quantity of their own sleep are commonplace among mothers of infants, suggesting considerable conflict between maternal attention to the infant's nocturnal needs and investment in her own somatic well-being. It is uncertain, however, whether the degree of this conflict arises largely as a consequence of current behavioral repertoires or if comparable trade-offs were faced by mothers throughout human evolution. We measured sleep and breastfeeding patterns in a natural fertility (non-contracepting) rural Bolivian population principally reliant on agropastoralism. Most homesteads lacked electricity and cooked with wood, scarce in this harsh cold environment (altitude 3800m, latitude 17°S). In contrast, those households closest to the main town were more likely to have electricity and use propane for cooking. Data are from 885 48-hour recording periods in 184 co-sleeping mother-infant pairs (infant age 22-730 days). Maternal sleep duration co-varied with natural photoperiod and was much longer than that typically reported by U.S. mothers of infants. Higher night breastfeeding rates were associated with fewer hours of maternal sleep. This association was mitigated as the nursling aged. Near-town mothers went to bed later than rural mothers. As their infants aged, near-town mothers slept less while rural mothers slept more. These patterns suggest that (1) more frequent night nursing is associated with less maternal sleep even in co-sleeping pairs, and (2) even modest increases in "modernization" (e.g., electricity) are associated with shorter maternal sleep. Funding: NSF#SBR9506107

09:30 *Randolph Nesse* and *Charles Nunn*

Does the tradeoff with short sleep explain vulnerability to Alzheimer's disease?

SPEAKER: unknown

ABSTRACT. The prevalence of Alzheimer's disease climbs dramatically from 8% among people in their upper 70's, to nearly 40% for those over 85. Why does the brain fail so consistently in this particular way? The weaker force of selection at advanced ages is relevant, but several recent discoveries suggest that additional evolutionary factors may be involved. First, the brain manifestations of Alzheimer's disease appear to be far more common for humans than for other primates. Second, humans sleep vastly less than other primates, and much less than predicted based on our brain size, activity pattern, body mass,

phylogeny, and other traits. Third, recently discovered glymphatic channels in mice expand by 60% during sleep, doubling the rate of amyloid beta exit from the brain. Finally, sleep deprivation causes tau accumulation in the brains of mice.

These findings lead us to propose the hypothesis that strong selection for shorter sleep in humans has compromised glymphatic function, resulting in vulnerability to Alzheimer's disease. Selection forces shaping shorter sleep durations in humans include risks from predators because of sleeping on the ground, and from hostile conspecifics who can be more active at night thanks to the controlled use of fire. Shorter sleeping also provides benefits from social learning and relationship building during nighttime socializing. The tradeoff for these benefits of less sleep is compromised glymphatic function, which may result in amyloid beta and tau accumulation with associated dementia later in life. Our hypothesis predicts that the risk of plaques and tangles in other primates is correlated with sleep durations. If confirmed, it would support recent initiatives to manipulate sleep and glymphatic function to see they can influence the prevention or progression of Alzheimer's disease.

09:45 *Gandhi Yetish*, *Hillard Kaplan* and *Michael Gurven*

Tsimane hunter-horticulturalists sleeping in more exposed sleeping sites have more sleep interruptions and lower sleep efficiency

SPEAKER: unknown

ABSTRACT. Recent sleep research conducted among small-scale subsistence societies (lacking electricity) has yielded novel findings about the nature of human sleep, especially with regard to timing and duration. Building on this, we aim to 1) quantitatively characterize the typical pattern of sleep fragmentation among Tsimane hunter-horticulturalists in lowland Bolivia, and 2) to explain variation in sleep efficiency (total sleep / time in bed) and sleep interruptions in relation to the degree of environmental exposure from lacking walls on one's house. Taking advantage of heterogeneity in the Tsimane sleep environment, we measured the normal, in-home sleep of 76 women aged (mean ± SEM) 36.5 ± 1.9 and 57 men aged 41.7 ± 2.2 for an average of 4.7 nights each (639 total). Sleep was measured using wrist-worn accelerometers, which have been validated as sleep monitors against polysomnography. 459 in-home interviews measured nocturnal awakenings and characteristics of the sleep environment. Mean total sleep was 6.7h ± .13, and the mean time awake in bed was 95.3m ± 1.8. The most common reported causes of sleep interruption were the need to perform childcare (32.3%), need to urinate (26.6%), and hearing animal noises (13.7%). Sleeping in houses missing at least one wall was associated with spending 14.4m more awake during the sleep period each night (t-test, p=.001), being 7.8% more likely to attribute sleep interruption to animal noises (t-test, p=.089), and being 16.3% more likely to attribute it to the need for childcare (t-test, p=.005). These results indicate that people sleep more soundly in fully-closed spaces, suggesting that without walls, people may need to maintain greater vigilance during sleeping hours. Based on these findings, we suggest that early humans likely faced nighttime dangers regularly, and that in response, we have evolved the ability and predisposition to inhibit sleep in response to stressors in our environment.

09:00-10:00 Session 3B: Selection, stress and homeostasis

CHAIR: *Mark Schwartz* LOCATION: Grand Ballroom III

09:00 *Chris von Rueden*, *Benjamin Trumble*, *Mellissa Emery Thompson*, *Jonathan Stieglitz*, *Paul Hooper*, *Aaron Blackwell*, *Hillard Kaplan* and *Michael Gurven*

Political influence associates with cortisol and health among egalitarian forager-farmers

SPEAKER: unknown

ABSTRACT. Low social status increases risk of disease due, in part, to the psychosocial stress that accompanies feeling subordinate or poor. Previous studies report that chronic stress and chronically elevated cortisol can impair cardiovascular and immune function. We test whether lower status is more benign in small-scale, relatively egalitarian societies, where leaders lack coercive authority and there is minimal material wealth to contest. Among Tsimane' forager-horticulturalists of lowland Bolivia, we compare informal political influence among men with urinary cortisol, immune activation (innate and acquired), and morbidity as assessed during routine medical exams. After controlling for potential confounds, we find that politically influential men have lower cortisol, and that this association is partly attributable to access to social support. Cortisol is positively associated with men's income, which may reflect chronic psychosocial stress from market involvement. Greater influence is also associated with lower probability of respiratory infection, which is a frequent source of morbidity among Tsimane'. Among men who lost influence over a 4-year period, cortisol and probability of respiratory infection were higher the greater the decline in influence. Deleterious effects of low status on health are not merely 'diseases of civilization' but may result from how (even subtle) status differences structure human behavior.

09:15 *Beverly Strassmann*, *Armin Dadkhah*, *Zachary Dolo* and *Claudius Vincenz*

A longitudinal study of the effects of stress and urbanization on blood pressure in Africa

SPEAKER: unknown

ABSTRACT. High blood pressure is the greatest single cause of the global burden of disease (Pouler et al. 2015). The prevalence of hypertension is higher in persons of African descent, yet there are few longitudinal cohort studies of non-communicable diseases in Sub-Saharan Africa. For 19 years we have conducted a prospective cohort study of the Dogon of Mali: following ~1700 subjects annually from early postnatal life to adulthood. Half of the subjects migrated to the capital city of Bamako where we have continued to follow ~85% annually. Our study is unique in that it longitudinally compares the health and developmental trajectories of subjects from the same cohort who either remained in the rural villages or who migrated to the city. Our statistical analyses employed linear mixed models in IBM SPSS 22. "White coat hypertension" emerged as the single variable with the largest effect size. For each additional measurement session, blood pressure fell significantly ($P < 0.001$) reflecting acclimation to the measurement protocol, with boys acclimating faster than girls. Controlling for the number of measurements, blood pressure increased with age, ambient temperature, height, and BMI and tended to decrease slightly with wealth. Of particular interest was that after adjusting for these variables, blood pressure was 4.6 mm Hg ($P < 0.001$) higher in the city than in the countryside. Thus, the increase in blood pressure in the city was not entirely mediated by body size, and may reflect the stress of adjusting to urban life. This possibility is supported by the 0.5 mm Hg ($P < 0.001$) decrease in blood pressure for each additional year of urban living. Research has focused on obesity and sedentary life styles, yet blood pressure is also strongly reactive to stress--an under-investigated factor in the epidemiological transition in low income countries.

09:30 *Djuke Veldhuis*

"Stress is the spice of life": an evolutionary perspective on the human stress response.
SPEAKER: *Djuke Veldhuis*

ABSTRACT. The human stress response governs our ability to deal with a wide range of stimuli that life throws at us. An evolutionary approach encourages us to consider the selective advantage this system provides, particularly given its associated costs (e.g. in metabolism and immune function).

However, given that our ancestors almost certainly experienced more stress, in the form of trauma, disease and starvation for example, one may question why stress appears to play such a large role in industrialised societies. One argument is that our stress response developed in the context of physical stressors, not the mental and social ones people in industrialised societies mainly encounter today. In other words, the idea that there is a mismatch between the evolutionary context in which our stress response evolved and the environment it operates in today.

To test this hypothesis, I report results from three distinct communities in Papua New Guinea. Depending on location, these communities face notably different stages of socioeconomic transition. I looked at the interaction between social change, lifestyle, and stress. A 'stress profile' was built using physiological (hormonal) measures of stress and psychological indicators of anxiety alongside socioeconomic surveys and ethnographic methods. The results suggest that with urbanization and, so called 'modernization' come a swathe of maladaptive coping behaviours and significantly heightened stress hormone levels.

Finally, I consider the challenge of translating the results from fieldwork to meaningful, applied public health (intervention) programs. I show how evolutionary biology and psychology provided a broader framework to tackle the existing disconnect between research and (health) policy.

09:45 *Diana Fleischman*, *Abbey Woods* and *Susan Girdler*

Baseline inflammation predicts higher disgust sensitivity but stronger inflammation in response to disease cues predicts lower disgust sensitivity: insights into evolved disease avoidance mechanisms from IL-6 levels
SPEAKER: unknown

ABSTRACT. Disgust is widely thought to have evolved to motivate humans away from contagious disease (Curtis et al., 2004). The compensatory behavioral prophylaxis hypothesis (Fleischman & Fessler, 2011) predicts those who are the most immunologically vulnerable will show the most disgust sensitivity. There is evidence that disease cues influence immunity. Previous research has found pictures of sick people and disgust eliciting images increase serum IL-6 (Schaller et al., 2010) as well as body temperature and oral immune markers (Stevenson et al., 2012). There is also some evidence that those who have suffered a recent infection and therefore are immunologically vulnerable show increased attention to disease cues (Miller & Maner, 2011). However, no previous study has investigated the connection between baseline immunity or immune activation in response to a stress paradigm on disgust sensitivity. In the current study, 150 women in the menopause

transition were exposed to a psychosocial stressor, the Trier Social Stress Test. During the protocol, plasma levels of interleukin 6 (IL-6) were collected at baseline and over a 60 minute recovery following the test. . After recovery, disgust measures including disgust response to images (Curtis et al., 2004) and the Three Domains of Disgust inventory (Tybur et al. 2009) were administered. We find that higher baseline IL-6 is associated with greater disgust sensitivity to both images and inventory items, especially those that reflect disease cues. However, we find that women who show a more robust IL-6 response to stress show lower disgust sensitivity. We hypothesize that baseline IL-6 may be indicative of recent infection or immune vulnerability but that IL-6 increase during the stress task could be indicative of healthy immune function. Results will be discussed in light of an adaptationist perspective on disgust and disease avoidance.

10:00-10:30 Session : Break

Coffee and snacks will be provided.

LOCATION: Grand Ballroom II

10:30-11:30 Session 4A: Selection, stress and homeostasis

CHAIR: *Melissa Wilson Sayres* LOCATION: Grand Ballroom I

10:30 *Edmund Legrand* and *Judy Day*

Self-harm with non-specific stressors to preferentially harm the pathogens within

SPEAKER: unknown

ABSTRACT. Much of a major part of host defense against pathogens is generally unrecognized—the active use of non-specific stressors which harm host cells as well as pathogens. These stressors include heat, reactive molecular species, nutrient and oxygen deprivation, and lactic acidosis. Hosts take advantage of two potential vulnerabilities of pathogens to stress: 1) the inherent vulnerability of growth and replication (more immediately crucial for pathogens than for host cells) and 2) the degree of localization of the pathogens. Each of the non-specific stressors listed above typically occurs within phagolysosomes (where their utility is well-recognized), as well as locally at the infected site, in the region of the infected site, and systemically as part of the acute-phase response (e.g., fever, anorexia, iron and zinc restriction). We used a simple agent-based model of a locally infected host to explore the efficacy of host defenses consisting of completely non-specific stress in controlling rapidly replicating pathogens. We found that local, regional, and systemic stress acted synergistically in eliminating pathogens. While local and regional stress functioned by restricting pathogen spread, systemic stress's efficacy was due to pathogens using their resources for more rapid replication compared to host cells, thus having fewer reserves to withstand stress. To the extent that hosts can harm themselves to preferentially harm the pathogens within, it should be expected that hosts actively use this strategy as a defense. This evolutionarily basic strategy complements more recently evolved specific anti-pathogen defenses which cause little collateral host harm but are more susceptible to the evolution of resistance.

10:45 *Robert Perlman*

Precision Medicine and Evolutionary Medicine

SPEAKER: *Robert Perlman*

ABSTRACT. Last year, President Obama launched the Precision Medicine Initiative (PMI). In brief, this ambitious program aims to improve health by tailoring the prevention and

treatment of disease to genetic, environmental, and lifestyle differences among individuals. The PMI grew out of a realization that the traditional “one size fits all” approach to medical care is imperfect and not always helpful or successful, because many preventive measures and therapies benefit only a small fraction of the patients who receive them. Medical practice is rapidly changing, however, at least for the treatment of patients with some forms of cancer. Because of progress in sequencing the genomes of cancer cells and in identifying mutations that are “drivers” of malignancy, the PMI will initially be focused on cancer therapy, but the leaders of this initiative plan to expand it to include virtually all diseases. Although the PMI may improve some aspects of medical practice, its potential is limited by its failure to incorporate principles of evolutionary medicine. The initiative is grounded on an appreciation of the abundant variation among individuals in susceptibility to disease and among patients in the pathophysiological pathways leading to disease but it retains a typological or essentialist view of illness. Moreover, while the PMI intends to integrate genomic information with physiological, clinical, behavioral, and environmental data, the initiative remains a gene-centric view of disease and does not give sufficient recognition to ecological determinants of illness. Finally, even though diseases of aging will be important targets of the PMI, the initiative does not yet incorporate life history theory into its analyses. The PMI can be improved by adoption of an evolutionary understanding of disease, and so this initiative offers new opportunities for members of the Evolution, Medicine, and Public Health community to contribute to medical research and practice.

11:00 *Charleston Chiang*, *Carlo Sidore*, *Magdalena Zoledziewska*, *Joseph Marcus*, *Hussein Al-Asadi*, *Goncalo Abecasis*, *David Schlessinger*, *Francesco Cucca* and *John Novembre*
Population genetic insight to the study of human height
SPEAKER: unknown

ABSTRACT. Genetic adaptations of many human traits are likely highly polygenic, occurring at many loci in the genome rather than at a single locus. Human height is one such example. It is a classic polygenic trait and is known to be differentiated across Europe. Powered by successful genome-wide association studies that provided us with hundreds of known loci, we detected a signature of widespread selection at height loci across Europe. Furthermore, we honed in on the isolated Southern European population of Sardinia. Using whole genome sequencing data, we investigated the population structure of Sardinia, its demographic history and relationship to ancient European farmers to gain insight on the peopling of the island. On this unique Sardinian genetic background, we identified two loci in which the derived alleles have increased frequency compared to mainland Europe and strongly decrease height in Sardinia, as well as an overall trend of lower stature being favored on the island by selection. These results generate additional hypotheses regarding height variation around the globe, and serve as examples of studying the evolution of polygenic traits when the genetic architecture is sufficiently known.

11:15 *Irina Morozova*, *Sergey Bruskin*, *Timofey Prodanov*, *Anton Afanasyev*, *Frank Rühli* and *Tatiana Tatarinova*
Evolution of evolution: changing of human adaptation reaction from the Bronze Age to the modern time
SPEAKER: unknown

ABSTRACT. One of the main goal of evolutionary medicine is to understand how evolution has shaped our body. During last several thousand years, mankind has been dispersed all

over the world, experienced agriculture, significant increasing in population density, domestication of animals and plants, and exposure to new pathogens. All of these effects have been selfimposed. Turning point in human evolution has started with beginning of civilization when humans, instead of reacting to the environment, began to actively shape it. Therefore, we should expect significant changes in human adaptive reactions on the exposure to the artificial environment created by man, and to the natural environment changed by man. These changes should be seen as selection signals in human genomes. Identifying and analysis of these selection signals is of great importance for understanding of connection between the human organism and its environment. We analysed the effect of recent selection on humans by direct comparison of whole genome data on individuals from two civilization steps, the Bronze Age and the modern time. We used an approach allowing us to study the evolution of biochemical pathways involving many different genes and regulatory regions. Thus, we detected selection on the systemic level. We revealed the biochemical pathways indicating the selection signals which were significantly different between the two groups. Our results show that most substantial changes took place in metabolism of some amino acids, lipids, and xenobiotics, in immune system, and in processes connected with some pathologies. In conclusion, we obtained direct proof of action of recent selection on human population during last five thousand years. We believe that our study revealed the strongest selection signals and opened new perspectives for more detailed investigations about when, exactly, and how civilization has been modifying human genomes.

10:30-11:30 Session 4B: Behavior and vulnerability

CHAIR: *Polly Wiessner* LOCATION: Grand Ballroom III

10:30 *Frazer Meacham* and *Carl Bergstrom*

Explaining the hedonic treadmill: opportunity costs and the evolution of mood

SPEAKER: unknown

ABSTRACT. Qualitative theories for the evolution of mood commonly posit that it is adaptive for mood to eventually return to some baseline set point. This idea is supported by the hedonic treadmill—the observation that happiness levels are resilient to both good and bad events. However, the few mathematical models that have been developed to provide evolutionary explanations of mood do not predict that mood should return to a baseline set point. Instead, these models assume that mood functions to decrease activity when the cost is greater than the benefit, and increase it when the benefit is greater than the cost. Thus, these models predict that if conditions stay bad (or good), mood will stay low (or high).

To explain the hedonic treadmill, we investigate a different hypothesis for the function of mood: In a complex environment, the main cost of pursuing a reward may be the opportunity cost of not being able to pursue other rewards. We describe a modeling framework based on opportunity cost in which individuals are presented with a sequence of opportunities, but the cost of pursuing one of the opportunities is giving up the ability to pursue following opportunities in the near future. The optimal strategy in such an environment will often be to adjust activity levels relative to the current expected reward size. This means that activity levels and mood should return to baseline even after the environment has become consistently better or consistently worse. Because depression and bipolar disorder are characterized by mood failing to return to baseline, this modeling

approach has good potential to give insights into pathological mood as well as giving an evolutionary account of normal mood.

10:45 *Molly Fox* and *Laura Glynn*

Testing the adaptive significance of postpartum depressive symptoms in a prospective longitudinal cohort

SPEAKER: unknown

ABSTRACT. Postpartum depression (PPD) is a critical health issue affecting women, children, and wider society. Despite injurious consequences and high incidence, PPD remains understudied and undertreated. Using data from a cohort of 308 pregnant California women studied longitudinally from early gestation through 9 years postpartum, we evaluate a new framework for understanding PPD in an evolutionary context. Previous theories are limited by narrow focus on social support 'benefits', and monolithic characterization of depression itself. Our approach was motivated by Nesse's model of major depressive disorder that focuses on symptoms and situations. We expand upon that model by adding childbirth to the list of situations that instigate depression, and identify symptoms that may be adaptive in this context based on principles of evolutionary anthropology. We predict certain symptoms should be more pronounced in PPD compared to depression during other life phases. To test our hypotheses, we compare PPD symptomology between postpartum women and a separate cohort of women assessed outside the perinatal phase. Because it is unknown whether PPD is fundamentally distinct from analogous syndromes with onset during other life phases, our study has clinical relevance as the first symptom-based characterization of PPD. It also remains unknown whether gestational endocrinology differentially promotes particular symptom clusters in PPD. We hypothesize that if there is a particular set of adaptive depressive symptoms during the postpartum phase, endocrinology is the most likely regulatory biological pathway. We test this hypothesis in our longitudinal cohort by measuring gonadotropin and stress hormone levels serially across each woman's pregnancy, and use regression models to evaluate relations between gestational hormone trajectories and postpartum depressive symptom clusters. Results suggest particular symptom profiles predicted to have adaptive relevance in PPD may be programmed by gestational endocrinology. Results also provide evidence for gestational neuroendocrinology as the target of selection, enacting psycho-behavioral adaptation.

11:00 *Levent Sipahi*, *Derek Wildman*, *Sandro Galea*, *Karestan Koenen*, *Allison Aiello* and *Monica Uddin*

Epigenetic Epidemiology of Epiphenomena: Applying Tinbergen's Four Questions to Posttraumatic Stress Disorder

SPEAKER: unknown

ABSTRACT. As a product of intersecting social-environmental exposures and innate biological states, Posttraumatic Stress Disorder (PTSD) is best understood by epigenetic explanations. Recent advances in measuring epigenetic variation have led to an explosion of epigenetic data related to PTSD, advancing our understanding of biological underpinnings and providing a basis for future developments in prevention and treatment modalities. This literature conceptualizes epigenetic variation that both preexists and arises in response to trauma exposure as causal of differential PTSD risk and resiliency. Despite growing understanding of PTSD epigenetics, few studies have undertaken evolutionary analyses nor leveraged evolutionary theory to inform hypothesis generation or study design. One such evolutionary

perspective that may guide studies of the epigenetic underpinnings of mental health disorders is that of Nikolaas Tinbergen's Four Questions. Here, I present original research and interpret the contemporary literature of PTSD epigenetics to address each of Tinbergen's Four Questions towards a theory of PTSD epigenetics that is informed by evolutionary theory. Specifically, I provide data showing that 1) epigenetic variation is involved in the physiological mechanism of PTSD, 2) epigenetic modifications are responsive to trauma and thus involved in the development of PTSD, 3) genetic potential for epigenetic regulation of PTSD has an ancient phylogenetic history, and 4) PTSD may represent a functional adaptation to the omnipresent threat of trauma. I argue that trauma responses generally and PTSD specifically represent an adaptive developmental plasticity with deep evolutionary roots that is underpinned by epigenetic variation. Appreciating these evolutionary insights, I conclude that PTSD is a biologically functional and appropriate response to trauma exposure. The "disorder" in PTSD is thus confined to a social dimension – the ills of PTSD are socially constructed, not biologically disordered. This theory of PTSD thus has far-reaching implications for research, clinical practice, and public policy.

11:15 *Kristin Tully*, *Alison Stuebe* and *Sarah Verbiest*

The 4th Trimester: Evolutionary Medicine as a Framework to Improve Clinical Support for New Families

SPEAKER: unknown

ABSTRACT. The term "4th Trimester" reflects the anthropological concept that during the first months of life, newborns continue to function like a fetus in many ways; they require months of intense, 'womb-like' nurturing. An evolutionary perspective views the mother and infant as a mutually dependent unit, behaviorally and physiologically intertwined via breastfeeding and other interactions such as skin-to-skin contact. In suboptimal conditions (such as early separation, maternal distraction, lack of safety, maternal anxiety or pain), the bidirectional processes inherent in maternal-infant functioning can be so severely disrupted that health, and even infant survival, is compromised. These infant demands require a substantial transformation for mothers, as Dr. Sheila Kitzinger has noted: There is a fourth trimester to pregnancy and we neglect it at our peril.

During this critical period, many women currently experience considerable challenges, including fatigue, pain, breastfeeding difficulties, depression, lack of sexual desire and incontinence. Amid these concerns, U.S. health care is often fragmented among maternal and pediatric providers. The 4th Trimester Project brings together patients, clinicians, researchers and other stakeholders to define patient-centered priorities in the first 12 weeks after birth. Key, interrelated health themes are (1) maternal mood; (2) infant feeding; (3) sleep and fatigue; (4) sexuality, contraception, and birth spacing; (5) substances, medications, and environmental exposures; and (6) physical recovery from childbirth. To fully address the health issues of the 4th Trimester, it is vital that the systems designed to support health better consider the realities of the lives they serve. The 4th Trimester Project is an example of applying evolutionary medicine concepts to reenvision health care and implement improvements in clinical support for new families.

11:30-12:30 Session 5: Poster session

All posters and presenters will available during this session.

LOCATION: Grand Ballroom II

12:30-13:30 Session : Lunch

This lunch will be provided.

LOCATION: Junior Ballrooms C and D

13:30-14:30 Session 6: Plenary Speaker: Martin Blaser

CHAIR: *Andrea Graham* LOCATION: Grand Ballroom I

13:30 *Martin Blaser*

Human Evolution 201: Our early life microbial metagenome guides developmental phenotypes

SPEAKER: *Martin Blaser*

ABSTRACT. not available

14:30-15:30 Session 7A: Somatic cell mutation, selection and evolution in health and disease

CHAIR: *Neil Greenspan* LOCATION: Grand Ballroom I

14:30 *Neil Greenspan*

A Perspective on the Role of Somatic Cell Evolution in Human Health and Disease

SPEAKER: *Neil Greenspan*

ABSTRACT. Practitioners of evolutionary medicine most typically focus on the consequences of human evolution for variation in health, survival, reproduction, and susceptibility to disease. However, a full accounting for variation in each of these traits must also address the contributions of somatic cell mutation, selection, and evolution, which have been implicated in the pathogenesis of numerous medical conditions, susceptibility to disease, and response to therapy. In addition to cancer, there are non-malignant diseases, such as WHIM (warts, hypogammaglobulinemia, infection, and myelokathexis) syndrome, that arise from competition among somatic cells, hematopoietic stem cells in the case of WHIM syndrome. As demonstrated by a recent study that will be discussed in this session, clonal competition among hematopoietic stem cells can lead to reversal of a disease, specifically WHIM syndrome. It is well known that mutation and selection of B lymphocytes is essential for many humoral immune responses that protect against pathogens such as HIV-1, examples of which will be presented. Another key role for somatic cell selection and evolution involves development of resistance to therapy for cancer and strategies to prevent such resistance, a final topic to be addressed. Additional examples of somatic cell mutation, selection, or evolution that affect health will also be discussed to demonstrate the broad range of these phenomena.

14:45 *Mattia Bonsignori*

B Cell Lineage Immunogen Design for HIV-1 Vaccine Development.

SPEAKER: *Mattia Bonsignori*

ABSTRACT. The HIV-1 pandemic remains a global emergency for which there is currently no cure. Vaccination has historically been the most effective measure for controlling the transmission of infectious agents and the development of a protective HIV-1 vaccine remains a global public health priority.

Many licensed vaccines induce specific antibodies that correlate with protection. Therefore, the induction of HIV-1 broadly neutralizing antibodies (bnAbs) capable of neutralizing

infectivity of the diverse population of HIV-1 is an appealing goal for a preventive HIV-1 vaccine. However, despite decades of intense research, attempts to formulate a protective HIV-1 vaccine through classic vaccine design strategies have not been successful.

Rare chronically HIV-1 infected individuals naturally develop bnAbs but this happens several years after infection - when natural eradication can no longer be achieved - and as a result of tortuous and disfavored B cell affinity maturation pathways. The application of new technologies has provided a clearer understanding of the mechanisms of induction of bnAbs, their co-evolution with autologous virus and their cooperation with other B cell lineages.

These studies have informed on how to recapitulate the key events in the naturally occurring B cell affinity maturation underlying bnAb development and provided a strategy to select HIV-1 envelope proteins that have directly participated in bnAb development to be used as immunogens.

15:00 *Kris Wood*

Targeting the convergent evolution of resistance to targeted therapies
SPEAKER: *Kris Wood*

ABSTRACT. My laboratory uses genomic, pharmacological, and biochemical approaches to define the pathways of resistance to targeted anticancer therapies. For example, we recently developed a technique in which engineered lentiviral cDNAs encoding activators of major oncogenic signaling pathways are introduced into cells and then profiled to identify those capable of conferring resistance to drugs. Using this approach, we have uncovered new pathways of resistance to a range of targeted therapies, and further, have used this information to rationally design more durable combination therapeutic strategies, some of which are currently being explored clinically. In the past two years, we have become particularly interested in the phenomenon of convergent resistance, wherein discrete resistance pathways function through common downstream signaling or transcriptional programs. By identifying these “common effectors”, it may be possible to define new, more robust therapeutic strategies that select against resistance evolution.

15:15 *David McDermott*, *Paejonette Jacobs* and *Philip Murphy*

Chromothriptic Cure of WHIM Syndrome
SPEAKER: unknown

ABSTRACT. Warts, Hypogammaglobulinemia, Infections and Myelokathexis Syndrome (WHIMS) is a rare, autosomal dominant immunodeficiency resulting from gain-of-function mutations in the chemokine receptor CXCR4. We recently described a unique WHIMS patient who underwent spontaneous genetic and phenotypic reversion at approximately age 30 after being severely affected as a child (McDermott, et al., Cell, Feb., 2015) . Her reversion was due to a single catastrophic genetic event known as chromothripsis (chromosome shattering) resulting in the deletion of one copy of 163 genes in addition to her mutant copy of CXCR4 on chromosome 2. This event was traced to a hematopoietic stem cell (HSC) that had spontaneously repopulated her bone marrow. Using mouse models we have found that Cxcr4 haploinsufficiency markedly enhances HSC engraftment potential in recipient WHIM mice whether the donor HSC were purified from whole bone marrow cells or not, and whether the recipient was conditioned by lethal irradiation or not. Enhanced engraftment by Cxcr4 haploinsufficient donor HSC also occurred in wild-type

mouse recipients, but to a lesser extent, and was also HSC intrinsic. Genome editing experiments have been successful at deleting one or both copies of CXCR4 in human cell lines in up to 40% of treated cells, and in reducing CXCR4 surface expression. While CXCR4 was already understood to be important in HSC biology, this patient and subsequent murine experiments have proven that the gene dosage of CXCR4 is a critical factor affecting HSC engraftment. Genome editing is a promising technology for deleting one copy of CXCR4, ideally the WHIM allele, in autologous HSC as a strategy to cure WHIM syndrome.

14:30-15:30 Session 7B: Microbiome and evolutionary medicine

CHAIR: *Richard Bribiescas* LOCATION: Grand Ballroom III

14:30 *Joe Alcock*, *Helen Wasielewski* and *C. Athena Aktipis*

Conflict and cooperation between host and gut microbiota: Implications for nutrition and human health

SPEAKER: unknown

ABSTRACT. The human gut has evolved to take advantage of a diet that is higher in nutrient energy by volume compared to any other primate diet. Industrial food processing continues this trend, but have we taken it too far? An evolutionary framework suggests that cooperation and conflict between host and gut microbes may explain features of the human digestive tract and shed light on diseases linked with the Western diet. Cooperation occurs when microbes provide host energy and protection from infection, and when hosts 'feed' complex carbohydrates to microbes and maintain microbial habitat. Conflict occurs when resident microbes cause tissue destruction, divert dietary energy from the host, and disseminate widely throughout the body, often leading to escalating microbial virulence and host inflammation. According to this framework, an alignment of host and gut microbe fitness interests should promote health, and conflicting fitness interests between host and gut microbes should contribute to disease and malnutrition. Can we prevent diseases by promoting host-microbiota cooperation and limiting conflict? This presentation explores the possibilities.

14:45 *Helen Wasielewski*, *Athena Aktipis*, *Joe Alcock*, *Naomi Mandel* and *Rosy Krajmalnik-Brown*

Two Minutes, Twice a Day: Evolutionary Dynamics of Oral Flora Manipulation in Humans

SPEAKER: unknown

ABSTRACT. Microscopic organisms of the human body are intimately involved in physiological function of their hosts, suggesting a long history of interdependency. Yet, because microbiomes and their hosts are genetically distinct, commensal relationships are only one outcome of co-evolution. Populations of the human microbiota are continually and rapidly evolving, and any genetic mutation that enables individual microbes to shift host behavior toward improved survival and reproductive success should be favored by natural selection. The idea of microbial manipulation of behavior has strong support from research on known pathogenic species: when acquired by a rodent, the protozoan parasite Taxoplasma gondii induces behavioral changes in the host to increase the probability that the parasite will be transmitted to the next required host – a feline. Bacteria that metabolize host foods could increase their access to these substances by evolving to exploit the mechanisms of host food intake. Oral bacteria that feed on dietary sugars, such as Streptococcus mutans, could be involved in shifting taste perception for sweet taste, thus increasing the intake of sugars. If sustained, excess sugar consumption mediated by oral

bacteria could contribute toward the development of obesity. Use of antimicrobial oral hygiene products should moderate this effect. Oral bacterial disease (e.g., periodontitis) and obesity have long been recognized to co-occur, and some evidence for a causal link between oral bacteria and obesity has been reported, but no studies directly examining the role of antimicrobial oral hygiene in this process have been published. Because gut microbes are seeded from the mouth, microbiota present here, either as transients or colonizers, are an easily-accessible system for better understanding the well documented relationships between gut microbiome and health status. Genomic analyses of oral microbiota along with data on host diet and oral hygiene behavior will be needed to evaluate these hypotheses.

15:00 *Sarah Council*, *Robert Dunn* and *Julie Horvath*

Host genetic variation influences skin microbe composition

SPEAKER: unknown

ABSTRACT. The microbes (microscopic organisms including bacteria and Archaea) living on human skin are responsible for immune system maturation, the fate of pathogens that land on the skin and production of body odors that affect mate selection. They therefore have the potential to affect both human health and fitness. Previous studies have identified numerous external and environmental factors that alter the composition and abundance of skin microbes including gender, diet and daily antiperspirant and/or deodorant usage. In order to address whether particular host genetic factors influence our skin microbiota abundance and composition, we analyzed microbial samples from participants of the Personal Genome Project through the Genomes, Environments, Traits conference in Boston in 2014. These participants have had their entire genome sequenced and often also provide their medical data to researchers. Eighty-four participants were swabbed for their axillary (armpit) microbes and answered a series of questions about their daily habits. Using high throughput sequencing, we assessed their 16S rRNA gene sequence (V4 region) to determine the abundance and composition of their axillary microbiota. After data quality control, 41 participants remained and we determined their genetic variants in 20 candidate genes associated with skin disorders or odor profiles. The abundance of key skin microbes was then compared to differences among humans in the variants of these key genes using a non-parametric Kruskal Wallis ANOVA test. We found at least five single nucleotide variants (across two genes) that associate with differential abundance of microbiota (e.g., Streptococcus, Staphylococcus and Corynebacterium). These data suggest an influence from the host genome on the microbes inhabiting our skin, and suggest future work will be valuable in identifying a more complete picture of the microbes we have co-evolved with.

15:30-16:00 Session 8: Poster Session and Break

A-K Last name of the submitting authors should stand by posters.

LOCATION: Grand Ballroom II

16:00-17:30 Session 9A: Immune response

CHAIR: *Cynthia Beall* LOCATION: Grand Ballroom I

16:00 *Aaron Blackwell*, *Benjamin Trumble*, *Ivan Maldonado Suarez*, *Jonathan Stieglitz*, *Bret Beheim*, *J. Josh Snodgrass*, *Hillard Kaplan* and *Michael Gurven*

Immune Function in Amazonian Horticulturalists

SPEAKER: unknown

ABSTRACT. Amazonian populations are exposed to diverse parasites and pathogens, including protozoal, bacterial, fungal, and helminthic infections. Yet much of our understanding of the immune system is based on industrialized populations living in evolutionarily novel environments, where these infections are rarer than they would have been through the majority of human history. We examine distributions and age-related changes in 22 measures of immune function for Bolivian forager-horticulturalists, and compare these to US and European populations. Subjects were 6,338 Tsimane aged 0-90 years. Blood samples collected between 2004-2014 were analyzed for 5-part blood differentials, C-reactive protein, erythrocyte sedimentation rate (ESR), and total immunoglobulins E, G, A, and M. Flow cytometry was used to quantify naive and non-naïve CD4 and CD8 T cells, natural killer cells, and B cells. Compared to reference populations, Tsimane have elevated levels of most immunological parameters, particularly immunoglobulins, eosinophils, ESR, B cells, and natural killer cells. However, monocytes and basophils are reduced and naïve CD4 cells depleted in older age groups. We conclude that infectious and parasitic exposures of the Tsimane ecology lead to lymphocyte repertoires and immunoglobulin profiles that differ from those observed in industrialized populations. These differences have consequences for disease susceptibility and co-vary with patterns of other life history traits, such as growth and reproduction. Moreover, an understanding of immune function under high pathogen stress may help us to understand the emergence of many non-infectious diseases in industrialized populations where pathogen stress is low.

16:15 *Seth Barribeau*, *Paul Schmid-Hempel* and *Ben Sadd*

Royal decree: gene expression in transgenerationally immune primed bumblebee workers mimics a primary immune response

SPEAKER: unknown

ABSTRACT. Invertebrates lack the cellular and physiological machinery of the adaptive immune system, but show specificity in their immune response and immune priming. Functionally, immune priming is comparable to immune memory in vertebrates. Individuals that have survived exposure to a given parasite are better protected against subsequent exposures. Protection may be cross-reactive, but demonstrations of persistent and specific protection in invertebrates are increasing. This immune priming can cross generations ("trans-generational" immune priming), preparing offspring for the prevailing parasite environment. While these phenomena gain increasing support, the mechanistic foundations underlying such immune priming, both within and across generations, remain largely unknown. Using a transcriptomic approach, we show a bacterial challenge to bumblebee queens, known to induce trans-generational immune priming, alters daughter (worker) gene expression. Daughters, even when unchallenged themselves, constitutively express a core set of the genes induced upon direct bacterial exposure, including high expression of antimicrobial peptides, a beta-glucan receptor protein implicated in bacterial recognition and the induction of the toll signaling pathway, and slit-3 which is important in honeybee immunity. Maternal challenge results in a distinct upregulation of their daughters' immune system, with a signature overlapping with the induced individual response to a direct immune challenge. This will mediate mother-offspring protection, but also associated costs related to reconfiguration of constitutive immune expression. Identification of conserved immune pathways in memory-like responses has important implications for our

understanding of the innate immune system, including the innate components in vertebrates, which share many of these pathways.

16:30 *Gabriele Sorci*, *Cédric Lippens* and *Bruno Faivre*
Disentangling immune protection and damage: a lesson from studies on KO models
SPEAKER: unknown

ABSTRACT. The immune system is often depicted as a two-edged sword, one edge providing protection against invading pathogens and proliferating malignant cells, the other edge incurring damage to the host if the immune response is misdirected or over-expressed. Disentangling immune protection and damage has been very challenging as the relative costs/benefits of immune activation might depend on several traits, including species-specific features, infectious dose, or the immune pathway involved. Here we conducted a large survey of studies on rodent models where animals knocked out for different cytokines (th1, th2, pro-, anti-inflammatory) have been compared to wild type individuals in terms of changes in parasitemia and survival. The literature survey encompasses about 100 studies covering a large spectrum of cytokines and pathogens (from viruses to protozoa). To our knowledge, this is one of the first attempts to provide a comprehensive assessment of the relative importance of immune protection and damage in shaping disease severity.

16:45 *Julie Baker Phillips*, *Juan Felipe Ortiz*, *Patrick Abbot* and *Antonis Rokas*
Rapid evolution of the Siglec Immune Receptor Family in Primates
SPEAKER: unknown

ABSTRACT. Sialic acid-binding immunoglobulin-type lectins (Siglecs) are a pan-mammalian family of immune receptors whose primary function is recognition of self and inducing immune tolerance. The CD33-related (CD33r) Siglecs are a sub-group of this diverse family; CD33r Siglecs show multiple genetic and biochemical differences between primates, and are believed to be rapidly evolving. For example, Siglec 11 has acquired a human-specific expression pattern in brain microglia, while Siglecs 5 and 14 are paired receptors that coordinate immune responses to pathogens. In the context of Group B Streptococcus (GBS) infection, polymorphisms in Siglec 14 influence prematurity risk in mothers colonized with the infection. To better understand the evolutionary history of the Siglec receptor family, we use a novel homology based algorithm to identify Siglec clusters present across ten primate species as well as in mouse and dog. Additionally, we reconstruct the phylogeny of this gene family across primate species using state-of-the art phylogenetic techniques. Finally, we compare within- and between-species population fixation indices to identify the genetic structure of polymorphisms within the Siglec family. Taken together, our data suggest that the Siglec family is one of the most rapidly evolving gene families in primate genomes. Because some of the tissues and functions that Siglecs are involved exhibit major phenotypic differences between humans and other primates, our work raises the hypothesis that understanding the evolution of this gene family may be relevant for understanding certain aspects of human health.

17:00 *Emily Wroblewski*, *Paul Norman*, *Lisbeth Guethlein*, *Yingying Li*, *Rebecca Rudicell*, *Miguel Ramirez*, *Christiana Shaw*, *Steve Ahuka-Mundeke*, *Martine Peeters*, *Anne Pusey*, *Beatrice Hahn* and *Peter Parham*
Comparison of MHC class I polymorphism in wild populations of chimpanzee and bonobo
SPEAKER: unknown

ABSTRACT. MHC (major histocompatibility complex) genes encode cell surface glycoproteins that present antigens to lymphocyte receptors to trigger and maintain the immune response to infection. Extremely high polymorphism of classical MHC genes is maintained by natural selection. The B*57 allele of HLA-B, which is the most polymorphic MHC gene in humans, associates more strongly than any other HLA allele with slower progression of infection with the HIV-1 lentivirus into AIDS. Wild ape populations are ideal for studying such host-pathogen evolution and dynamics. Chimpanzee (Pan troglodytes) subspecies can be endemically infected with SIV (simian immunodeficiency virus), whereas bonobos (Pan paniscus) are not. We compared the polymorphism of HLA-B orthologs in wild populations of chimpanzee (Patr-B) and bonobo (Papa-B). These include the entire population of 125 P. t. schweinfurthii chimpanzees from Gombe National Park, Tanzania, which harbor SIVcpz. Also studied were 130 bonobos from six populations in the Democratic Republic of the Congo. Patr-B and Papa-B allelic variations were characterized by PCR amplification and sequencing of exons 2 and 3, using DNA extracted non-invasively from feces. In the Gombe chimpanzees, we discovered 11 Patr-B alleles, of which seven were novel. Four Patr-B alleles differed significantly in frequency between SIVcpz-infected and uninfected chimpanzees, including Patr-B*06:03. We show Patr-B*06:03 is phylogenetically related to HLA-B*57 and part of a lineage that also includes gorilla Gogo-B alleles. Patr-B*06:03 also associates with reduction in SIVcpz viral load, assessed from feces. In bonobos, we defined >20 alleles of Papa-B. These alleles are maintained within bonobo populations with number and frequency distributions similar to chimpanzee and indigenous human populations of comparable size. However, finding no alleles belonging to the conserved B*57 lineage suggests bonobo Papa-B has experienced a different history of selective pressure from immunodeficiency-causing lentiviruses than the MHC-B genes of other African apes and humans.

17:15 *Caroline Amoroso* and *Charles Nunn*

Human parasitism in a comparative context: are humans over- or under-parasitized?
SPEAKER: unknown

ABSTRACT. Many studies have investigated the origins of specific human diseases, but fewer have examined how parasite richness changed along the human lineage. Here, we investigated three hypotheses. (1) The hyper-parasitism hypothesis views humans as especially parasitized compared to other primates. This widely accepted hypothesis is attributed to contact with domesticated animals, sedentary lifestyles, and high densities. (2) Conversely, the cultural benefits hypothesis proposes that behavioral and psychological traits – like medicinal plant use, hygienic behaviors, and disgust responses – have reduced the number of parasites infecting humans. (3) The null hypothesis states that epidemiological transitions had weak effects on parasite richness, and humans therefore have as many infectious agents as expected given our characteristics.

In sheer numbers, humans host many more disease-causing organisms (1415) than any other primate (maximum of 82). This would seem to support the hyper-parasitism hypothesis. However, humans also have enormous populations, live globally, and are better studied than any other primate; these factors may account for high parasite richness without invoking distinct factors unique to humans. Thus, we built a statistical model using predictors of parasite richness in non-human primates, including population density, latitudinal range, geographic range, body mass, and phylogeny. To avoid extrapolating

beyond the primate data, we focused on infectious diseases in two countries: Nigeria and Madagascar. We used species accumulation curves to estimate parasite richness when holding sampling constant, and Bayesian approaches to fit the model and make predictions.

The primate model predicts the observed virus and helminth richness of humans in Madagascar and Nigeria, consistent with the null hypothesis. Remarkably, however, these populations appear to be under-parasitized by protozoa (observations are outside the predicted 95% credible intervals), supporting the cultural benefits hypothesis. Overall, our results challenge current thinking about epidemiological transitions in humans. We are expanding the analysis to seven additional countries.

16:00-17:30 Session 9B: Reproductive ecology and human health

CHAIR: *Grazyna Jasienska* LOCATION: Grand Ballroom III

16:00 *Grazyna Jasienska*

Women's reproductive ecology and the most effective breast cancer prevention strategies

SPEAKER: *Grazyna Jasienska*

ABSTRACT. The most common breast cancers are estrogen receptor-positive, therefore risk of breast cancer in women increases with high lifetime exposure to estrogens. Many factors that increase risk of breast cancer have been identified. However, most of these factors cannot be easily modified and thus knowledge about them has a limited practical use for designing strategies of breast cancer prevention.

Studies in human reproductive ecology show that the availability of metabolic energy has a significant impact on the levels of ovarian hormones, including estrogens. Differences among women in lifetime exposure to estrogens can, in part, be explained by variation in adult lifestyle conditions that determine levels of physical activity or energy balance. In addition, the ovarian function is, to some extent, programmed in utero and subsequently influenced by the conditions experienced during childhood growth and development.

The relative importance and interactive impact of different energetic factors on ovarian function are not well understood. However, it is now clear that physical activity is one of the most powerful factors with the ability to lower the estrogens levels and reduce the risk of breast cancer. Surprisingly, it is still not known what amount of physical activity is needed for a meaningful reduction in the levels of reproductive hormones. It is likely that the beneficial dose depends on fetal and childhood developmental conditions that change the sensitivity of the ovarian function to energetic factors in adulthood. Studies on the interactive effects of factors capable of influencing the levels of estrogens, operating during all life stages, are needed to suggest more effective breast cancer prevention programs.

16:15 *Richard Bribiescas*

How evolutionary biology can inform the risks and benefits of testosterone supplementation in healthy men

SPEAKER: *Richard Bribiescas*

ABSTRACT. The deployment of testosterone supplementation to healthy men, especially those that are older has become increasingly common within the United States and throughout the globe. While the reported effects include greater muscle mass, strength,

increased libido, and improved affect, the long term consequences of testosterone supplementation are poorly known. Limited evidence from the clinical literature as well as from non-human animal models suggest that testosterone supplementation may lead to detrimental outcomes that are consistent with trade off predictions made by life history theory. Moreover natural variation in testosterone levels between and within populations is seldom considered by physicians or discussed within the clinical literature when considering the benefits and risks of testosterone supplementation. This presentation outlines (1) the significance of normal variation in male neuroendocrine function, specifically in regards to between population differences in testosterone levels as well as variation in age associated changes in testosterone; (2) physiological sources of variation that contribute to normal differences in testosterone levels such as production, clearance rates, carrier protein binding, and genetic variation in regulatory enzymes and gonadotropins such as luteinizing hormone. Recent anthropological, clinical, and epidemiological literature are presented to (1) illustrate that normal testosterone variation between and within populations should be considered in the development and application of testosterone supplementation in healthy men; (2) predictions from evolutionary and life history as well as field studies motivated to test these predictions can inform the risks and benefits of testosterone supplementation in health men.

16:30 *Katie Hinde*

Liquid Gold Standards: Complexities of Breast Milk and Implications for Precision Medicine
SPEAKER: *Katie Hinde*

ABSTRACT. Public health efforts promote the first 1000 days of life as influential for health and well-being across the lifespan. This developmental period has both vulnerability and opportunity for the integration of infant physical, behavioral, and microbial systems. Previous research of this developmental stage has primarily targeted physiological influences before birth and behavioral care during infancy, but mammals produce milk extending physiological investment post-natally. Unlike adults in Westernized, Educated, Industrial, Rich, Democratic nations, far removed from the ancestral conditions that shaped our bodies, the breastfed infant develops within an “adaptively relevant environment.” Cross-cultural investigations combined with an evolutionary approach to biomedical models yield new perspectives of mothers, milk, and infants. Most importantly milk is an integrated food, medicine, and signal as milk nourishes, protects, and informs the developing neonate through nutrients, immunofactors, and hormones. Milk varies across evolutionary time, populations, individuals within populations, and within mother longitudinally. In these ways, mother’s milk reflects the “here and now” and the “there and then.” Biological and social scientific research on this topic can directly translate to more personalized clinical recommendations and health optimization for mothers and their infants as well as substantiate the importance of infrastructure and institutional support for breastfeeding. Further, a better understanding of the composition and function of milk informs the composition of a more representative infant formula or donor milk selection for those mothers facing obstacles or contraindications to breastfeeding. Lastly, decoding mother’s milk will allow for enhanced precision medicine for the most fragile infants and children in neonatal and pediatric intensive care units. Transdisciplinary approaches to mother’s milk research, along with public engagement, facilitate discoveries at the bench and their translation to applications at the bedside.

16:45 *Kathryn Clancy*

Clinical implications for normal variation in female reproductive physiology
SPEAKER: *Kathryn Clancy*

ABSTRACT. Ovarian follicular dynamics show the ovaries to be constantly active, with consequences for fecundity and the experience of the menstrual cycle. The thickness of the endometrium also varies through the window of implantation, even among normo-ovulatory women. Variation in these aspects of reproductive physiology demonstrate that genes, life history trajectories, lived experiences, and current energetic status contribute to fecundity. They also point a path forward for understanding the responsiveness of different individuals to exogenous hormonal treatments. At this time the major points of variation in exogenous hormonal treatments for contraceptive purposes are in drug delivery methods, not concentration, of synthetic sex steroids. While many more synthetic hormone preparations exist for assisted reproductive technologies, doctors choose between these treatments based on the historical preferences of their practice. This presentation describes a path forward in leveraging our understanding of genetic and lifestyle variation in reproductive function to produce personalized medicine strategies to better meet women's reproductive health needs. Adopting personalized medicine strategies will reduce side effects and increase efficacy of existing methods, while also pointing towards future novel therapies.

17:00 *Alejandra Nunez-De La Mora*

Developmental plasticity of human reproductive function and its implications for epidemiological and demographic trends: an evolutionary viewpoint
SPEAKER: *Alejandra Nunez-De La Mora*

ABSTRACT. Population-based studies have documented significant variation in reproductive maturation and function among diverse human groups in relation to the socio-ecological environments in which they live. Recent empirical data show that human reproductive plasticity has, to a large extent, a developmental origin. Data on the influence of pre- and post-natal nutritional status on different human reproductive traits indicates that energetic conditions during development influence the size and characteristics of reproductive organs, levels of adult gonadal endocrine function, its regulation and its sensitivity to energetic stress. Such influences are likely to underpin the associations between developmental conditions and duration of adolescent subfertility, age at first pregnancy, proportion of ovulatory cycles and reproductive behaviour, which ultimately underlie differences in fertility. At another level, developmental conditions affect an individual's lifetime reproductive success by determining the length of the reproductive span by influencing the tempo and timing of reproductive maturation and reproductive senescence. Medical interest in the developmental plasticity of human reproductive function is typically focused on elucidating the mechanisms involved with a goal of devising diagnostic and therapeutic tools. A life history perspective in contrast, extends beyond proximal causation and offers insights into what the costs and benefits of alternative developmental trajectories may be, in terms not only of fertility, but of survival and disease risk. In this paper I will review what we know (and don´t) about developmental plasticity of human reproductive function, analyze its impact on current epidemiological and demographic trends, compare the clinical and evolutionary approaches to the evidence, and highlight the contribution of an evolutionary viewpoint to our understanding of such patterns, particularly in the context of rapidly changing socio-economic and ecological systems worldwide.

17:30-19:30 Session : Food truck rodeo

Use this link to view the location on google maps.

LOCATION: Durham Farmer's Market- 501 Foster St, Durham, NC 27701

PROGRAM FOR FRIDAY, JUNE 24TH

07:00-08:00 Session : Continental Breakfast

LOCATION: Grand Ballroom Lobby

08:00-09:00 Session 10: Plenary Speaker: Carl Zimmer

CHAIR: *Stephen Stearns* LOCATION: Grand Ballroom I

08:00 *Carl Zimmer*

Evolutionary Medicine and the Media: Engaging Stories and Tricky Concepts

SPEAKER: *Carl Zimmer*

ABSTRACT. In this talk, I discuss the media coverage of evolutionary medicine since it first emerged in the 1990s. Reporters have been drawn to a wide range of examples, from antibiotic resistance to the evolution of cancer defense mechanisms. But they have also neglected some of the most important concepts, including maladaptation and genetic drift, because few readers understand their scientific foundations. Journalism can help introduce the public to evolutionary medicine, but without better science education, it will be difficult to explore its full implications.

09:00-10:15 Session 11A: Genetics, vulnerability and selection

CHAIR: *Alejandra Nuñez-De La Mora* LOCATION: Grand Ballroom I

09:00 *Melissa Wilson Sayres*

Population history and patterns of sex-biased evolution

SPEAKER: *Melissa Wilson Sayres*

ABSTRACT. The mammalian sex chromosomes, X and Y, originated from a pair of homologous autosomes, but, over time, suppression of recombination between them led to the degradation of the Y chromosome, and tremendous divergence between the X and Y chromosomes. This divergence, and the unique inheritance patterns of sex chromosomes, also means that sex-biased genomic regions can be used to infer the relative influences of demographic history and selection acting on populations. This is because, while natural selection and demographic history may result in similar patterns on any one genomic region, they will leave unique signatures when considering all genome regions together. By simulating patterns of variation across all genomic regions (autosomes, X chromosome, Y chromosome, and mtDNA), we characterize the consequences of different demographic scenarios (notable variance in male reproductive success and population bottlenecks) on genome-wide patterns of diversity. These patterns will form the basis for accurately interpreting empirical patterns of diversity observed across genomes, especially across human populations.

09:15 *Guido A. Gnecchi Ruscone*, *Choongwon Jeong*, *Sara De Fanti*, *Michela Trancucci*, *Davide Gentilini*, *Anna Maria Di Blasio*, *Geoff Childs*, *Sienna R. Craig*, *Buddha Basnyat*, *Mingma G.*

Sherpa, *Phurba T. Sherpa*, *Giorgio Marinelli*, *Luca Natali*, *Davide Peluzzi*, *Cynthia M. Beall*, *Anna Di Rienzo*, *Davide Pettener*, *Donata Luiselli* and *Marco Sazzini*

Exploring evolutionary causes of differential susceptibility to acute mountain sickness in Nepali populations from the Gaurishankar Area

SPEAKER: unknown

ABSTRACT. Populations settled in remote Himalayan valleys coming up to the Nepali Gaurishankar mountain range at the border with the Tibetan plateau belong to three main ethnic groups that are distributed along a wide altitudinal range (900-4,900 m a.s.l.). People speaking Indo-Aryan languages appear to be biologically and culturally related to populations from the Indian subcontinent and live exclusively at low altitudes. Groups speaking Tibeto-Burman languages (e.g. Tamangs) and Sherpas are instead supposed to be tightly related to high-altitude Tibetans and to have crossed the Himalayan range in recent historical periods. Tamangs have then largely spread across Gaurishankar valleys up to ~2,500 m a.s.l., whereas most local Sherpa communities remained considerably isolated at high-altitude up to the recently abandoned Bomdok village beside the Ripimo Glacier (4,900 m a.s.l). Coupled with cases of Acute Mountain Sickness (AMS) reported for Tamangs hired as porters in mountaineering expeditions, such pattern of population structure questions their actual adaptation to hypoxia and, indirectly, their presumed common ancestry with respect to Sherpas and high-altitude Tibetans. To disentangle this complex anthropological scenario and to investigate evolutionary causes of different AMS susceptibility between Tamangs and Sherpas, we inferred their genetic histories from genome-wide data generated for more than 700,000 SNPs on 75 individuals collected during three humanitarian and scientific field expeditions. Their genomic relationships with other Sherpa, Tibetan, South Asian and East Asian populations were also explored by comparison with genotype data from 1,152 additional subjects belonging to 72 human groups. Finally, we searched for shared or private signatures of natural selection on the Tamang and Sherpa genomes that could be ascribable to adaptive processes triggered by high-altitude hypoxia and that could provide crucial insights into their different susceptibilities to AMS.

This work was supported by ERC-2011-AdG295733 to DP, NSF Award 1153911 to CMB, NSF Grant BCS-0924726 to ADR.

09:30 *Fred Nijhout*

Evolution of homeostatic mechanisms, cryptic genetic variation, and predisposition to disease

SPEAKER: *Fred Nijhout*

ABSTRACT. Metabolic and physiological systems have evolved a broad diversity of homeostatic mechanisms that stabilize phenotypes against genetic and environmental variation. Deterministic mathematical models of such systems enable one to study the properties of these stabilization mechanisms and see how they are influenced by genetic and environmental variables. This work has shown that phenotypic stability in these systems is a dynamic property that is actively maintained. When homeostatic mechanisms operate normally, they allow for the accumulation of cryptic genetic variation. Incorporating data from human genetic diseases allows us to document the extent of this genetic variation and explain why it is “cryptic” at the phenotypic level even though some mutations have very severe effects at the molecular level. We show that mutations, or environmental factors,

that alter the homeostatic dynamics allow certain cryptic mutations to become phenotypic, and give a natural explanation of why certain conditions “predispose” to disease. Analysis of the distributions of mutations in phenotypic landscapes, and statistical analyses of corresponding population models, allows one to design strategies for personalized medicine. Moreover, population versions of the deterministic models allow one to study how phenotypic homeostasis can evolve.

09:45 *Nicole Mideo*, *Jeffrey Bailey*, *Andrew Read* and *Jonathan Juliano*
A deep sequencing tool for detecting drug resistance in polyclonal malaria infections
SPEAKER: unknown

ABSTRACT. Current tools struggle to detect drug resistant malaria parasites when infections contain multiple parasite clones, which is the norm in high transmission settings in Africa. Our aim was to develop and apply an approach for detecting resistance that overcomes the challenges of polyclonal infections without requiring a genetic marker for resistance. Clinical samples from patients treated with artemisinin combination therapy were collected from Tanzania and Cambodia. By deeply sequencing a hypervariable locus, we quantified the relative abundance of parasite subpopulations within infections and revealed evolutionary dynamics during treatment. Slow clearance is a phenotypic, clinical marker of artemisinin resistance; we analyzed variation in clearance rates within infections by fitting parasite clearance curves to subpopulation data. In Tanzania (where resistance is not yet thought to be a problem) we found substantial variation in clearance rates within individual patients. Some parasite subpopulations cleared as slowly as resistant parasites observed in Cambodia. All else being equal, simulated infections predict that modest increases in the frequency of these subpopulations could substantially increase time to cure. Our method can detect rare, slow clearing parasites in vivo whose phenotypic effects would otherwise be masked. Since our approach can be applied to polyclonal infections even when the genetics underlying resistance are unknown, it could aid in monitoring the emergence of artemisinin resistance. Our application to Tanzanian samples uncovers rare subpopulations with worrying phenotypes for closer examination.

10:00 *Courtney Babbitt*, *Jason Pizzollo* and *Gregory Wray*
Identifying genomic loci involved epithelial cancer using comparative genomics
SPEAKER: unknown

ABSTRACT. Epithelial cancers, such as breast, ovary, and prostate, account for up to 20% of deaths in human populations. In our nearest living evolutionary ancestor, the chimpanzee, however, rates of epithelial cancer are significantly lower (2-4%) while rates for other types of cancers are comparable. Although part of this difference is likely due to environmental factors, we believe there is a genetic component as well. To study this difference we employ an assay in fibroblasts isolated from healthy skin tissue. Previous studies show that fibroblasts in culture exposed to a "serum challenge" engage in a pattern of gene expression that mimics that found in tumors. Therefore, we used this assay to compare how human and chimpanzee cells behave in this cancer-like response. We performed RNA-seq and DNase-seq to investigate differences in gene expression and gene regulation, respectively. Our data show significant differences in expression and in areas of open chromatin between our species. In particular, genes involved in cell adhesion, inflammation, and homeostasis pathways are differentially expressed between human and chimpanzee, which may help explain differences in epithelial cancer rates.

09:00-10:15 Session 11B: Lessons from our primate cousins: Evolutionary medicine in nonhuman primate studies

CHAIR: *Jenny Tung* LOCATION: Grand Ballroom III

09:00 *Jenny Tung*, *Elizabeth Archie*, *Jeanne Altmann* and *Susan Alberts*

Cumulative early life adversity predicts longevity in wild baboons

SPEAKER: unknown

ABSTRACT. Adverse experiences in early life can have profound and pervasive effects on human health and survival. These observations cut across study designs, national boundaries, and disease types. However, the roots of early life effects likely reach much further back in our evolutionary history. In nonhuman animals, early adversity has also been shown to predict components of fitness, especially adult fertility. Multiple adverse conditions are thought to be especially toxic, but this hypothesis has rarely been tested in a prospective, longitudinal framework, especially in long-lived mammals. Here, we use prospective data on 196 wild female baboons to show that cumulative adversity from six early life sources—drought, high density social groups, low maternal status, low maternal social integration, maternal loss, and the presence of a competing younger sibling—predicts natural adult lifespan. Females who experience ≥3 sources of early adversity die a median of 10 years earlier than females who experience ≤1 adverse circumstances (median lifespan is 18.5 years). Females who experience the most adversity are also socially isolated in adulthood, suggesting that social processes partially explain the link between early adversity and adult survival. Because age at death strongly predicts the total number of surviving offspring in this population (r=0.95), females exposed to high adversity in life paid a cost both in years of their own lives and in overall Darwinian fitness. Together, our results provide powerful evidence for the developmental origins of health and disease and indicate that close ties between early adversity and survival arise even in the absence of health habit and health care-related explanations.

09:15 *Jessica Brinkworth*, *Jordan Kohn*, *Lanford Robert*, *Zach Johnson* and *Luis Barreiro*

Comparative genomics of innate immune responses to infection in primates

SPEAKER: unknown

ABSTRACT. Primates exhibit striking differences in susceptibility to multiple pathogens. For example, humans are highly susceptible to bacterial sepsis and chronic hepatitis C infection, while many other catarrhines are not. Innate immunity is strongly implicated in such disease progression, however a lack of comparative immune response data from major primate clades inhibits our understanding of how this response has evolved in susceptible and resistant primates. Here we report a genome-wide comparative study of primate innate immune responses to bacterial and viral molecules associated with severe infections. We stimulated leukocytes from humans, chimpanzees, rhesus macaques, olive baboons and ring-tailed lemurs with molecular motifs representing Gram-negative bacterial (LPS) and viral (Gardiquimod) pathogens. Blood was stimulated for 4 and 24 hours and leukocytes responses assessed via RNA-seq. Overall, whole transcriptome responses agreed with species phylogeny and we found a considerable number of genes and entire regulatory networks, that showed species-specific responses (SSR) to both immune-stimuli. We show that a significant number of genes associated in SSR have signatures of rapid evolution in either their coding sequence of promoter regions, which suggests that some of the lineage-specific changes have been adaptive. We also found a considerable overlap between

species-specific response genes and genes known to be associated with susceptibility to immune-related disorders in humans suggesting that the observed changes might contribute to inter-species differences in immunity and severe infection manifestation.

09:30 *Nelson Ting*, *Noah Simons*, *Diana Christie*, *Geeta Eick*, *Maria Ruiz-Lopez*, *Colin Chapman*, *Tony Goldberg* and *Kirstin Sterner*

Understanding how evolution has shaped disease susceptibility in the Ugandan red colobus monkey (Procolobus rufomitratus tephrosceles)

SPEAKER: unknown

ABSTRACT. The distribution and dynamics of infectious diseases are influenced by a variety of environmental and evolutionary factors. Over the past 11 years, the Kibale EcoHealth Project has documented patterns of infectious disease both within and between various species across the Kibale region in Western Uganda. It is now clear that certain aspects of these pathogen distributions cannot be explained by ecology and/or demography alone. We are thus currently using this system to investigate the influence of host genetics on disease prevalence in wild primates. In doing so, we hope to reveal the genetic architecture of primate disease phenotypes present in the Kibale community and to test evolutionary hypotheses for disease susceptibility. An initial example of this work focuses on the Ugandan red colobus, which shows individual variation in infection intensity from whipworm (Trichuris sp.) – a gastrointestinal parasite that has known zoonotic potential and human health consequences. We identified 15 SNPs located within transcription factor binding sites of the Ugandan red colobus MHC-DQA1 core promoter, two of which were associated with whipworm infection intensity. Reporter assays suggest that these two SNPs have the potential to drive expression of MHC-DQA1 differently in vitro, and we are currently investigating patterns of MHC-DQA1 expression in vivo using RNAseq. Interestingly, we also found evidence that variation in this regulatory region is associated with changes in gut microbial diversity in these animals. Lastly, we detected a strong signal of balancing selection on this MHC regulatory region that is likely maintaining these functional polymorphisms in this population. Taken together, this work suggests that evolution of regulatory regions have played an important role in shaping disease susceptibility in humans and nonhuman primates. Ongoing work in the Kibale EcoHealth Project is focusing on such approaches to further elucidate relationships between evolution and health.

09:45 *Noah Snyder-Mackler*, *Joaquin Sanz Remon*, *Jordan Kohn*, *Jessica Brinkworth*, *Zachary Johnson*, *Mark Wilson*, *Luis Barreiro* and *Jenny Tung*

The genomic signature of social adversity in rhesus macaques

SPEAKER: unknown

ABSTRACT. Social interactions can exert strong selective pressures on group-living animals, including humans. However, the proximate mechanisms that underlie such pressures remain unclear, especially on the molecular level. Recent studies suggest that changes in gene regulation may play a role, but we still know little about the biological pathways influenced by social adversity, the behaviors most responsible, and the degree to which animals continue to respond to changes in the social environment throughout life. Here, we used experimental manipulations of social status (i.e., dominance rank) in 9 rhesus macaque social groups (n=45 females) to investigate its consequences for genome-wide gene expression. Among purified populations of white blood cells, we found that Natural Killer (NK) cells were by far the most sensitive to social status, with a secondary contribution from

helper T cells. This effect was partly attributable to rank-associated affiliative relationships, and to a lesser extent to rank-associated differences in aggression. Further, using an ex vivo model of bacterial infection, we found that a substantial fraction of genes exhibited an exaggerated response to immune stimulation in low ranking females. Our findings are consistent with glucocorticoid resistance and baseline inflammation in low status animals. Finally, we conducted a mid-study intervention that rearranged the ranks of all study subjects. Gene expression profiles changed in accordance with changes in rank, indicating large-scale plasticity in gene expression for social status-associated genes. Together, our findings provide novel insight into the importance of both behavioral and molecular mechanisms in linking social status to health and fitness-related consequences.

10:00 *Katherine Amato*

Using the gut microbiota to understand primate ecology and evolution

SPEAKER: *Katherine Amato*

ABSTRACT. Clinical-type research aimed at understanding the impacts of the gut microbiota on human health is currently exploding. However, while necessary for putting clinical research into context, broader, ecological and evolutionary perspectives on host-gut microbe interactions in wild animals under selective pressure are less common. Here, I integrate gut microbes into a basic model of primate bioenergetics by discussing the impact of host age and sex, seasonal shifts in host diet, and host habitat differences on the gut microbiota of wild, black howler monkeys (Alouatta pigra) in southeastern Mexico. Data suggest that the gut microbiota buffers howler monkeys against nutritional shortfalls during periods of growth and reproduction as well as during periods of reduced energy intake. Relatedly, a reduction in gut microbial diversity appears to contribute to nutritional stress and increased health risks in howler monkeys inhabiting anthropogenically degraded forests. These patterns imply that the gut microbiota has multiple effects on host nutrition, health, and ultimately, fitness, and provides an impetus for further studies of host-microbe-environment interactions in wild primates. These data also emphasize the need for recognizing the influence of gut microbes on human ecology and evolution and implications for human health.

10:15-10:30 Session : Break

Coffee and snacks will be provided.

LOCATION: Grand Ballroom II

10:30-11:45 Session 12A: General evolution and medicine

CHAIR: *Nicole Burt* LOCATION: Grand Ballroom I

10:30 *Camille Jacqueline*, *Frédéric Thomas* and *Benjamin Roche*

An eco-immunological approach for cancer: a new role for infectious diseases?

SPEAKER: unknown

ABSTRACT. Since the beginning of the 20th century, parasitism has emerged as a fundamental mechanism for cancer causation with a growing number of pathogens recognized as oncogenic. Meanwhile, oncolytic viruses have also attracted considerable interest as possible agents of tumor control. Lost in this dichotomy between oncogenic and oncolytic agents, the indirect influence of parasitic communities on cancer, notably through the multiple trade-offs involved in immune system, has been largely unexplored. Here, we address the various ways by which parasitic organisms can lead to immune system

deregulation and then interfere with oncogenic processes. Using first a theoretical framework, we show that repeated acute infections could impact the accumulation of cancerous cells through continuous perturbation of immune system efficiency. Through a drosophila model, we report the activity of immune genes and the accumulation of cancerous cells after experimental infections to test these theoretical predictions. We finally challenge our new theory with a cutting-edge statistical analysis of databases reporting human cancer incidences and parasite occurrence throughout the world to report evidences for an indirect impact of infectious diseases on carcinogenesis. We conclude by discussing how integrating the community of parasitic organisms may improve public health strategies against most of cancer, which could represent a new step towards a "global health" perspective.

10:45 *Amy Boddy*, *Angelo Fortunato*, *Melissa Wilson Sayres* and *Athena Aktipis*
Cooperation and conflict beyond the womb: Fetal microchimerism and maternal health
SPEAKER: unknown

ABSTRACT. During pregnancy, there is a bi-directional exchange of fetal and maternal cells across the placenta. The presence of fetal cells has been associated with both positive and negative effects on maternal health. These paradoxical effects may be due to the fact that maternal and offspring fitness interests are aligned in certain domains and conflicting in others. Here we use a cooperation and conflict theory framework to propose an explanation for this paradox. Considering the evolutionary and phylogenetic origins of microchimerism, fetal cells may have a similar function to the placenta. Just as the placenta's physiology is designed to transfer resources from the maternal body to the offspring in the womb, the physiology of fetal cells in maternal tissues may enhance resource transfer to the offspring after parturition. This resource transfer may be mutually beneficially for both maternal and offspring fitness interests, or fetal manipulation may push maternal tissues beyond the maternal optimum leading to conflict over resource allocation. Depending on the ecological context (the mothers body), fetal cells may function both to contribute to maternal somatic maintenance (e.g. wound healing) and to manipulate maternal physiology. We suggest fetal cells may play important roles in continued maternal investment in the offspring through manipulation of lactation, thermoregulation, and attachment systems. The framework proposes fetal cells should be more common in tissues that are the site of resource transfers (e.g. the breast, thyroid, and brain) and we offer testable predictions about the role of fetal microchimerism in lactation, thyroid function, autoimmune disease, cancer and maternal emotional, and psychological health.

11:00 *Paul Norman*, *Neda Nemat-Gorgani*, *Hugo Hilton*, *Jill Hollenbach*, *Elham Ashouri*, *Emily Wroblewski*, *Ketevan Gendzekhadze*, *Laurent Abi-Rached*, *Lisbeth Guethlein* and *Peter Parham*
Coevolution of the highly complex HLA and KIR gene families impacts human immunity and reproduction.
SPEAKER: unknown

ABSTRACT. The physiological functions of natural killer (NK) cells in human immunity and reproduction depend upon diverse interactions between killer cell immunoglobulin-like receptors (KIR) and their HLA class I ligands. The genomic regions containing the KIR and HLA class I genes are unlinked, structurally complex, and highly polymorphic. They are also strongly associated with a wide spectrum of disease, including infections, autoimmunities,

cancers, and pregnancy disorders, as well as the efficacy of transplantation and other immunotherapies. Although it is clear this polymorphism directly affects NK cell function and human immunity, population studies of KIR allelic diversity have been few. To facilitate study of these extraordinary genes, we developed a method that captures, sequences and analyzes the 13 KIR genes and the HLA genes from genomic DNA. We also devised a bioinformatics pipeline that attributes sequencing-reads to specific KIR genes, determines copy number by read depth, and calls high-resolution genotypes for each of the KIR genes. To sample the world's KIR allelic diversity, we analyzed populations of low genetic diversity from Polynesia and South America and, accounting for ancient population substructure in Africa, seven populations from sub-Saharan Africa. In all populations the majority of individuals studied had unique KIR/HLA genotypes. In every population we identified private alleles including those with dramatic effect on NK function, such as 2DL1*022, common and unique to the KhoeSan hunter-gatherers from Southern Africa that has switched specificity from one HLA ligand to another. Using phylogenetic analysis and simulations we show that natural selection is exquisitely targeted to the sites of KIR that contact HLA and demonstrate strong evidence for balancing selection of the KIR locus. We also show that co-evolution of the HLA and KIR molecules remains ongoing in extant populations. Studying the evolution of KIR and HLA has multiple benefits and insights for human health

11:15 *India A. Schneider-Crease*, *John C. Noh*, *Thore J. Bergman* and *Jacinta C. Beehner*

Diagnosing Taenia serialis in wild geladas: Novel use of adapted urine Ag-ELISA for assessing wildlife health.

SPEAKER: unknown

ABSTRACT. Six percent of wild geladas (Theropithecus gelada) in the Simien Mountains National Park, Ethiopia, exhibit bulging cysts caused by the tapeworm parasite Taenia serialis. This parasite, spread through contact with canid feces, can also infect humans, and anthropogenic change may affect the patterns of infection in geladas as well as the risk of infection for humans. Understanding the ecology of T. serialis is thus critical for identifying at-risk wildlife and human populations. However, identifying infection based on visual diagnosis of cysts is of limited use because internal cysts are undetectable with this method. Unfortunately, classical diagnostic imaging and serological methods are often prohibited in wild populations, and may not be available for human diagnosis in remote areas. To address this problem, we adapted a monoclonal antibody-based sandwich ELISA (Dorny et al. 2000) to non-invasively diagnose T. serialis infection in dried urine samples. Sample index values were calculated using the average negative and positive control values for the plate on which each sample was run. Because unweaned infants do not consume grass and are not exposed to T. serialis eggs, a positive cutoff was set by averaging the index values for infants (n=58) and adding two standard deviations. With this cutoff, the specificity of our test is 98.21% and the sensitivity 97.65%. While only 6.3% (n= 17) of sampled geladas had cysts, 15.1% (n=41) of sampled geladas were Taenia-positive. Furthermore, an additional 6.2% of sampled geladas (n=12) exhibited 'transient' infections, in which animals become positive but are presumably able to fight off infection. This system presents a unique opportunity to investigate the drivers of susceptibility and the fitness impacts of a costly parasite on a wild primate population and to identify parasites of potential risk to humans in remote areas.

11:30 *Rui Diogo*

Evolutionary Developmental Pathology and Anthropology: a new field linking development, comparative anatomy, human evolution, morphological variations and defects, and medicine
SPEAKER: *Rui Diogo*

ABSTRACT. We introduce a new subfield of the recently created field of Evolutionary Developmental Anthropology (Evo-Devo-Anth): Evolutionary Developmental Pathology and Anthropology (Evo-Devo-P'Anth). This subfield combines experimental and developmental studies of non-human model organisms, biological anthropology, chordate comparative anatomy and evolution, and the study of normal and pathological development in humans. Above all, instead of focusing on studies of other organisms to try to better understand human development, evolution, anatomy and pathology, it places humans as the central case study, i.e. as truly model organism themselves. We summarize the results of our recent Evo-Devo-P'Anth studies and discuss long-standing questions in each of the broader biological fields combined in this subfield, paying special attention to the links between: 1) Human anomalies and variations, non-pentadactyly, homeotic transformations, and "nearest neighbor" vs "find and seek" muscle-skeleton associations in limb+facial muscles vs other head muscles; 2) Developmental constraints, the notion of "phylotypic stage", internalism vs externalism, and the "logic of monsters" vs "lack of homeostasis" views about human birth defects; 3) Human evolution, reversions, atavisms, paedomorphosis and peromorphosis; 4) Scala naturae, Haeckelian recapitulation, von Baer's laws, and the parallelism between phylogeny and development, here formally defined as "Phylo-Devo parallelism"; and 5) Patau, Edwards, and Down, Syndrome (trisomies 13, 18, 21), atavisms, apoptosis, heart malformations and medical implications.

11:45 *Chelsea Landolin* and *Carlos J. Suarez*
Evidence for Applications of Evolutionary Biology Across Health Care Disciplines
SPEAKER: unknown

ABSTRACT. Background: Applications of evolutionary biology to medicine and public health have become increasingly recognized over the past 25 years. However, these two disciplines only represent a subset of all health care sciences, with physicians comprising just 13% of all licensed U.S. health professionals. Objective: To determine the frequency with which terms related to evolutionary biology are used in the literature of health care disciplines outside of medicine and public health. Method: Google Scholar, PubMed, CINAHL, and Social Services Abstracts were search for English language publications between 1980 and 2016 containing the keywords “evolutionary biology,” “biological evolution,” “natural selection,” “Charles Darwin,” and “Darwinian” anywhere in the article. The search was limited to journals with titles or subjects including the words pharmacy, dentistry, nursing, social work, physical therapy, speech and language pathology, and nutrition. Clinical psychology was excluded as evolutionary psychology is already well established. Results: Approximately 9,313 publications containing the specified keywords were found in the overall health care literature, including medicine and public health. Of these, 1,331 (14%) corresponded to disciplines outside of medicine and public health. Nutritional science accounted for the vast majority of these publications (62%) followed in descending order by nursing (25%), social work (20%), pharmacy (6%), dentistry (4%), physical therapy (1.6%), and speech and language pathology (0.5%). Discussion: Although the relative contribution of health care disciplines other than medicine and public health to the body of literature in evolutionary

health sciences is low, the finding suggests that there is interest by professionals in those disciplines to apply concepts of evolutionary biology in their fields. In order to capitalize on that interest, the evolutionary health care community must actively engage these practitioners and expand educational efforts to include a broad spectrum of health care professionals.

10:30-11:45 Session 12B: Human evolution, adaptation and disease in Africa

CHAIR: *Sarah Tishkoff* LOCATION: Grand Ballroom III

10:30 *Joseph Lachance*, *Ali Berens*, *Matthew Hansen*, *Andrew Teng*, *Sarah Tishkoff* and *Timothy Rebbeck*

Population and evolutionary genomics of prostate cancer-associated variants: implications for health disparities in men of African descent

SPEAKER: unknown

ABSTRACT. To determine why men of African descent are more likely to suffer from prostate cancer, we integrated GWAS results and scans of selection with allele frequency data from 45 African and 19 non-African populations. Although there is substantial overlap in predicted risk across populations, genetic risk scores indicate that prostate cancer risk is highest in West African populations and lowest in non-African populations. Genetic risk scores also correctly predict clinical differences in prostate cancer risk between African-Americans and Europeans. Despite the polygenic nature of prostate cancer, we find that a small number of loci drive the difference in predicted risk across populations (e.g. rs10505483, rs1447295, rs9623117, and rs2660753). Although the majority of prostate cancer-associated loci are in neutrally evolving genomic regions, we found multiple instances where alleles at prostate cancer-associated loci have hitchhiked with linked alleles that are locally adaptive. Positively selected genomic regions that overlap with GWAS hits include 2q37 (Europe) and 22q13 (West Africa).

10:45 *Sophie Limou*, *George W Nelson*, *Jeffrey B Kopp* and *Cheryl A Winkler*

Balancing the risk: APOL1 variants, African sleeping sickness and chronic kidney disease

SPEAKER: unknown

ABSTRACT. The burden of chronic and end-stage kidney disease in the United States is considerable and exceeds colorectal and breast cancer combined in annual mortality rate. Individuals of African ancestry are at increased risk for kidney disease compared to their non-African counterparts. Much of this excess risk has been attributed to two coding variants from the APOL1 gene encoding the apolipoprotein L1, an innate immunity protein involved in protection against Trypanosoma brucei infections. Carriage of two APOL1 risk alleles is strongly associated with non-diabetic chronic and end-stage kidney disease (odds-ratio 2 to 17) and strongly interacts with HIV to cause HIV-associated nephropathy (odds-ratio 29 to 89). These variants, which are restricted to African-derived chromosomes, are common in African Americans (13-14% carry the high-risk genotype) and found throughout Sub-Saharan Africa with allelic frequency >40% in West Africa. Evidence of a recent selective sweep in West Africa would explain why the APOL1 kidney risk variants have raised to such high frequencies. The prevailing hypothesis is a positive selection event in response to T.b. rhodesiense, the subspecies causing acute African sleeping sickness: this pathogen can evade trypanolysis from the APOL1 wild-type isoform, but the APOL1 kidney risk variants restore protection against T.b. rhodesiense infections. This unusual story of high-frequency

variants with strong effect size is an example opposing the “common disease-common variant” paradigm that echoes the malaria-sickle cell disease story: individuals carrying at least one copy of APOL1 variants are protected from infection by T.b. rhodesiense, while individuals carrying two APOL1 risk alleles are at excess risk for chronic kidney disease. Here, we review the evolution, population history, and clinical consequences of the APOL1 trypanolytic kidney risk variants in the United States and in Africa.

11:00 *Cheryl Winkler*, *George Nelson*, *Kareshma Ramcharan* and *Rajendra Bhimma*
Seeking Rare Variants in Diverse Populations for Precision Medicine: NPHS2 V260E homozygosity is a frequent cause of sporadic steroid resistant nephrotic syndrome in Black South African children
SPEAKER: unknown

ABSTRACT. Founder effects and genetic drift in diverse populations may inflate frequency of disease-causing monogenic variants. Steroid resistant nephrotic syndrome (SRNS), which frequently progresses to kidney failure, is more frequent among Black South African children compared to White or Indian children with NS, who are more likely to be steroid sensitive. To identify the basis for this health disparity, we sequenced NPHS2, which is frequently mutated in autosomal recessive SRNS, in 64 NS Black and Indian cases and 107 healthy controls from Durban, South Africa. Children were analyzed for consanguineous inheritance of a shared mutation by haplotype analysis and for response to immunosuppressive therapy. Among unrelated NS children, 55% of Indians and 97% of Blacks were steroid resistant ($p<10-5$); 27% of SRNS Black children, all of whom had biopsy-proven focal segmental glomerulosclerosis (FSGS), were homozygous for NPHS2 V260E. No SSNS case and no Indian SRNS case or control carried V260E; notably one Black blood donor was heterozygous for V260E, indicating that this variant is polymorphic in this mostly Zulu population. This variant was previously observed in a few consanguineous families in Oman and regions at one time part of the Omani Empire. Coalescence analysis suggested that the variant is at least 400 years old and most likely flowed from the Black population living in the great lakes region to the Omani prior to the migration to SA by the ancestors of the present Zulu. Testing a single mutation in Black African children with NS will provide a precision diagnosis for SR-FSGS making it possible to avoid kidney biopsy and ineffective steroid treatment. The age of the variant suggests that it may be broadly distributed amongst Black Africans migrating from the Great Lakes Region in the last 400 years. This study highlights the importance of sequencing diverse populations for rare, disease-causing variants.

11:15 *Scott Williams*, *Minjun Huang* and *Shirley Russell*
Pleiotropic effects of immune responses explain variation in the prevalence of fibroproliferative diseases
SPEAKER: unknown

ABSTRACT. Many diseases are differentially distributed among human populations. Differential selection on genetic variants in ancestral environments that coincidentally predispose to disease can be an underlying cause of these unequal prevalence patterns. Selected genes may be pleiotropic, affecting multiple phenotypes and resulting in more than one disease or trait. Patterns of pleiotropy may be helpful in understanding the underlying causes of an array of conditions in a population. For example, several fibroproliferative diseases are more prevalent and severe in populations of sub-Saharan ancestry. We propose that this disparity is due to selection for an enhanced Th2 response that confers resistance

to helminthic infections, and concurrently increases susceptibility to fibrosis due to the profibrotic action of Th2 cytokines. Many studies on selection of Th2-related genes for host resistance to helminths have been reported, but the pleiotropic impact of this selection on the distribution of fibrotic disorders has not been explicitly investigated. We discuss the disproportionate occurrence of fibroproliferative diseases in individuals of African ancestry and provide evidence that adaptation of the immune system has shaped the genetic structure of these human populations in ways that alter the distribution of multiple fibroproliferative diseases.

11:30 *Meagan Rubel*, *Matthew Hansen*, *Aubrey Bailey*, *Kyle Bittinger*, *Alice Laughlin*, *William Beggs*, *Alessia Ranciaro*, *Simon Thompson*, *Fd Bushman* and *Sarah Tishkoff*
Diet, Environment, and Parasites: Factors Shaping Rural African Gut Microbiomes
SPEAKER: unknown

ABSTRACT. The gut microbiome (i.e., the spectrum of bacteria, archaea, fungi, and other microscopic organisms in fecal matter) consists of microbes that span the tree of life and are involved in complex interactions with one another and their human hosts. African populations have adapted to a range of environments and foods as they spread through the continent, and their gut microbiomes (GMs) may have co-evolved with them. To interrogate the degree that GM composition is shaped by potential covariates such as traditional diet, parasites, geography, and genetic ancestry, we analyzed the GMs from sixty ethnically diverse rural Tanzanians practicing different subsistence strategies (Hadza hunter-gatherers, Burunge agriculturalists, Maasai pastoralists, recently-settled Sandawe hunter-gatherers) with urban European and African-Americans in Philadelphia, USA using ribosomal marker classification (16s RNA V1/V2) from fecal samples. We also report results on molecular quantification of nine parasites endemic to the region and implicated in gut dysbiosis (Ascaris lumbricoides, Trichuris trichiura, Necator americanus, Schistosoma mansoni, Strongyloides stercoralis, Giardia sp., Entamoeba histolytica, Ancylostoma duodenale, and Cryptosporidium sp.) by quantitative PCR . This data was paired with nutritional and ethnographic surveys as well as genetic data from an Illumina 5M Omni SNP Array. Bacterial compositional analysis shows that Hadza have lower within-group diversity than other populations. Principal coordinate analysis of bacterial families revealed that Tanzanians have two predominant bacterial gradients associated with broad global enterotypes: A strong Prevotellaceae-Ruminococcaceae gradient and a weak Bacteroidales-Ruminococcaceae gradient. Bacteroidales is associated with diets high in protein and fats, whereas Prevotellaceae and Ruminococcaceae are associated with diets rich in plants and fiber, and this result affirms expectations for populations eating rural, nonwestern foods. This represents one of the largest GM studies to date of ethnically diverse Africans and provides novel microbiome and parasitology data from sparsely characterized African groups.

11:45 *Matthew Hansen*, *Joseph Lachance*, *Sameer Soi*, *Laura Scheinfeldt*, *Alessia Ranciaro*, *Simon Thompson*, *Jibril Hirbo* and *Sarah Tishkoff*
The impact of ancestry and subsistence practice on cardiovascular and anthropometric traits in sub-Saharan Africans
SPEAKER: unknown

ABSTRACT. The African continent is home to a diverse range of indigenous peoples that have adapted to a wide range of ecological environments and subsistence lifestyles. Many complex traits are expected to display variation between populations due to demographic

history and/or natural selection to these diverse environments. In an effort to survey phenotypic variation in Africa and begin to understand the genetic and environmental factors that contribute to this variation, we have collected trait measurements on height, BMI, grip strength, systolic and diastolic blood pressure, and pulse from agricultural, pastoral, and hunter-gatherer communities across eastern and western sub-Saharan Africa. We present the observed variation in these traits between genders, across populations, and across subsistence practices. As expected, males tend to be taller, have stronger grip strength, and have a lower heart rate than females. The difference between the sexes in blood pressure and BMI is detectable but relatively small, although for BMI the male distribution is more sharply peaked about the mean. We find that agriculturalists tend to have higher BMI and blood pressure, while pastoralists tend to have lower BMI and blood pressure. A subset of individuals were genotyped at ~1 million autosomal SNPs, and we performed a GWAS using a linear mixed model approach. Only height replicated GWAS top hits from non-African cohorts (p-value enrichment, sign test). To assess the impact of broad genetic ancestry on trait variation, we performed STRUCTURE analysis to estimate ancestral/genetic cluster proportions, and calculated their correlation with trait values. We observe strong correlations between ancestry and height, grip strength, and blood pressure, respectively. For each trait, this correlation is also quantified by the proportion of heritability attributable to the broad ancestry make-up of each individual. The implications for future genotype/phenotype analysis within sub-Saharan Africa for these traits will be discussed.

12:00-13:30 Session : Lunch on your own

12:00-13:30 Session 13: Education and outreach committee meeting

LOCATION: Meeting Room I- Durham Convention Center

13:30-14:30 Session 14: Plenary Speaker: Joshua Schiffman

CHAIR: *Athena Aktipis* LOCATION: Grand Ballroom I

13:30 *Joshua Schiffman*

Comparative Oncology and the Search for Better Cancer Therapeutics

SPEAKER: *Joshua Schiffman*

ABSTRACT. The field of Comparative Oncology continues to expand at a rapid pace. In this talk, the power of comparative oncology will be explored for identifying universal pathways for the development of cancer, as well as for the prevention of cancer. The focus will be on hereditary cancer predisposition in humans, cancer risk in canines, and cancer resistance in elephants. Special attention will be given to how comparative oncology intersects with evolutionary medicine, and what can be translated from animals into treatment and prevention for cancer in human patients.

14:30-15:45 Session 15A: Cancer

CHAIR: *Robert Perlman* LOCATION: Grand Ballroom I

14:30 *Leonard Nunney*

Identifying the intrinsic and extrinsic risks of cancer.

SPEAKER: *Leonard Nunney*

ABSTRACT. In the past year there have been two influential articles (one in Science, the other in Nature), purporting to separate the contributions of intrinsic and extrinsic factors to the overall incidence of cancer. In this context, intrinsic factors were defined as factors

causing random errors in DNA replication, while extrinsic factors were defined as environmental factors that further increase mutation rates. Unfortunately both articles derive estimates based on false assumptions. Here I adopt an evolutionary perspective to examine the feasibility of accurately defining and separating the influence of these effects.

14:45 *Athena Aktipis*

What to do with cellular cheaters? The cheater detection problem in multicellularity and cancer susceptibility

SPEAKER: *Athena Aktipis*

ABSTRACT. The cheater detection problem has been widely explored in the context of human sociality. Research has shown that people detect cheating in social rules like “If you take the benefit, you must pay the cost” or “You should not ask unless you are in need.” But a similar cheater detection problem exists in cellular sociality. Multicellularity is an extreme example of cooperation and coordination, and one that is possible largely because of the close relatedness of constituent cells. However, mutations can give rise to cellular cheaters that signal for more resources than they should, proliferate when they should not and shirk their cellular duties. If unchecked, these cells grow in frequency in the population, accumulate more mutations and eventually can lead to cancer. How has multicellularity solved this problem of detecting pre-cancerous cheaters? Multicellular bodies are equipped with an arsenal of cheater suppression mechanisms, many of which employ the principles of cheater detection. One of these is the cancer suppression gene TP53. TP53 is a central node in a complex cellular information processing system that integrates diverse signals to ‘decide’ whether a cell can continue its cell cycle, requires DNA repair or should undergo programmed cell death (apoptosis). The costs and benefits of these different alternatives differ for organisms with different sizes, life spans and reproductive strategies. By applying cheater detection and signal detection theory to the problem of cancer suppression, we can better understand the function of complex gene regulatory networks that protect multicellular bodies from cancer.

15:00 *Zi-Ming Zhao* and *Jeffrey Townsend*

Cancer Selection Intensity using Model-Averaged Clustering

SPEAKER: unknown

ABSTRACT. Tumorigenesis is an evolutionary process associated with the accumulation of somatic mutations. Somatic mutations can be deleterious to cancer cell lineages, neutral "passenger mutations", or they can be positively selected, increasing in frequency within tumors because they enhance any of a number of hallmarks of cancer in tumor cells. While methodologies for detecting statistical significance of mutations as "drivers" have become increasingly advanced, little has been done to quantify the extent to which positive selection operates on individual mutations in cancer genes.Positively selected somatic mutations increase survival and/or reproduction of tumor cells, increasing the fitness of cell lineages and driving the genesis and progression of cancer. To quantify the selective effects of mutations, we have developed an approach to estimate selection intensity of somatic single nucleotide mutations using model-averaged clustering. We analyze the clustering of mutations within gene sequences, comparing variant frequencies to the expectation to ascertain whether genes, gene regions, or individual sites within genes have been affected by selection as well as mutation, yielding an estimate (and 95% intervals of uncertainty) for the selection intensity conveyed by mutation at every position within the gene. Our

approach can be used 1) to identify genes, gene regions, and sites that contribute to tumorigenesis when mutated, 2) to estimate the relative contribution of those genes, gene regions, and mutations to the somatic evolution of cancer, and 3) to evaluate the distribution of selection coefficients of all mutations within cancer types. Estimation of the effect of mutations on growth and survival of cancer is necessary to provide guidance toward the potential of directed cancer therapeutics and to design optimal therapeutic regimens against evolving cancer tissues.

15:15 *Carlo Maley*

Cure by Control: Evolutionary approaches to cancer therapy and prevention
SPEAKER: *Carlo Maley*

ABSTRACT. Cancers are highly evolvable, with large population sizes, high mutation rates, and a large genome filled with molecular tools that can be repurposed for the fitness of the cancer cells. Most therapies attempt to cure cancers through eradication of all the cancer cells, which, in disseminated disease, typically results in selection for resistant clones, failure of the therapy, recurrence of the tumor, and death of the patient. An alternative approach is control the cancer, without necessarily eradicating it, thereby transforming cancer from an acute disease to a chronic disease. An additional way to control cancer is to target its evolvability, slowing its evolution. Since most cancers require decades to evolve from the first initiated cell to a life-threatening disease, slowing its evolution by just a factor of 2 would eliminate cancer as a cause of death in most cases. I will present results from a variety of approaches, from sensitivity analyses of evolutionary simulations in order to identify effective targets for controlling cancer, to in vitro experiments to slow the evolution of eukaryotic cells (yeast), to in vivo adaptive therapy experiments in mice, in collaboration with Bob Gatenby.

15:30 *Diego Mallo*, *Rumen Kostadinov*, *Luis Cisneros*, *Mary Kuhner* and *Carlo Maley*

Agent-based simulation of somatic evolution: Modeling the progression of Barrett's esophagus to Esophageal adenocarcinoma
SPEAKER: unknown

ABSTRACT. Despite almost four decades of research since the evolutionary theory of cancer was published, little is known about the clonal evolutionary dynamics of neoplastic progression. We developed an agent-based model of Barrett's esophagus (BE) in order to explore and make testable predictions about these dynamics. BE is a medical condition that is considered a precursor of Esophageal adenocarcinoma (EA). It provides a unique opportunity to study the evolutionary process of neoplastic progression, since BE is not removed upon diagnosis, and instead, is followed through serial endoscopies with multi-region sampling at each endoscopy. We will present a simulation study in order to assess the effect of clonal evolutionary dynamics on tumor heterogeneity and cancer progression from BE to EA. In our generative model crypts constitute the proliferative units, which can mutate, replicate, die, and expand into neighboring locations in the tissue, according to independent rates and neighbor interaction parameters. Each crypt carries its own genotype, composed of a variable number of neutral and selective loci, which modulate three types of fitness advantages (survival, reproduction and mutation rates). Importantly, this process takes place within a hexagonal 2D spatial model, which allow us to account for spatial constraints and interactions with neighbors, and the phylogenetic relationships of the crypts are traced through time. These simulations were carried out using different

combinations of parameters across a range of biologically realistic values that resemble the conditions of BE crypts. Thus, we could observe whether or not clonal expansions cause transient drops in the clonal diversity of the neoplasm. Moreover, by defining cancer as the expansion of a clone with a set of sufficient mutations, we studied the sensitivity of neoplastic progression to the different parameters of the model, thereby identifying the critical aspects of neoplastic progression that are the most promising targets for cancer prevention.

14:30-15:45 Session 15B: Paleopathology as part of evolutionary medicine

CHAIR: *Frank Rühli* LOCATION: Grand Ballroom III

14:30 *Frank Rühli*, *Katherine van Schaik* and *Francesco Galassi*

Evolving humans health: Insights from the paleopathological record

SPEAKER: unknown

ABSTRACT. Paleopathology – the study of diseases of the past - can contribute significantly to the emerging research field of evolutionary medicine. Human disease patterns changed substantially through time. In this presentation we use various sources of "evidence" to show such short term alterations of human disease. Main influencing factors such as changes in environment, socio-economic stratification, influence prevalence and impact of diseases in pre- and historic populations. Data sources include thoughtfully interpreted text-based and iconographic evidence but also skeletal and mummified remains. Thus, state-of-the-art paleopathological studies contribute fundamental data to the understanding of the on-going evolution of human health. Disease load of the past – despite certain lack of medical data – shall be assessed hereby by using data of modern pathology reference collections (such as the Galler pathology collection at the University of Zurich) and meta-analysis data of e.g. mummies of ancient Egypt. Finally, the diagnostic pitfalls of paleopathological research and some recommendations how to improve the medical impact of such unique studies on sort term adaptation of human health shall be addressed too.

14:45 *Bruce Rothschild*

Evolutionary perspectives of rheumatologic disease

SPEAKER: *Bruce Rothschild*

ABSTRACT. Evolution is a term suggesting change and that does apply to infectious diseases such as tuberculosis. There is a clear transition in sequences and speciation from the earliest DNA isolation in the fossil record to that in contemporary organisms, although the skeletal damage is indistinguishable from what is observed in patients today. Identification of similar variation/evolution has actually proven elusive in both the paleontological and archeologic record of rheumatologic disease. The skeletal manifestations of rheumatoid arthritis, first recognized in 6500 ybp cemeteries from the western portion of the Tennessee and Green Rivers in the southeastern United States, are indistinguishable from those found today in contemporary patients. Diseases which occur as population phenomenon allow use of epidemiology as a valuable tool in their recognition. Such allows confident rejection of alleged cases of rheumatoid arthritis in the Old World prior to 1492. Rheumatoid arthritis was quite limited in geographic distribution for 5000 years, spreading 1000 years ago into Ohio, and beyond North America, only 300 years ago. A second form of inflammatory arthritis is actually much older. Currently referred to as spondyloarthropathy, it differs in pattern and character from rheumatoid arthritis, permitting its earliest recognition pre-

dating the advent of the dinosaur. Not only are ancient patterns and character of skeletal alterations in archeologic sites dating 6000 ypb indistinguishable from those of contemporary patients, the same is true of the zoologic and paleontologic record. The prevalence varies with sanitation conditions in the archeologic record, but examination of the paleontologic record reveals a dramatic geometric increase in prevalence from the Oligocene in horses and rhinoceros from one and five percent respectively to eight and 35% today. Rheumatologic diseases have increased in prevalence over geologic time with little change, except for the appearance of a new disease in the form of rheumatoid arthritis 6500 ybp.

15:00 *Michelle Blyth* and *Frank Ruehli*

A medical perspective to study syphilis in human remains

SPEAKER: unknown

ABSTRACT. The origin of syphilis has long been a subject of much debate for decades. Much of this debate centers on whether or not particular findings in human remains can be considered syphilitic in origin. Many criteria have been proposed, some highly stringent, and some quite lax. We believe that taking a medical diagnostic point of view could help to bring clarity to some of these debates. Currently, most syphilis diagnoses in developed countries are made utilizing molecular methods. However, historical methods, practices in resource poor environments, and utilization of clinical suspicion to elucidate false negatives can help illuminate methods of diagnosis in human remains. After a review of medical and paleopathological literature, we found five findings that can be considered pathognomonic for congenital or acquired syphilis. One of these, thymic cysts, are limited to mummified remains. We also found eight signs that when found with another sign, make the diagnosis of syphilis likely. The remaining signs can be used with a differential diagnosis process to determine the likelihood that they represent a syphilis infection. Two of these signs can only be found in mummified remains. We would also like to stress that we believe that several of these signs are not routinely looked for in human remains, and that methodological scrutiny for all these findings may bring further clarity to the pre-Columbian prevalence of syphilis. As several of these signs are only found in mummified remains, the use of diagnostic imaging in searching for these signs may prove fruitful. We feel as though this interdisciplinary blending of medical diagnosis and paleopathology is a unique approach that has the possibly of being utilized in the study of the origins of other human diseases.

15:15 *Rebecca Crawford*, *Markus Melloh*, *Frank Rühli* and *Martin Haeusler*

Low back pain as a trade-off to efficient walking: A new perspective on connecting evolutionary medicine with public health

SPEAKER: unknown

ABSTRACT. Modern man is the epitome of efficient upright walking, yet with up to 80% lifetime prevalence for low back pain (LBP) as a potential trade-off, the consequences to present day society are vast. Despite significant global resources directed at understanding and managing this condition, outcomes have not improved, incidence has not decreased, and it is projected to worsen with our ageing society. New approaches to combatting LBP are therefore urgently needed. Evolutionary adaptations of bipedalism that potentially contribute to the origin of LBP include features like our relatively long lumbar spine coupled with our characteristic spinal curves,, shortened transverse and spinous processes, vertebral invagination within the thorax, and modified disc architecture. Yet, theories defining a

common denominator that underpins this susceptibility to one of the world's most disabling diseases remain relatively immature. Here, we discuss the role of our unique capacity for trunk rotation in combination with the reorganized epaxial muscles for understanding LBP. We speculate that these muscles represent a promising target for early, informed, personalized and preventive interventions. However, it would be remiss of us to lay sole blame on evolutionary inadequacies for a condition with proven complexity, particularly when the sufferers' beliefs and expectations are such strong determinants of outcome. But what if we can influence the latter by informing the public about the former? What if we can indicate that LBP might be expected on the basis of our ancestral beginnings? Transporting our understanding of evolution to a condition with global relevance and applying this knowledge as a basis for public health provision represents a promising approach to a new understanding and management of LBP.

15:30 *Sandra Mathews*, *Nakita Frater*, *Noémie Bonneau* and *Martin Haeusler*

Osteoarthritis and Human Evolution

SPEAKER: unknown

ABSTRACT. Musculoskeletal pathologies including osteoarthritis, osteoporosis and problems of the lower back, knee and shoulder are a growing contributor to health costs. In contrast to the high prevalence of musculoskeletal disorders in modern and prehistoric humans, they are surprisingly uncommon among wild-living non-human primates. This can only partly be explained by the increased lifespan of modern humans. Another hypothesis describes these disorders as evolutionary trade-offs of bipedalism. Bipedalism was the key innovation in the evolution of early hominids and involved several adaptations in the musculoskeletal system, such as the adoption of the lumbar lordosis and a reorganization of the shoulder and pelvic girdles, knee joint, foot. In contrast to the predictions of this hypothesis, however, no osteoarthritic changes are known so far from the hominid fossil record of the appendicular skeleton predating Neanderthals. The only exception is an isolated proximal femur of an Australopithecus africanus that perhaps can be explained in the context of a haematological condition like sickle cell anaemia rather than as degenerative joint disease. Here, we analyze the remarkably complete two million year old skeleton of MH2 (Australopithecus sediba) from Malapa, South Africa. Evidence from the pelvis and advanced dental attrition suggest that MH2 is a relatively old female. A close inspection of the skeleton revealed several pathological alterations at multiple large joints. These pathological findings at the skeleton of this early biped give us one of the first indications for osteoarthritis in human evolution. We discuss the implications of these findings in the context of an evolutionary theory explaining the pathogenesis of musculoskeletal disorders in correlation with bipedalism.

15:45-16:15 Session 16: Poster Session and Break

L-Z Last name of the submitting authors should stand by posters.

LOCATION: Grand Ballroom II

16:15-17:30 Session 17A: Translating evolutionary medicine to the clinic--practical lessons for patient care

CHAIR: *Joe Alcock* LOCATION: Grand Ballroom I

16:15 *Robert Woods*, *Michael Mwangi*, *Juan Garay* and *Andrew Read*

Clinical management of resistance evolution: A case study

SPEAKER: unknown

ABSTRACT. We report the case of a patient with a chronic bacterial infection that could not be cured. Drug treatment became progressively less effective due to antibiotic resistance, and the patient died, in effect from overwhelming evolution. Even though the evolution of drug resistance was recognized as a major threat, and the fundamentals of drug resistance evolution are well understood, it was impossible to make evidence-based decisions in real time about the evolutionary risks associated with the various treatment options. An evolutionary framework is presented that considers possible routes of antibiotic resistance evolution and allows one to compare antibiotic strategies. The results of post hoc whole genome sequencing of clinical isolates from this patient reveal which of these possible routes of resistance actually evolved as a consequence of the treatment decisions that were made. This evolutionary framework will be used to highlight tractable future research directions that can improve clinical decision-making. Finally, the value of this case as a teaching resource for evolutionary medicine courses will be discussed.

16:30 *Joe Alcock*

When evidence-based medicine is evolutionary medicine.

SPEAKER: *Joe Alcock*

ABSTRACT. In the hospital and clinic an ethical obligation exists to withhold treatments when their risks outweigh the benefits. At the same time, the risks/benefits of many interventions are incompletely understood by both physicians and patients, and they continue to be used with little evidence. Evidence-based tools - the number needed to treat (NNT), and its converse, the number needed to harm (NNH) - are useful in reducing harm from powerful but overused interventions, such as antibiotics and opioids. Evolutionary concepts may speed the adoption of evidence-based treatments by providing a rationale for potential tradeoffs in their use. Can understanding the tradeoffs surrounding resistance evolution, addiction to novel substances, and interference with host defenses result in more appropriate care? This presentation will give examples of how evolutionary and evidence-based medicine can work in concert to produce better outcomes for patients.

16:45 *Mark Schwartz*

Evolution in the Clinic

SPEAKER: *Mark Schwartz*

ABSTRACT. While evolutionary biology has its most profound impact as a foundational science for medicine and public health, shaping new, important, and sometimes disruptive research questions about why our bodies are vulnerable to disease, there are occasions when it can be quite useful in the clinic. It can provide clinicians with meaningful explanations for illness and offer a context for patients' suffering.

Two anecdotes typify ways clinicians might use evolutionary explanations in practice.

When the patient complains of fever and a cough productive of sputum, the doctor may begin thinking about antipyretics and cough suppressants. Alternatively, the doctor might encourage the patient for his healthy, evolved defense mechanisms saying, "your body is doing exactly what it needs to do, what it has evolved to do, to fight off this infection." And thus avoid the disruption of these well conserved defenses.

In geriatrics, caring for patients in their 80s, 90s and beyond, the doctor often hears complaints about loss - not just of old friends and family members but of energy, appetite, sleep, bowel and bladder function, memory, etc. Here evolutionary theories of senescence (antagonistic pleiotropy, disposable soma, etc.) can couch such distressing losses in the context of a patient's life history, with its inevitable tradeoffs, and entirely predictable decline in physical and mental functions.

Whether such evolutionary explanations reduce suffering or deepen meaning in illness remains to be proven, but they provide physicians with another toolkit to help their patients understand and navigate sickness.

17:00 *Shelley Hwang* and *Carlo Maley*

What evolution can teach us about cancer

SPEAKER: unknown

ABSTRACT. Genetic diversity in a population is the fuel for natural selection and is a key determinant of the rate of evolution. The more genetic and microenvironmental diversity, the more opportunities for selection to drive clonal expansions and for the neoplasm to adapt to new selective pressures, including interventions. Measures of the somatic evolutionary process itself represent new forms of biomarkers. Because all neoplasms progress through a process of somatic evolution, measures of somatic evolution have the potential to predict progression across many cancers, not just breast cancer. In essence, they may be universal biomarkers. We are applying this approach to study the earliest breast cancers, ductal carcinoma in situ and propose applying this concept to more precisely guide the management of early stage breast cancer. The heuristic is based upon application of metapopulation and dispersal theories from ecology to predict cancer progression based on their effects on natural selection. This framework represents an innovative approach that is a significant departure from traditional cancer biology, and could yield a universally applicable construct for understanding interactions between tumors and their environments.

17:15 *Chelsea Landolin*

Exploring Clinical Applications of an Evolutionary Biology Perspective in Nursing

SPEAKER: *Chelsea Landolin*

ABSTRACT. Evolutionary biology provides a distinctly different perspective on what it means to be human and to be healthy. For the nurse in clinical practice, what are the advantages and disadvantages of carrying this perspective into a clinical setting? What progress has been made and what barriers exist to applications in clinical decision-making and patient education? What are the real opportunities to use knowledge of evolutionary history and evolutionary principles, and where might we stumble? What are the distinct strengths and challenges for nursing compared to other health professions? We present the case of a young man diagnosed with schizophrenia and comorbid conditions who is treated across several settings by nurses to illustrate how these issues interact in the real world.

(2016 ISEMPH special session on translating evolutionary medicine to the clinic)

16:15-17:15 Session 17B: Life history

CHAIR: *Kathryn Clancy* LOCATION: Grand Ballroom III

16:15 *Caleb Finch* and *Mafalda Cacciottolo*

ApoE alleles in the evolution of human brain aging

SPEAKER: unknown

ABSTRACT. Humans are unique among primates and other animals in their multiple APOE alleles. APOE4 is recognized as a risk factor for Alzheimer disease (AD) that also increases damage from cerebral trauma. Moreover, APOE4 shows interactions with sex that differ by species. While male APOE4 carriers with AD have more cerebral microbleeds, mice carrying the human gene show the opposite sex difference. Nonetheless, females of both species have greater load of brain amyloid in APOE4 vs APOE3 carriers (Cacciottolo et al, Neurobiology of Aging, 2016;PMID 26686669). These findings on sex differences give a basis for examining gender differences in APOE influences on brain development and on resistance to infections. We anticipate an expanded discussion of APOE allele pleiotropies that may underlie the large differences in APOE allele frequencies between populations.

16:30 *Paul Turke*

Childhood food allergies: an evolutionary mismatch hypothesis

SPEAKER: *Paul Turke*

ABSTRACT. Through placental transfer, breastfeeding, and the introduction of first solid foods, children are exposed to a wide range of food antigens. During the Plio-Pleistocene those early exposures would have matched the food antigen exposures expected over the remaining lifespan. With the advent of farming, long-distance trade, and the steady march of advancing technology, the potential for mismatch between early and late food antigen exposure has been increasing--slowly at first, and exponentially in the past few decades in countries where the cuisine has rapidly become less and less insular. In turn, since the development of immunological tolerance must be accomplished early in the lifespan, and since selection has accordingly honed the process to work best in the very young, each increase in the mismatch identified above is expected to produce a corresponding increase in childhood food allergies. Supporting evidence is presented.

16:45 *Daniel Kruger* and *Jessica Kruger*

Understanding health behaviors and outcomes in a life history framework

SPEAKER: unknown

ABSTRACT. Life History Theory is a powerful framework that can help promote understanding of variation in health-related behavioral patterns and why they vary consistent with environmental conditions. An organism's life history reflects trade-offs made in the allocation of effort towards specific aspects of survival and reproduction across the lifespan. Human health and longevity have improved dramatically in technologically advanced societies due to scientific research and intervention. Advances in health and medical technologies continue to extend the possibilities of saving lives. However, efforts to promote healthy behaviors and discourage health adverse behaviors struggle with diminishing returns. Short time horizons, substantial future discounting, and risky behaviors contribute to a wide variety of health issues, concerns, and outcomes. The future-oriented strategies that health promotion efforts intend to promote depend on environmental conditions that will be relatively stable over time. Individuals developing in relatively less predictable environments will exhibit riskier, immediate outcome oriented, behavioral

strategies because of the historical low probability of reproductive success for more cautious approaches. This study examines the relationship between psychological indicators of life history strategy and health related behaviors in a demographically representative sample in the Midwestern USA. Slower life histories and longer time horizons predicted higher levels of health promoting behaviors and lower levels of health adverse behaviors, even when controlling for relevant socio-demographic factors, and mediated the relationships of neighborhood conditions and life experiences. The analyses provide a strong test of the hypothesized relationship between life history and health behavior indicators, as life history variation co-varies with socio-demographic factors. Traditional public health efforts may be reaching their limits of effectiveness in encouraging health-promoting behaviors. Integrating an evolutionary framework may revitalize behavioral health promotion efforts. Novel methods for health promotion will be discussed.

17:00 *Benjamin Trumble*, *Aaron Blackwell*, *Jonathan Stieglitz*, *Caleb Finch*, *Michael Gurven* and *Hillard Kaplan*

Protective impact of ApoE4 on cognitive performance of older adult Tsimane forager-horticulturalists.

SPEAKER: unknown

ABSTRACT. Antagonistic pleiotropy is a useful concept for understanding genes that may be beneficial only in certain environments or life stages, with otherwise deleterious consequences. One potential example is the Apolipoprotein E4 (ApoE4) allele, which is the single strongest genetic predictor for Alzheimer's Dementia. Despite significant social and economic costs of dementia worldwide, the ApoE4 allele is common in many world regions, though whether this allele confers protective advantages is unclear. Recent evidence suggests that in high parasite environments ApoE4 allele may confer benefits to both child stature and cognitive development. We test whether there is a protective impact of the E4 allele on cognitive ageing in a subsistence population facing a high parasite load. Tsimane forager horticulturalists (n=266) aged 30-88 (mean 49.2 years, 50.9% male) participated in a cognitive battery (short and long term recall, digit forward, category fluency, visual scan), and gave blood samples for ApoE genotyping and eosinophil counts, a measure of parasitic load. Controlling for age, education, Spanish fluency, and sex, ApoE4 negatively impacted cognitive performance on all tasks (Std. β from -0.08 to -0.25), as did higher eosinophil counts (all tasks except category fluency; Std. β from -0.10 to -0.32). However, there was a significant interaction between eosinophils and ApoE4 on cognitive performance in all fluid cognition tasks including short (Std. β=0.45, p=0.013) and long term recall (Std. β=0.35, p=0.05), digit span (Std. β=0.22, p=0.035) and visual scan tasks (Std. β=0.39, p=0.01); in the presence of high eosinophil counts, individuals with ApoE4 alleles out performed those monozygotic for ApoE3. There was no significant interaction effect on category fluency tasks. These results suggest that while ApoE4 is associated with cognitive declines in industrialized populations with low pathogen loads, in the presence high rates of parasitic infection the ApoE4 variant may have protective effects on cognitive performance.

17:00-18:30 Session 18: Meeting and Programs committee meeting

LOCATION: Meeting Room I- Durham Convention Center

19:00-20:30 Session 19: Board of directors meeting and dinner

PROGRAM FOR SATURDAY, JUNE 25TH

07:00-08:00 Session : Continental Breakfast

LOCATION: Grand Ballroom Lobby

08:00-09:00 Session 20: Plenary Speaker: Andrea Graham

CHAIR: *Andrew Read* LOCATION: Grand Ballroom I

08:00 *Andrea Graham*

Why do immune systems harm their bearers? The evolutionary biology of "friendly fire"

SPEAKER: *Andrea Graham*

ABSTRACT. Immune-mediated diseases ranging from septic shock to multiple sclerosis exact a huge toll on human health. Many of the molecular and cellular mechanisms by which the immune system can harm a host's own tissues or even cause death are well understood. However, evolutionary explanations for self-harm have received less attention. What forces of natural selection have generated such a remarkable immune system – capable of feats like memory responses that protect against particular influenza strains decades after first exposure – that also is capable of causing such tremendous damage to our own bodies?

This talk will focus on our emerging understanding of the evolutionary causes of immune-mediated disease, including important roles for susceptibility trade-offs and for long-term co-evolution with parasites such as gastrointestinal worms. For example, in wild sheep, autoimmunity is associated with enhanced resistance to infectious diseases. Hosts may thus experience a trade-off: a host could be susceptible to autoimmune diseases OR infections, but not both. Such a trade-off could help to explain the persistence of diseases like lupus. Recent tests suggest that this trade-off is borne out in human populations. Furthermore, the clearance of our co-evolved gastrointestinal worms can alter immune system balance in a way that exacerbates autoimmune disease. Will the future of medicine entail "restoration ecology" of the human gut, reinstating worms to rein in diseases like ulcerative colitis? These and other clinical implications of an evolutionary understanding of immune-mediated disease will be discussed.

09:00-10:00 Session 21A: Evolutionary medicine: A comparative cross species perspective

CHAIR: *Elizabeth Uhl* LOCATION: Grand Ballroom I

09:00 *Michelle L. Osborn* and *Elizabeth W. Uhl*

The Pathomechanics of Degenerative Joint Disease: An Evolutionary, Comparative, and Functional Approach

SPEAKER: unknown

ABSTRACT. The common body plan of vertebrates allows for the comparison across species of disease processes and treatments, a tenet of the One Health Initiative. The most common disease affecting humans and animals is degenerative joint disease (DJD, osteoarthritis) caused by pathomechanical forces, which are forces induced by how an individual structurally interacts with its environment that directly cause joint injury. Therapeutics based upon identification of the sources of mechanical stress are critically needed as treatments focused only on controlling pain and tissue pathology mostly fail to prevent disease progression. The comparative approach emphasizes that the causal relationship between pathomechanical forces and DJD are based upon the same principles across species. However, the selection of which structures to compare should be approached with

caution. In some natural diseases, like DJD of the dog and of the human spine, the structures of interest (in this case the spine) can be directly correlated between species (although differences, like the presence or absence of disc degeneration, must be considered). But in other instances, as in the Achilles enthesis organ of humans and the Navicular enthesis organ of horses, different structures have developed similar adaptations to similar force regimes, a finding that would be ignored if 1:1 comparisons were the only ones being made. In the case of DJD, animal models based on pathomechanics and tissue responses rather than exact anatomic correlations, can facilitate a better understanding of the shared susceptibility to a very common disease and the transfer of therapeutic approaches between human and veterinary medicine.

09:15 *Natalie Warner*

Animal Models, Evolution and Drug Development

SPEAKER: *Natalie Warner*

ABSTRACT. The recent death of a volunteer in a Phase 1 clinical trial has emphasized concerns about the "prediction problem" associated with the use of animal models to evaluate the effect of xenobiotics in humans. Toxicology testing in 2 species, required by the regulatory authorities for compounds that will be tested in humans, predicts correctly in only approximately 70% of cases, although the result is rarely as dramatic as the death of a Phase 1 volunteer. Evolutionary similarities and differences among different species and among individuals within species underlies both the utility and the failure of animal models. Adaptations to environmental exposures, including diet, have resulted in differences in absorption, distribution, metabolism and excretion (ADME) of xenobiotics both across species and among individuals within the human population. These differences are increasingly recognized and taken into account when developing and when prescribing medications. Mice with "humanized" livers are available and genetic tests for variants in drug metabolizing enzymes are recommended prior to initiation of therapy with certain drugs. ADME is not the only area where it is important to consider both evolution based similarities and differences among species. Studies in animals have shown that genetic variants in, for example, the dystrophin or cystic fibrosis transmembrane conductance regulator genes result in different phenotypes in different species. In addition, not all individuals with a genetic variant that is associated with a disease will develop the disease phenotype and a disease phenotype may result from different genetic variants. Discovering why the interspecies and inter-individual differences occur is leading to more predictive animal models and to new therapeutic approaches. It has also led to interest in a more predictive classification of disease.

09:30 *Elizabeth Uhl*

Cancer in Animals: Impacts of Selective Breeding, Husbandry and Domestic Environments

SPEAKER: *Elizabeth Uhl*

ABSTRACT. Cancer is an evolutionary process in which genetic and environmental factors have been documented as affecting the incidence of cancer in humans. Animals have been selectively bred and raised in a variety of environments quite different from those of their ancestors. Both factors have impacted the occurrence of cancer in domesticated species. Selective breeding has increased the incidence of melanoma in horses and pigs, but has had the biggest impact on cancer incidence in dogs, making them especially good models for studying cancer pathogenesis, as well as identifying phenotypes at risk. For example,

osteosarcoma of the long bones is a rare cancer in most species but is very common in large breed dogs. In production animals, which have relatively short lifespans, viruses, especially those infecting the lymphatic system, induce several of the most common cancers. Environmental exposures and lifestyle (husbandry) factors also impact cancer in domestic animals. As in people, squamous cell carcinoma in a variety of animal species is induced by sun exposure, but is also exacerbated by selection for white markings. Other husbandry factors that have impacted cancer in domestic animals include spaying and neutering, which is associated with both decreases and increases in cancer risk, and the development of treatments and prophylactics against infectious diseases. Examples of the latter include the decline of tumors associated with parasite infections and the increased incidence of vaccination–induced sarcomas in cats. While comparative cross-species studies can provide important insights into both the pathogenesis and incidence of cancer, an evolutionary perspective that includes an understanding of how genetic, environmental and lifestyle/husbandry factors can interact to influence cancer development is critical. It is also important to take into account that for many cancers, the incidence data for animals is currently not very comprehensive compared to that available for humans.

09:45 *Rita McManamon*, *Linda J. Lowenstine*, *Karen A. Terio*, *Marietta Dindo Danforth* and *Hayley Murphy*

Cross-Disciplinary Efforts to Understand, Treat and Prevent Ape Heart Disease, through the Great Ape Heart Project

SPEAKER: unknown

ABSTRACT. All four great ape taxa (gorillas, orangutans, chimpanzees, bonobos) are endangered or critically endangered in the wild. Cardiovascular disease (CVD) is a significant cause of mortality in captive great apes and is documented in wild gorillas and chimpanzees. The Great Ape Heart Project (GAHP; www.greatapeheartproject.org) is a cross-disciplinary, multi-institutional, multinational effort headquartered at Zoo Atlanta. It seeks to understand, address and prevent ape heart disease, through coordinated, collaborative efforts currently funded by the Institute of Museum and Library Services. The close phylogenetic relationship between human and nonhuman apes makes it likely that a comparative approach incorporating human and veterinary medicine, evolutionary biology and genetics will provide valuable insights into contributing and ameliorating factors. Some CVD presentations, such as viral and bacterial myocarditis, have similarities among apes and humans. However, based on compiled zoo-housed ape necropsy reports, there are some species differences (e.g. aortic aneurysms are seen in gorillas, bonobos and chimpanzees, but not orangutans). In contrast, the pattern of myocardial dissecting fibrosis noted in all apes with CVD, is different from the pattern of post-myocardial infarction in humans. Atheromatous lesions in major (extrinsic) coronary arteries are common in humans, but less significant in apes. Whether these differences (or commonalities) are genetically based or multifactorial requires rigorous study. A newly-developed database, including antemortem and postmortem data, will allow future clinicopathologic analyses. Standardization of data collection (e.g., using a veterinary postmortem cardiac evaluation closer to the human autopsy approach) has been initiated. Consensus on diagnostic criteria and terminology is an ongoing goal. While nonhuman apes do not indulge in some human lifestyle choices such as smoking and alcohol consumption, other factors such as genetics, demographics, social housing, diet (e.g. salt, sugar, fiber intake), metabolic factors (obesity or diabetes), hypertension,exercise, or social stress, warrant exploration as contributing factors.

09:00-10:00 Session 21B: Metabolism and mismatch

CHAIR: *Benjamin Trumble* LOCATION: Grand Ballroom III

09:00 *Ariel Aspiras*, *Cliff Tabin* and *Nicolas Rohner*

Cavefish as a natural model for insulin resistance and fatty liver disease

SPEAKER: unknown

ABSTRACT. Understanding the genetic basis of adaptation has broad applications not only for a basic understanding of evolution, but also for human pathologies given that many human diseases are a consequence of mis-adaptation to modern societies. The emerging model system Astyanax mexicanus has become an important fish species to address adaptation to extreme environments due to its unique ecology and the availability of genetic tools and genomic resources. Cave environments are typically dark and nutrient deprived. We have previously shown that cavefish have acquired hyperphagia (increased appetite), starvation resistance and altered feeding behaviors to cope with these conditions. Here, we have focused on the fatty livers and symptoms reminiscent of diabetes these fish develop. Interestingly, we detected only very low insulin levels in cavefish (compared to surface fish) partially due to lower numbers of beta-insulin producing cells in the pancreas. In addition, cavefish display strong insulin resistance when administered with ectopic insulin. Despite the consequential fluctuating blood glucose levels, cavefish live long and healthy lives, probing the question whether they have acquired mechanisms allowing them to cope with extreme nutritional levels. Taking advantage of the newly available genome of Astyanax mexicanus, we identified mutations in the insulin receptor of cavefish most likely responsible for the observed insulin resistant phenotype. Importantly, the same mutations were found in cases of Type-II diabetic patients in human populations. Our findings in independently derived cavefish populations suggest that cavefish are inherently insulin resistant, potentially as an additional strategy to acquire better starvation resistance. We are currently using genome editing to functionally test these and other candidate mutations in zebrafish and cavefish itself to study in detail the molecular mechanisms underlying the adaptation of cavefish to the extreme and nutrient poor environments, thereby providing potential new insights into human health.

09:15 *Robert Chevalier*

Nephron maladaptation and progression of kidney disease: a new paradigm is needed

SPEAKER: *Robert Chevalier*

ABSTRACT. There is a global epidemic of chronic kidney disease (CKD): diagnosis and treatment are limited by incomplete understanding of pathophysiology. The current paradigm for progression of CKD postulates that nephron loss leads to adaptive hyperfiltration by remaining nephrons, resulting in maladaptive glomerulosclerosis and interstitial fibrosis. Recently, we have developed mouse models of CKD that point to proximal tubular injury as an early initiator of CKD, with fibrosis as a late event. Following complete ureteral obstruction, proximal tubules undergo rapid cell death with disconnection of proximal tubules from glomeruli. A similar, more gradual process takes place in polycystic kidney disease, in which intact nephrons are compressed by enlarging cysts. In contrast, cystinosis (an inherited disorder of cystine transport) results in proximal tubular oxidative injury, mitochondrial loss, and marked thinning of proximal tubular cells, with late glomerulotubular disconnection. Rather than regarding these as maladaptive physiologic responses, we have considered them as evidence of evolutionary adaptation. The kidney is

the product of evolutionary adaptation, transitioning between marine, freshwater and land environments. In mammals, high glomerular filtration rates necessitated the development of energy-consuming tubular reclamation, making the proximal tubule vulnerable to hypoxia and oxidative injury. Glomerulotubular disconnection in the mammalian kidney may represent an atavism conserved by the sculpin, a marine fish that benefits from reduced filtration by decreasing urinary water losses. Thinning of the proximal tubule in cystinosis prolongs tubular integrity by reducing cystine uptake and consequent oxidative injury. Both result in energy conservation that can be allocated to reproductive success (tradeoff). Future investigation of CKD should include deep sequencing of nephron segments to elucidate proximal tubular gene regulatory networks, mitochondrial bioenergetics, and epigenetics (microRNAs). These could be complemented by newly described kidney organoids, grown from human induced pluripotent stem cells as well as those from novel model organisms to provide phylogenetic comparisons.

09:30 *Sasha Makohon-Moore* and *Gregory Wray*

Primate iPSCs provide insights into the evolution of human metabolic traits

SPEAKER: unknown

ABSTRACT. Understanding of the evolutionary basis and molecular underpinnings of many uniquely human traits and disease susceptibilities has been hampered by the limited ability to perform experiments on and access to samples from our closest relatives. The development of induced pluripotent stem cell (iPSC) lines allows one to control for genetic effects, remove environmental variability, and carry out experimental manipulations. We are using iPSCs to identify genetic, epigenetic and environmental effects on the evolution of physiology during human origins. We differentiated iPSCs from humans and chimpanzees into adipocytes, the primary cell type of white adipose tissue.. We then used RNA-seq to identify genes whose expression differs in humans, and from these data inferred how specific metabolic pathways may have changed.These results demonstrate the utility of stem cells for providing insights into key metabolic traits of both evolutionary and medical importance.

09:45 *Nicholas Grebe*, *Melissa Emery Thompson* and *Steven Gangestad*

Oxidative Stress and Facultative Adjustment of Energy Allocation

SPEAKER: unknown

ABSTRACT. Reactive oxidative species (ROS) are a necessary byproduct of energy production. For decades, physiologists have investigated the etiological role of ROS in the disease process. While all organisms harness anti-oxidant mechanisms to combat the deleterious effects of ROS, individuals vary in their capacity to control oxidative stress, a state in which ROS production exceeds anti-oxidant efforts. More recently, evolutionary biologists have posed arguments framing oxidative stress as a potential indicator of genetic quality and/or ability to allocate energetic resources to somatic maintenance, with some preliminary empirical work in humans providing support for each of these possibilities. Here, we investigate associations between two biomarkers of oxidative stress (8-OHdG and isoprostane), activity levels, sleep patterns, and grandparental incidence of Alzheimer's Disease/dementia in two independent non-clinical samples of young adults (Ns = 150 and 98). Oxidative stress is thought to be one consequence of sleep disruption (and associated processes such as intermittent hypoxemia) within clinical populations suffering from sleep apnea; here we find mixed support for a link between sleep quality and oxidative stress. We

also find that oxidative stress biomarkers correlate positively with incidence of Alzheimer's disease/dementia in participants' grandparents (an effect replicated across both samples). Interestingly, in spite of past findings indicating stability in oxidative stress levels across time, many of the patterns we report diverge depending on time of collection. Oxidative stress levels assessed upon waking (possibly reflecting the extent of somatic repair processes overnight), but not at other times, relate negatively to physical activity levels, suggesting that individuals may facultatively adjust activity levels based on what they can energetically afford. Additionally, contemporary sedentary lifestyles might create an evolutionary mismatch with our evolved oxidative stress management systems. We conclude, tentatively, that an assessment of oxidative stress might provide information regarding allocation strategies, rather than overall 'quality' or fitness.

10:00-10:30 Session : Break

Coffee and snacks will be provided.

LOCATION: Grand Ballroom Lobby

10:30-11:00 Session 22: Human Evolution

CHAIR: *Michelle Blyth* LOCATION: Grand Ballroom I

10:30 *Stephen Corbett*, *Alexandre Courtiol*, *Virpi Lummaa*, *Jacob Moorad* and *Stephen Stearns*

A Fiery Forge: The Industrial Revolution, Recent Human Evolution and the Global Burden of Non-Communicable Disease

SPEAKER: unknown

ABSTRACT. The profound changes to human demography, life history, morphology, diet and environment wrought by the Industrial Revolution have been of an intensity, velocity and consequence with little precedent in the entire history of our species. These changes to have precipitated abrupt shifts in selection pressures that rival or exceed those associated with the other great transformations in human history, such as the advent of fire, weapons, language, writing, and agriculture. The growing global burden of chronic disease is a direct consequence of this upheaval and threatens to erode the hard won improvements in standard of living wrought by economic development. Here we review the dynamics that link demography, biology and genetics during this period of unprecedented change, and how they are likely to have had an impact on the recent evolution of genes associated with chronic and degenerative disease.

10:45 *John Pepper*

Why mammal meat is bad for humans (and humans only)

SPEAKER: *John Pepper*

ABSTRACT. Multiple studies have shown that eating red meat (mammal meat) increases illness and death from a wide range of causes, including cancer, but the reasons why haven't been widely known. It is now clear that this wide range of negative health effects all involve chronic inflammation through auto-immunity, caused by a uniquely human peculiarity of biochemistry. This talk will review the evidence for this causal link, and explain the biochemical and evolutionary mechanisms behind it.

11:00-12:00 Session 23: ISEMPH Annual Meeting

LOCATION: Grand Ballroom I

12:00-13:30 Session : Lunch on your own

13:30-14:30 Session 24: Plenary Speaker: Marion Koopmans

CHAIR: *Joseph Graves* LOCATION: Grand Ballroom I

13:30 *Marion Koopmans*

Smart genes: evolution as a driver for emerging infectious diseases

SPEAKER: *Marion Koopmans*

ABSTRACT. An estimated 70% of emerging infectious diseases (EID) in humans are zoonotic infections, where humans become infected after direct or indirect exposure to animals and the microbes that they carry. The impact of such zoonotic infections may be limited unless the pathogens are widespread and exposure is frequent, but zoonotic infections may become a global public health threat when they acquire the ability to spread efficiently between humans and develop into regional or global outbreaks called pandemics. The history of mankind has been shaped by such events, with for instance the plague epidemics caused by Yersinia pestis that were associated with waves of globalization in the Middle Ages through the colonial history of Europe, the emergence of HIV, introduced into the human population in the first half of the 20th century, or the history of influenza pandemics of which the Spanish flu caused a sizable dip in the projected population level life expectancy through its selective impact on young adults. While the burden of infectious diseases has been reduced hugely with the development of public health programs like water and food sanitation, and introduction of vaccines and antibiotics in the 20th century, the fast expansion of the human and livestock population and globalization of travel and (food and animal) trade have led to a rebound with increasing problems with EID outbreaks. Notable examples are the emergence and spread of avian influenza viruses (AIV) H5N1 and H7N9 in the past decade, with major impact on the animal sector and a continuing threat to human health, Middle East Respiratory Syndrome (MERS) Coronavirus that is widespread in the most popular livestock across the Arabian peninsula and continues to cause zoonotic infections and outbreaks, the West African multi-country outbreak of Ebola virus. The advances in human and veterinary medicine also have a downside and meet with the new challenge of increasing resistance to antimicrobial drugs, resulting from selective pressures on micro-organisms through selection of resistant mutants, and cross-species transmission of bacteria, plasmids and resistance genes, and decreasing resistance of the human population to new diseases due to the growing size of the population that has impaired immune systems and thereby lower barriers to infections. Combined, the changing dynamics of infectious diseases lead to the new challenge of our times: emergence of potential pandemic disease problems (PPP) resulting from complex interactions between humans, animals and their environment, each with their own healthy and disease causing microorganisms.

14:30-15:00 Session 25: Omenn Prize

CHAIRS: *Randolph Nesse* and *Andrew Read*
LOCATION: Grand Ballroom I

14:30 *João Barroso-Batista*, *Jocelyne Demengeot* and *Isabel Gordo*

Adaptive immunity increases the pace and predictability of evolutionary change in commensal gut bacteria

SPEAKER: unknown

ABSTRACT. Co-evolution between the mammalian immune system and the gut microbiota is believed to have shaped the microbiota's astonishing diversity. Here we test the corollary

hypothesis that the adaptive immune system, directly or indirectly, influences the evolution of commensal species. We compare the evolution of Escherichia coli upon colonization of the gut of wild-type and Rag2-/- mice, which lack lymphocytes. We show that bacterial adaptation is slower in immune-compromised animals, a phenomenon explained by differences in the action of natural selection within each host. Emerging mutations exhibit strong beneficial effects in healthy hosts but substantial antagonistic pleiotropy in immune-deficient mice. This feature is due to changes in the composition of the gut microbiota, which differs according to the immune status of the host. Our results indicate that the adaptive immune system influences the tempo and predictability of E. coli adaptation to the mouse gut.

15:00-15:30 Session 26: Williams Prize

CHAIRS: *Randolph Nesse* and *Andrew Read*LOCATION: Grand Ballroom I

15:00 *Pete C. Trimmer*, *Andrew D. Higginson*, *Tim W. Fawcett*, *John M. McNamara* and *Alasdair I. Houston*

Adaptive decision-making systems with limited information may cause ill health

SPEAKER: unknown

ABSTRACT. Non-communicable illnesses such as obesity, depression, and anxiety disorder are the dominant medical problems in the developed world, but their causes are poorly understood. Medical treatments are predicated on the assumption that such disorders are caused by pathological malfunction, but pharmacological treatments are often ineffective. Evolutionary explanations are limited to reasons why the deleterious condition could be adaptive and often fail to capture critical phenomena. For instance, explanations for depression focus on depressive behaviour as a way to avoid costly effort where benefits are small and/or unlikely, but fail to explain why low mood persists when the situation improves. Animals, including humans, do not always make optimal decisions but have evolved decision-making systems (or 'rules') that are adaptive generally. We developed an adaptive learning model in which an individual has repeated choices of whether to invest costly effort that may result in a net benefit. Investing effort also provides information about the current conditions and the rate of change in those conditions. Among a population of individuals all following the adaptive rule a significant minority remain inactive when conditions are favourable (i.e. when it would be better to invest effort), thus mimicking an effect of depression. Initially benign conditions can predispose an individual to inactivity after a relatively brief period of negative experiences. This explanation for depression contrasts strongly with the idea that the brain is somehow malfunctioning: brains of reactively depressed individuals may be working perfectly but have inaccurate beliefs about current conditions. This insight has allowed us to construct models that mimic the behaviour associated with anxiety disorder and that predict the storage of excessive fat. Pharmacological treatments for these illnesses are unlikely to work because they do not adjust beliefs; effective treatments are likely to involve altering the experiences of adaptive decision makers.

15:30-15:45 Session : Break

Coffee and snacks will be provided.

LOCATION: Grand Ballroom Lobby

15:45-17:15 Session 27A: Frontiers of evolutionary medicine

CHAIR: *Stephen Stearns* LOCATION: Grand Ballroom I

15:45 *Jang Ik Cho*, *Choongwong Jeong*, *Jiayang Sun*, *Anna Di Rienzo*, *Buddha Basnyat*, *Geoff Childs*, *Sienna Craig* and *Cynthia Beall*

Hemoglobin concentration and reproductive success of Tibetan highlanders

SPEAKER: unknown

ABSTRACT. Evolutionary medicine concerns adaptations and their consequences for disease vulnerability. Adaptations resulting from natural selection can be difficult to detect among arrays of phenotypes. This study considers the extent to which a distinctive phenotype of Tibetan highlanders, comparatively low hemoglobin concentration, is adaptive. To illustrate, at 3900m Andean Aymara women averaged 17.8 gm/dL hemoglobin concentration as compared with Tibetan women who averaged 14.2. The present study tested the hypothesis that relatively low hemoglobin concentration within a Tibetan sample associated with higher reproductive success and an opportunity for selection favoring associated genetic variants.

We collected reproductive histories by interviews in native dialects with a sample of 1,006 Tibetan women 39+ years of age residing at altitudes from 3000-4100m in Nepal. Fitness outcomes included the number of pregnancies and the rate of successful livebirths/pregnancy.

Six women had complete reproductive failure (no pregnancies became livebirths), 208 reported pregnancy loss and 720 had complete reproductive success (all reported pregnancies became livebirths). Hemoglobin concentration averaged 14.7 + 1.5, 14.2 + 1.3, and 13.7+ 1.5 gm/dL among women with no, intermediate and complete success in converting pregnancies to livebirths. Women married throughout their reproductive years had more pregnancies and thus more risk of pregnancy loss. Among those women, higher hemoglobin concentration correlated with a lower rate of successful livebirths.

We conclude that post-reproductive Tibetan women residing at 3000-4000m in Nepal having relatively lower hemoglobin concentrations have greater reproductive success than those with higher concentrations. Whether hemoglobin concentration itself is adaptive or is a proxy for another trait is unknown. The findings support the hypothesis that relatively low average hemoglobin concentration, as compared with Andean highlanders, reflects an adaptive phenotype among Tibetans at high altitude.

SUPPORT FROM NSF award 1153911 to CMB

16:00 *Gillian Bentley*, *James Curtis*, *James Firth*, *Samuel Foley*, *Dugald Foster*, *Michele Freed*, *Bliss Gibbons*, *Savanna Hamilton*, *Ángel Jiménez*, *Hyun Jung*, *Kunil Kim*, *Christopher Lawson*, *Francis Oliver*,*Alexandra Newman*, *Andrea Silva-Caballero*, *Jie Yan*, *Alice White* and *Samantha Green*

Is it Time to Re-evaluate the Mismatch Concept?

SPEAKER: *Michele Freed*

ABSTRACT. The concept of “Mismatch” is inextricably linked to the psychologist, John Bowlby’s, original formulation of the Environment of Evolutionary Adaptedness, which has come under heavy criticism as evidence mounts for continuing human microevolution. That aside, the Mismatch formulation has stimulated ongoing research about human conditions including nutrition and obesity, susceptibility to cardiovascular and metabolic disorders, and

the absence of helminths and prevalence of allergies, among many others. While Mismatch continues to be useful as an overarching framework, details concerning differences in lifestyle and disease prevalence among our human ancestors in prehistory continue to be illuminated, and call into question assumptions that have been made about ancestral conditions. Here, we take issue specifically with palaeodiets, prevalence of obesity, energy output, helminth infestations, specific cardiovascular conditions, and sleep patterns among ancestral populations. We argue that the palaeodiet was much more diverse across human groups than originally thought, that obesity was present among Palaeolithic populations, that exercise was more limited, that helminth infestations became much more prevalent among agriculturalists once this subsistence strategy emerged, that cardiovascular conditions such as atherosclerosis are not just limited to contemporary, sedentary populations, and that sleep deprivation may also have plagued hunter-gatherer groups. Our goal in criticising "Mismatch" is not to argue that the notion should be eliminated from common usage; rather, we argue that the concept needs to be refined further as our current knowledge expands about evolutionary medicine and its applications.

16:15 *Emmanuel Milot*, *Claudia Moreau*, *Alan A. Cohen*, *Damian Labuda*, *Jacinthe Gosselin* and *Francine M. Mayer*
Eco-evolutionary dynamics and natural selection on health-related traits in humans
SPEAKER: *Emmanuel Milot*

ABSTRACT. Natural selection can alter the frequency of genetic variants affecting health when these variants also affect fitness. Moreover, demographic changes can modulate the strength of the selection exerted on these variants due to a dependency of selection on age-specific survival and fertility in a population. In theory, this can result in an evolutionary feedback loop, whereby the response to selection, i.e. the change in a variant frequency, modifies the demography and vice versa. We study this complex dynamics using the French-Canadian population as a model. Deep genealogies (> 300 years) and molecular data for this population allow measuring selection and genetic variation. We found that selection in favour of juvenile survival has increased during the history of a local population, île aux Coudres, as a result of demographic changes. This implies that mutations reducing juvenile survival where more strongly selected against after 1900 than before 1900. One of these mutations, T14484C, is located in the mitochondrial genome and causes the Leber hereditary optical neuropathy. Our genealogical analyses revealed a strong effect of T14484C on infant male mortality that was previously undocumented in the medical literature. In contrast to infant mortality, maternal mortality in childbirth, a critical concern in preindustrial societies, occurred at ages where selection on survival was very weak. These results illustrate how evolutionary approaches can provide insights into the prevalence of genetic disease in modern populations.

16:30 *Hillard Kaplan*, *Benjamin Trumble*, *Jonathan Stieglitz*, *Daniel Eid* and *Michael Gurven*
Cancer in an Indigenous Native South American Population: Initial insights into the natural history of cancer in traditional subsistence populations.
SPEAKER: unknown

ABSTRACT. Little is known about the epidemiology of chronic diseases in past human populations or in populations living under traditional subsistence conditions. Evidence suggests that such populations experienced higher infectious burden throughout life, high total fertility, and different dietary and exercise regimes. We present data on cancer cases

observed among Tsimane Native South Americans over a six year period from 2008 to 2014. Cancer observed among Tsimane come from two data sources; A) screening for cervical and prostate cancer, and B) other cancers seen in symptomatic patients seeking medical attention or reported in verbal autopsies (suggesting the incidence of such cases are underestimates of true rates). The observed incidence of cervical cancer was about six times higher among Tsimane compared to age-matched U.S. women. In contrast, estimated incidence of breast cancers are one sixth the U.S rate. Little cancer was observed among Tsimane men in general, with skin cancers (basal cell carcinoma and melanoma) the most commonly reported cancer among men. Strikingly, there were no reported cases of prostate cancer among the Tsimane, nor among 348 male Tsimane screened with prostate ultrasound and serum PSA; whereas prostate cancer is the leading cause of male cancer in the U.S. These results may reflect broad trends regarding cancer rates in traditional societies. Lower rates of steroid dependent breast cancer among women and prostate cancer among men may reflect different hormonal exposures throughout life. Women in traditional societies experienced fewer menstrual cycles during their lives and thus less unopposed estrogen exposure, while men in such populations appear to have lower testosterone. The high rate of cervical cancer among Tsimane women, with its infectious routes, requires reflection about its incidence in the past and how modern routes of transmission may be affecting even remote populations.

15:45-17:15 Session 27B: Pathogen evolution

CHAIR: *Jon Laman* LOCATION: Grand Ballroom III

15:45 *Joseph Graves*, *Mehrdad Tajkarimi*, *Adero Campbell*, *Jaminah Norman* and *Marjan Assefi*

Does Nanoparticle shape impact the evolution of resistance?

SPEAKER: unknown

ABSTRACT. Recently metallic nanoparticles (e.g. silver, AgNPs) have been used as antimicrobial agents. It had been proposed that due to the multiple impacts of AgNPs that it would be difficult for bacteria to evolve resistance to them. However the Graves laboratory has demonstrated the rapid evolution of resistance to AgNPs as well as to ionic silver in Escherichia coli. This study examines the effect of nanoparticle shape on the ability of bacteria to evolve resistance to silver. In the first selection experiment, both lines selected for resistance to ionic and spherical silver nanoparticles increased their minimum inhibitory concentration (MIC) in AgNO3 relative to their controls. However, the AgNPl (triangular)-selected lines actually showed a decrease in MIC 12.5 +/- 0.0 to 6.25 +/- 0.0 mg/L in generation 442. In a second experiment, the triangular NP selected lines did show resistance relative to controls in generation 476 (MIC of AgNPl-selected: 250.37 +/- 27.35 versus controls 33.33 +/- 2.15). This suggests that resistance to triangular silver nanoparticles was much harder to achieve compared to either spherical NPs or ionic silver.

16:00 *Katia Koelle* and *David Rasmussen*

The role of deleterious mutations in shaping influenza's antigenic evolution in humans

SPEAKER: unknown

ABSTRACT. Recent phylogenetic analyses indicate that RNA virus populations carry a significant deleterious mutation load. This mutation load has the potential to shape patterns of adaptive evolution via genetic linkage to beneficial mutations. Here, we examine the effect of deleterious mutations on patterns of influenza A subtype H3N2's antigenic

evolution in humans. By first analyzing simple models of influenza that incorporate a mutation load, we show that deleterious mutations, as expected, act to slow the virus's rate of antigenic evolution, while making it more punctuated in nature. These models further predict three distinct molecular pathways by which antigenic cluster transitions occur, and we find phylogenetic patterns consistent with each of these pathways in influenza virus sequences. Simulations of a more complex phylodynamic model further indicate that antigenic mutations act in concert with deleterious mutations to reproduce influenza's spindly hemagglutinin phylogeny, co-circulation of antigenic variants, and high annual attack rates. We end by presenting in progress work that shows the important role that deleterious mutations may play in shaping influenza's phylogeographic patterns.

16:15 *Elsa Hansen*, *Robert Woods* and *Andrew Read*

On the use of a chemotherapeutic agent when resistance to it threatens the patient

SPEAKER: unknown

ABSTRACT. Evolution of resistance to drug treatment severely limits our ability to successfully treat patients. Results from clinical, experimental and theoretical studies have been mixed and the best way to manage resistance is still vigorously debated. At the center of this debate is whether aggressive drug-treatment is best or if more moderate approaches might be better. In this talk I will present a mathematical framework for defining and evaluating the performance of aggressive and moderate treatment strategies. Specific conditions will be given which clearly delineate when aggressive and moderate treatment should be used.

16:30 *Alison Feder*, *Christopher Kline*, *Brandon Keele*, *Shiu-Lok Hu*, *Dmitri Petrov*, *Pleuni Pennings* and *Zandrea Ambrose*

Evolutionary dynamics of drug resistance evolution in RT-SHIV through space and time

SPEAKER: unknown

ABSTRACT. There is mounting evidence that intrahost viral evolution is a non-homogenous process within the body and therefore must be understood spatially, temporally, and with respect to both latent and active viruses. To better understand how drug resistance spreads and establishes within a patient, we examined >3300 single-genome sequences from four macaques infected with RT-SHIV, an SIV with an HIV reverse transcriptase (RT), and treated with weak monotherapies to induce the emergence of drug resistance. We sampled both viral RNA and DNA (vRNA and vDNA) from four different compartments (lymph node, vagina, gut and PBMC) and vRNA from the plasma from 13 to 30 weeks post-infection. We find that even when drug resistance develops, a stable proportion of vDNA is maintained as wild-type without any drug resistance mutations. Further, only a small percentage of vDNA encodes most vRNA present within a compartment. This suggests that sampling vRNA may provide only a narrow view of the evolutionary potential of the virus. Although there is evidence for a strong role of migration between tissue types, we find that different compartments have notably different dynamics. In particular, gut vRNA has higher rates of turnover, and gut vDNA maintains less wild-type virus, than the vRNA and vDNA from other compartments. Characterizing the relationships between compartments and between vDNA and vRNA will be important in understanding how multidrug resistance emerges, particularly outside of the blood, and can inform treatment and eradication strategies. That many of these findings are reliant on the sampling scheme of both vDNA and vRNA, across compartments and time

demonstrates the importance of varied sampling to obtain a more complete picture of how intrahost evolution proceeds.

16:45 *Ruian Ke*, *Ruy Ribeiro* and *Alan Perelson*

Cure and superinfection of infected cells facilitate extremely rapid HCV resistance development to an direct-acting antiviral

SPEAKER: unknown

ABSTRACT. Direct-acting antivirals (DAAs) are revolutionizing the treatment of hepatitis C virus (HCV) infection. Yet, our understanding of the impact of DAAs, how HCV population responds to drug pressure and the mechanism of resistance development remains incomplete. Previous theory in general assumed resistant viruses arise through infection of newly generated cells. Here we take longitudinal clinical samples from five patients who were treated with an HCV protease inhibitor once daily for 7 days. Measurement of viral load and single genome sequencing of viral population reveal extremely rapid resistance development and surprising turnover of dominant resistant mutants over 7 weeks' period after treatment. Developing evolutionary models to simultaneously describe the viral load and viral sequence data, we show that predictions of previous theory with realistic biological parameters are inconsistent with data. Incorporating cure and superinfection of already infected cells reconciles model prediction with the extremely rapid resistant development and mutant turnovers, suggesting their important roles in accelerating within-host resistant evolution. Further, we find that the stability of resistant mutants in the viral population long after treatment cessation is likely to be due to compensatory mutations, highlighting the risk of resistant mutant transmission, especially when treatment is interrupted or after treatment failure.

17:00 *Qixin He* and *Mercedes Pascual*

Does specific immunity structure the Plasmodium falciparum population into strains from the perspective of the major blood antigen PfEMP1?

SPEAKER: unknown

ABSTRACT. Parasite antigen genes are directly involved in the arms race with the host immune system, which results in a frequency-dependent manner in competition for hosts and associated immune selection. . The Var genes (~60 per parasite genome) are a multi-copy gene family of the malaria parasite, Plasmodium falciparum, encoding the major antigenic protein (PfEMP1) on the surface of red blood cells. Standard signatures of frequency-dependent selection in the Var system are potentially confounded by the underlying parasite transmission dynamics and by non-homologous recombination. Previous modeling work posited that multi-copy antigenic genes could organize themselves into distinct minimum-overlapping strains under strong cross immunity despite high recombination. Such strain structure would have important implications for transmission dynamics and control. However, these models are far from describing and characterizing the immense diversity of Var genes observed in endemic regions. Here, we incorporate further realism on evolutionary processes into an epidemiological model of Var genes, in order to compare the patterns of structure and diversity within and between parasites. Three scenarios are compared concerning epidemiological dynamics and the duration of infection: epitope-specific immune selection, general immunity and neutral genetic drift. Distinctive signatures of specific immune selection are described, with an investigation of summary statistics of genetic diversity and population structure of Var genes. Our findings provide

theoretical expectations for patterns of empirical Var gene diversity, which we discuss in the context of existing empirical observations.

PROGRAM FOR SUNDAY, JUNE 26TH

Days:

09:00-11:30 Session : Excursion to the Duke Lemur Center

Meet in the Marriott hotel lobby at 8:50am.

LOCATION: Duke Lemur Center- 3705 Erwin Rd, Durham, NC 27705

11:30-15:00 Session : Excursion to the North Carolina Museum of Natural Sciences

Meet in the Marriott hotel lobby at 11:20am.

LOCATION: North Carolina Museum of Natural Sciences- 11 W Jones St, Raleigh, NC 27601