2016 ISEMPH Meeting Poster Presentations Abstracts

1. Immunity, iron, and reproductive status in the Bolivian Amazon

Amy Anderson, Ben Trumble, Hillard Kaplan, Michael Gurven and Aaron Blackwell

Regulation of iron status is a critical issue for populations in high-pathogen environments. Iron can promote pathogen growth, but is also required for immune response and optimal functioning of the host. This creates a delicate balance, and this trade-off may be even more pronounced during pregnancy when iron is needed both for oxygen transport to a fetus and for fetal growth, and when maternal immunity may be altered in order to promote fetal tolerance. As a major contributor to morbidity in the developing world, the dynamics of anemia risk and associated health outcomes merit further examination. To investigate causal links between iron status, immunity, and reproductive state, this study assesses longitudinal data from the Tsimane forager-horticulturalists of lowland Bolivia (n = 2,939 observations across 1,427 women between ages 18 and 50) between 2006 and 2015. 506 observations were of pregnant women. Prevalence of hookworm was 53%, and prevalence of anemia was 21%. Controlling for age, BMI, hookworm infection, lymphocyte, neutrophil, and eosinophil count, and reproductive status (pregnant or lactating), hookworm infection was associated with lower hemoglobin, hematocrit, and mean corpuscular hemoglobin concentration (MCHC) (all $p < 0.001$; Odds ratio for anemia risk = 1.32, $p = 0.006$). Lymphocyte count was positively associated with hemoglobin and hematocrit but negatively associated with MCHC (all $p < 0.01$). Pregnancy was associated with lower hemoglobin and hematocrit ($p \leq 0.001$), an expected effect of pregnancy-related hemodilution. Eosinophils, often indicative of parasitic infection, were negatively associated with hemoglobin and MCHC for all groups except pregnant women, for whom higher eosinophils were associated with higher hemoglobin and hematocrit (p's < 0.05). Our results suggest that eosinophils may protect against iron loss during pregnancy in a pathogen-rich environment, possibly by limiting parasitic infection when other forms of immunity are suppressed.

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2. Pulmonary artery pressure and arterial oxygen saturation in people living at high or low altitude: Implications for human adaptation to high altitude

Nicole Bender, Rodrigo Soria, Matthias Egger, Urs Scherrer and Stefano Rimoldi

Background. Several genetic analyses show evidence for recent evolutionary adaptations to high altitudes (HA, > 2.500m above sea level) in Andean, Tibetan, and Ethiopian populations. Pulmonary artery pressure (PAP) and pulmonary vascular resistance represent an important feature. While there is agreement that pulmonary vascular maladaptation may affect the health of HA dwellers, little is known on the distribution of PAP and oxygen saturation (SaO2) in people living at HA.

Methods. We conducted a systematic review on systolic PAP measured by Doppler echocardiography and SaO2 in people living above 2500m, and compared them to people living at low altitudes (LA, <1500m above sea level). We used random-effects meta-analyses to combine results.

Results. The combined mean systolic PAP at rest was 25.2 mmHg (95% CI 23.8-26.6) at HA, compared to 18.6 mmHg (17.2-19.9) at LA. The combined estimates for SaO2 were 90.8% (89.6-91.9%) for HA dwellers and 98.1% (97.8-98.4%) at LA.

Conclusion. Our results contribute to the understanding of physiological adaptations to HA in humans. However, as in our study most HA dwellers were Andean natives and most LA dwellers were Caucasians, further studies are needed to distinguish between evolutionary and physiological adaptation (acclimatization).

3. Integration of Embryology into an Ontophylogenetic Systems-Based Medical School Curriculum

Noel Boaz

A subcommittee of the American Association of Anatomists Curricular Task Force recently reviewed and updated the essential concepts and clinical correlations of Embryology in the medical curriculum. An Evo-Devo perspective, which encompasses Embryology, is central to a new ontophylogenetic systems-based medical school curriculum that is vectored along structural-functional adaptive levels from simple to complex and from early to late geological time. Organizing the AAA Embryology Subcommittee's topics within the framework of the new curriculum presents a novel series of learning objectives in a rich evolutionary biological context, underscoring the relevance of Embryology for an understanding of patterns of structure, function, and pathology in Evolutionary Medicine.

4. Designing the Role of Informal Education in Teaching Evolutionary Medicine in the USA

Nicole Burt

Evolutionary medicine is not widely taught in US colleges and medical schools despite increased awareness of the field. Formal education in the field is growing, but there is little attention paid to informal education. Informal Education has the potential to reach the general public and enhance formal education. There are only a handful of museums with human health galleries. Currently, none of these use an overtly evolutionary perspective. Here we present some of the work we are doing at CMNH to teach concepts of health and evolution to the public.

Our Human Origins Gallery is essential to educating students in Ohio about evolution. It is currently used to help teach both formal and informal programs to K-12 students and medical residents. In these programs, we supplement the story of human origins with evolutionary medicine and the role evolution plays in human health. To better teach and present the topic of Human Health, we are creating a unique permanent gallery focused on the evolution of health, which highlights evolutionary medicine. The gallery will be the first exposure to this topic for most of our visitors and is aimed at families. We are also working to expand our formal education programs that accompany the gallery spaces. Our joint program with Louis Stokes, Cleveland VA Medical Center, focuses on how medical practitioners can

apply new knowledge about human evolution and the evolution of human populations to disease in their practice. The feedback from participants has been overwhelmingly positive.

It is important to focus the promotion of evolutionary medicine not only on advanced learners, but also the general public if we are going to find widespread acceptance and understanding in the US. We hope to connect with others teaching evolutionary medicine to determine what is working and what can be done.

5. The Blemishes of Modern Society? Acne prevalence in the Dogon of Mali

Christine Campbell and Beverly Strassmann

Background & Objectives: To investigate whether acne vulgaris is a "disease of western civilization," we assessed the prevalence and severity of acne in the adolescents of the Dogon, a rural-dwelling population of Mali. Of the same cohort, we also investigated the effect of urban migration while controlling for age, puberty, BMI, and wealth.

Methodology: Using identification photos taken in 2011 as part of a prospective cohort study, we assessed the severity and prevalence of acne in 1182 Dogon adolescents between the ages of 11-18 years. We used multivariable logistic regression to estimate the effect of predictor variables (age, breast stage, testosterone level, BMI, urban vs. rural living, and wealth) on the presence of acne, which was coded as a binary dependent variable.

Results: The prevalence of acne in Dogon adolescents (age 11-18) in Mali was 28%, with 90% of the cases of acne being mild or very mild. Controlling for age, puberty, and BMI, and wealth z-score (which was non-significant), boys who had moved to the capital city of Bamako had 85% less acne than those who remained in the rural village. Wealth and urban living were not found to be significant predictors of acne in girls.

Conclusion and Implications: The low prevalence and severity of acne in the Dogon compared to other more urban or affluent populations may be caused by their low glycemic diet, limited milk consumption and other lifestyle factors. Since we did not find acne to increase when moving to a city, or in response to wealth status, it is difficult to conclude that acne is a disease of modern societies. However, the observation that the severity of acne is low in the Dogon compared with high-income populations, suggests that the hypothesis merits further consideration and testing.

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7. Better outcome on cancer patients subjected to bio-psychosocial (BPS) approach. Cost-effectiveness report on a small outpatient clinic located in southern Brazil

James Fleck, Luis Fernando Venegas, Ricardo Preger, Rosangela Dambros, Leonor Gonçalo and Simone Fardo

Despite the universal well-recognized importance of the BPS approach, most of the reviews showed an intrinsically methodological difficulty to evaluate the intervention. We proposed a BPS approach, which required a human changing management directed both to the patients and to the clinic staff. After several consensual meetings we sequentially adopted seven BPS interventions: Removing self-protection, improving the sense of belonging, applying to a tutorial, creating a virtuous wheel, promoting collective intelligence, producing a realistic scenario and developing self-management of an open clouding computing IT patient's file. We critically reviewed the deaths and evaluated the overall survival of 35 metastatic cancer patients who were subjected to at least three BPS interventions. Patients were categorized according to the tumor anatomical site, pathologic, molecular and immunohistochemical characteristics, clinical stage and treatment. The observed survival (OS) in each case was paired with the median expected survival (ES) previously reported on prospective randomised trials that better fit both group of patients into the same prognostic factors. The treatment cost of each patient was converted in American dollars in a daily exchange basis and the cost of the treatment periods were compared with those analyzed by Avalere Health which was commissioned by Community Oncology Alliance to evaluate chemotherapy cost in four large USA commercial managed care plans. Our results showed a 55% increase in median survival and a 40% decrease in cost, conducting to an impact benefit of 95% in cost-effectiveness. Despite the small number of patients, this is the first study, which could prospectively indicate a cost-effectiveness advantage obtained with BPS approach, supporting a low-cost standard treatment of metastatic cancer patients through behavioral changes.

8. A Mathematical Model for Celiac Disease

Alyssa Greenhouse and Frederik Nijhout

Celiac disease is an autoimmune disorder resulting in the inability to correctly digest gluten and transport it across the intestinal membrane. Although disease prevalence is 1 in 100, it remains widely undiagnosed. An estimated 2.5 million Americans remain undiagnosed and at serious risk of long-term health complications, including the development of other autoimmune diseases and neurological conditions. It is not fully understood how celiac disease starts, with both genetic and environmental factors playing critical roles. One possibility includes the onset of inflammation, which then triggers the immune response. Somatic mutations in the various enzymes involved in the breakdown pathway could also lead to disease activation. In order to develop a better quantitative understanding of the development of celiac disease, we constructed a mathematical model of the pathway by which gluten is broken down, imported through the intestinal membrane, and then becomes the signal for immune attack. The model shows how celiac disease can be initiated by inflammatory reactions in the bowel, as well as from misregulation of several critical enzymes. Further, the model incorporates the important role that specific genes play in the pathway, and what effect their activation or inactivation has. Thus, the model provides a holistic view of the diverse processes leading to and arising from celiac disease. By providing a more complete understanding of the various factors, the model can be used to predict optimal places for medical intervention, and potentially, find strategies for preventing the disease from developing in the first place.

9. Does Including Evolutionary Medicine in an Anatomy and Physiology Course Change Student Attitudes Towards Evolutionary Theory?

Laura Hechtel, Kimberly Bernosky-Smith, John Holz, Stacy Ruvio and Frank Stephen

Several studies have demonstrated a change in student attitudes towards evolutionary theory after being exposed to misconceptions about evolution, the nature of science, and/or epistemological views. But these studies have not intentionally looked at the use of examples in evolutionary medicine as the main focus to affect student attitudes towards evolutionary theory. In this study, we examined the effect of including evolutionary medicine concepts to an Anatomy and Physiology course on student attitudes towards evolutionary theory. This course is ideally suited for such a study as it contains both science and non-science majors, and is taken mostly by students seeking a career in either medicine or an allied health field. Students were given the Measuring Attitudes Towards Evolution (MATE) instrument at the beginning and end of the semester in each of 8 sections of an Anatomy and Physiology II course taught at D'Youville College. Three sections were exposed to examples of evolutionary medicine throughout the semester (experimental group) while the remaining 5 sections were not (control group). Average scores in the MATE per section for both pre-and post-tests were treated as individual samples and compared between the experimental and control groups. Results from the study indicate that exposure to evolutionary medicine improves student attitude toward evolutionary theory especially for non-science majors. These results seem to indicate that using practical or "real life" examples of evolutionary theory give students a different perspective of the importance and/or validity of evolutionary theory and therefore alters their attitudes towards it. Therefore, the authors suggest that using evolutionary medicine in combination with other factors affecting student attitude toward evolution (listed above) should be included in secondary and college biology curricula. Such inclusion may be an effective way to change student and public attitudes toward evolutionary theory.

10. Co-evolution of host and pathogen in major infections: a paleopathological perspective

Maciej Henneberg

Humans, like all other organisms, including microorganisms, undergo continuous evolutionary changes in response to a multitude of stimuli. Paleopathological studies enable observations of changes occurring in the relations between humans and their pathogens in relatively long periods of about 1000 generations. Though this is a benefit, the drawback is that major systemic infections – tuberculosis, treponemal diseases, leprosy – do not produce bone lesions in all sufferers. Thus they are not always observable. A large number of paleopathological descriptions of various past skeletal materials has been published enabling a meta-analysis, provided a careful interpretation of varying in quality descriptions of pathological signs is performed. This analysis shows that all three chronic and widespread infections, when their skeletal signs are studied in the context of paleodemographic situations of populations where they occurred, were gradually decreasing their severity. In the last 5000 years skeletal signs of tuberculosis become less common, skeletal manifestations of leprosy in Europe decline after the end of the Middle Ages, while skeletal signs of treponematoses are mild in areas of its endemic presence, becoming much more severe when members of foreign populations are exposed to local pathogen strains. The evolution of tuberculosis and treponematoses entered a new phase when the use of antibiotics became widespread. It has always been an ongoing process.

11. Immune Modulation during Pregnancy for Women in a High Pathogen Environment

Carmen M. Hové, Aaron D. Blackwell, Benjamin C. Trumble, Ivan Maldonado Suarez, Jonathan Stieglitz, Bret Beheim, J. Josh Snodgrass, Michael Gurven and Hillard Kaplan

Female immune function varies depending on reproductive state, presumably to negotiate trade-offs between maintaining maternal immune defenses, supporting conception, increasing fetal tolerance, and maintaining energy balance. Such shifts have been mostly documented in WEIRD (Western, Educated, Industrial, Rich, Democratic) populations, where the consequences of trade-offs are likely to be attenuated by low pathogen prevalence and high energy balance. Few data are available from populations experiencing high pathogen load and low energy balance. To determine whether changes in immunity during pregnancy are comparable in a population with chronic immune activation, we collected data from the Tsimane, an Amazonian, subsistence, natural fertility, forager-horticulturalist population living in lowland Bolivia. Tsimane have a total fertility rate of 9.1 children per woman and generally exhibit elevated immunoglobulins, eosinophils, and erythrocyte sedimentation rate (ESR).

Between 2004-2013, pregnant and non-pregnant Tsimane women ages 18 to 50 (n=948) provided blood samples. Women with lactational amenorrhea were excluded. Samples were assayed to determine total leukocytes, lymphocytes, neutrophils, basophils, eosinophils, and monocytes. For a subset (n=149), counts of total CD4+, naïve CD4+, non-naïve CD4+, total CD8+, naïve CD8+, non-naïve CD8+, CD4+:CD8+, NK cells, and B cells were measured with flow cytometry. Immunoglobulins (IgE, IgA, IgM and IgG), and two indicators of inflammation (C-reactive protein (CRP) and ESR) were also measured.

Mixed effect models controlling for repeated measures were used for our analysis. Compared to cycling women and controlling for age, pregnant women displayed elevated CRP ($p=0.019$), ESR ($p<0.001$), and

neutrophils ($p<0.001$), and lower total lymphocytes ($p<0.001$), CD8+ cells ($p=0.036$), eosinophils ($p=0.004$), monocytes ($p=0.02$) and total IgE ($p=0.019$).

These results echo studies in WEIRD populations indicating that pregnancy is characterized by elevated inflammation and repressed cellular immunity. These data suggest that even under high pathogen stress pregnancy is associated with shifts in immunity that may alter parasite and pathogen susceptibility.

12. Tobramycin and Bicarbonate synergize to kill planktonic Pseudomonas aeruginosa, but antagonize to promote biofilm survival

Karishma Kaushik, Jake Stolhandske, Orrin Shindell, Hugh Smyth and Vernita Gordon

Rising antibiotic resistance and decline in new antibiotics motivates approaches to increase the efficacy of existing antibiotics. For the opportunistic human pathogen Pseudomonas aeruginosa, we previously observed that alkalis including sodium bicarbonate enhance the bactericidal effect of aminoglycoside antibiotics against antibiotic-resistant mutants. Here, we examine the possibility of using bicarbonate to enhance the efficacy of aminoglycosides against P. aeruginosa infections.

The aminoglycoside tobramycin is standard-of-care for P. aeruginosa infections, including acute, planktonic infections, and chronic, biofilm infections, such as those found in lungs of cystic fibrosis (CF) patients. Inhaled bicarbonate is being evaluated as a therapy to improve antimicrobial activity of the airway surface liquid and decrease the viscosity of CF mucus. Using checkerboard microdilution assays for planktonic cells and in vitro biofilms, we measure the effect of combining tobramycin and bicarbonate against P. aeruginosa, for laboratory and clinical CF strains. Bicarbonate synergizes with tobramycin to enhance the killing of planktonic bacteria. In contrast, bicarbonate antagonizes with tobramycin to promote better biofilm growth. This suggests caution when evaluating bicarbonate as a therapy for CF lungs infected with P. aeruginosa biofilms.

We analyze the above drug interactions using an interpolated dose-response surface. This allows more accurate estimation of therapeutic combinations than do standard isobolograms. Using predictions based on Loewe additivity, we consolidate information on a wide range of combinations across the dose-response surface into a net effect, enabling rapid initial estimation of the potential benefit or harm of a therapeutic combination.

The mechanism(s) underlying antagonism of tobramycin and bicarbonate in biofilm treatment is unknown, but one possibility is binding of tobramycin to the extracellular biofilm matrix. To evaluate this, we are currently testing the effect of combining bicarbonate with a chemically modified form of tobramycin (conjugated to polyethylene glycol), which has reduced affinity for matrix polymers and greater efficacy against biofilms.

13. Sleep, immunity, and life history: associations between time of sleep onset, sleep duration, and leukocyte counts

Nikka Keivanfar, Angela Garcia, Sarah Bay and Aaron Blackwell

Organisms with varying energetic constraints and life history strategies should prefer disparate suites of the immune response, given the different costs and benefits of different branches of immunity. Previous

studies have suggested associations between both sleep duration and the timing of sleep onset, and immunological parameters. Most of these studies have focused on sleep deprivation, rather than naturally occurring variation in sleep cycles. In this study, we examined the immunological correlates of naturally occurring variation in sleep duration and time of sleep onset. Subjects consisted of 59 adults between the ages of 18 and 40. Whole blood samples were collected via finger prick and analyzed on a guava easyCyte HT flow cytometer. Data regarding previous night's sleep were obtained via self-report. For each hour less sleep obtained, the total quantity of leukocytes increased (290 cell/uL/hour, $p = 0.05$), particularly granulocytes (220 cells/uL/hour, $p = 0.06$). Total sleep time was not associated with differences in T-lymphocyte counts (CD4 or CD8) or percent of naïve T-lymphocytes; however, later sleep onset (controlling for sleep duration) was associated with increased T-lymphocytes (+2.2%/hour), particularly CD8 T-lymphocytes (+1.5%/hour, $p = 0.06$), and decreased natural killer cells (-1.2%/hour, $p = 0.04$). Our results suggest that sleep and the circadian rhythm play a regulatory role on immunological functions. Reduced sleep duration is associated with a heightened innate immune response, as indicated by elevated granulocytes. Later time of sleep onset is associated with a depressed natural killer immune response as well as elevated T-cell mediated cytotoxicity. This heightened adaptive response that defends against communicable infections may be favored by a faster life history strategy. Such findings suggest that lifestyle or circadian clock differences may be associated with trade-off between branches of immunity.

14. Calcium, zinc, and iron in mothers' milk from four diverse populations

Laura D Klein, Alicia A Breakey, Brooke Scelza, Claudia Valeggia, Grazyna Jasienska and Katie Hinde

In addition to containing macronutrients, mother's milk also provides essential micronutrients. The aim of this study was to characterize the concentrations of three minerals essential for growth, development, and immune function in early life across four populations with diverse nutritional and disease ecologies. Milk samples (n=70) were collected from Poland, Argentina, Namibia, and the United States. Milk samples were analyzed for concentrations of zinc, calcium, and iron using ICP-MS analysis at the Trace Metals Lab at the Harvard School of Public Health. Concentrations of all minerals varied across populations when controlled for infant age. Calcium concentrations were significantly higher in the US samples than any other population in the study. Zinc and iron concentrations were highest in the Namibian samples. Notably, Namibian milk samples were "contaminated" with otjize, a traditional cosmetic paste made of fat and red ochre that is applied to the hair and skin (including the breasts). While this limits our ability to assess the maternal synthesis of minerals in the Namibian milk samples, the results suggest Namibian infants are ingesting minerals through milk and suckling contact. Zinc and iron are essential for proper immune function; however, too much iron may allow pathogenic iron-requiring bacteria to proliferate. We do not yet understand if or how zinc or iron from the otjize may be utilized by the infant, but these results highlight the importance of evaluating mother's milk within the context of cultural ecology.

15. Medicine in light of the body as a highly evolved ecosystem containing multiple symbionts: conceptual and regulatory hurdles

Henry Kou, Dillan Bono-Lunn, Matthew Harker and William Parker

The understanding of the human body as a complex ecosystem containing multiple symbionts with deeply intertwined relationships has important implications for modern medicine. Foremost among the considerations is the presence of a potentially devastating evolutionary mismatch in Western culture caused by the profound alteration of biodiversity in the ecosystem of the human body. Indeed, alteration of the life associated with the human body, the human biome, is an underlying cause of pandemics of allergies, autoimmune conditions, neuropsychiatric disorders, and other inflammation-associated diseases in Western societies. Although this mismatch is well understood from a scientific perspective, translation into the clinic has been extraordinarily slow. For example, highly effective treatments based on biome restoration have been established for recurrent C. difficile colitis, Crohn's colitis, and multiple sclerosis for 58, 11, and 9 years, respectively. Despite the facts that biome restoration is associated with little to no adverse side effects, and that pharmaceutical approaches offer no effective alternatives, clinical utilization of biome restoration is not standard of care, and in some cases is completely unavailable to patients. Hurdles impeding the translation of knowledge into the clinic are multifactorial. First, the difference between the biological and clinical importance of various components of the human biome is not widely appreciated. While the microbiome contributes more to immune development and to homeostasis, more complex symbionts such as helminths have greater potential for clinical utility. This conclusion is based on observations in laboratory models and in clinical studies, and has its basis in the relative degree of alteration of the respective components of the biome by Western society. Other issues impeding clinical use of biome restoration involve the current drug development pipeline. Circumventing these hurdles may require substantive changes to government policy and regulation and to the processes associated with reimbursement for medical care.

16. Habitual physical activity: considering health behavior from a broader perspective

Katharine Lee, Mary Rogers, Andzrej Galbarczyk, Grazyna Jasienska, John Polk and Kathryn Clancy

Current public health recommendations regarding physical activitiy emphasize short-duration moderate-to-intense activities in the form of leisure time physical activity and exercise. From an evolutionary perspective, selective pressures for fitness may not have acted on primarily on short duration, high intensity activity, but rather on consistent low to moderate levels of physical activity. Using data from a transitioning agricultural population in rural Poland, I will discuss a variety of ways to measure physical activity levels and the effects of habitual physical activity on women of reproductive age. The Polish women in our study (n=33) travelled a median of 9629 steps per day, 86% (median) of which were at low intensity. There is no difference in the average number of daily steps or the percent of daily time spent in light activity (via Wilcoxon rank sum, $p = 0.56$ and 0.46, respectively) between women at healthy weight vs women who are overweight or obese (defined as BMI < 25 and BMI >= 25, per CDC guidelines). Results thus far on calculations of sedentary time for a subset of these women (n=7), indicate that they spend an average of 607 +/- 43 (mean+/-S.E) minutes of their waking hours engaged in sedentary behavior and 359 +/- 48 (mean+/-S.E.) minutes engaged in non-sedentary behavior. Results thus far indicate that physical activity levels for this population are largely a result of expected domestic labor and transportation behaviors. I argue that long-duration low levels of physical activity are physiologically relevant, especially among women who are responsible for domestic labor in more traditional settings. Effective public health recommendations regarding physical activity should consciously expand their scope beyond concepts of leisure time activity and exercise.

17. Morphological integration and changes in pelvic dimensions with age in adult female humans

Angela Mallard, Kristen Savell and Benjamin Auerbach

This study examines whether dimensions in the pelvis covary identically in adult humans as they age, as measured through morphological integration (MI). Despite morphological differences, it is assumed that patterns of covariance within the human pelvis are the same regardless of sex or age once adulthood is reached. However, studies by Tague (1994) and Auerbach et al. (in review) show that older adult females have mediolaterally wider pelvic outlets (MLPO) and anteroposteriorly deeper pelvic inlets (APPI).

In this study, 18 linear dimensions were measured from the rearticulated pelves of 327 adult human skeletons (188 females, 139 males) recovered from archaeological sites in North America dating from the last millennium. We aged the skeletons and placed them into two groups: "Young" (<~25 years) and "Not Young" (>~25 years). MI was measured by comparing relative eigenvalue variances between sex and age-and-sex groups, following Pavličev et al. (2009. Evol Biol 36:157-170), as well as by comparing mean-scaled covariance matrices of the traits within each group.

Results indicate that MI differs notably between age groups within sex, but not between the sexes. Both females and males have similar relative eigenvalues (females = 0.162; males = 0.172). However, the Young female group has a relative eigenvalue variance of 0.139, while the Not Young female group has relative eigenvalue variance of 0.202. This indicates that younger females have less integration than older females. Examination of the covariance matrices indicates lower covariances among most traits, but especially between MLPO and APPI. This suggests that covariation of traits within the pelvis continue to change in adults, which has implications for obstetrics, pelvic floor pathologies, and other clinical applications, as well as for evolution of the human pelvis.

18. GEneSTATION: a computational platform for studying the evolution of pregnancy-associated processes and phenotypes through the integration of evolutionary analyses and functional genomic data

Mara Kim, Brian Cooper, Julie Baker Phillips, Haley Eidem, Jibril Hirbo, Scott Williams, Lou Muglia, J. Anthony Capra, Kenneth Petren, Patrick Abbot, Antonis Rokas and Kriston McGary

Due to their rapid evolution, the processes, physiology, and anatomy of gestation demonstrate high diversity across mammals. This diversity complicates the translation of pregnancy-related discoveries from model organisms to humans. The GEneSTATION computational platform (http://genestation.org) integrates diverse types of omics data and evolutionary analyses to accelerate the discovery and translation of the genetic basis of gestation and pregnancy-associated phenotypes across mammals. GEneSTATION provides curated life history data on pregnancy and reproduction for 23 mammals with high-quality genomes. GEneSTATION provides easy access to diverse evolutionary (e.g. gene age, population genetic and molecular evolutionary statistics), organismal (e.g. tissue-specific gene and protein expression, differential gene expression, disease phenotype), and molecular data types (e.g. Gene Ontology Annotation, protein interactions). To encourage further exploration, we provide direct links to both general (e.g. Entrez, PubMed) and pregnancy disease-specific (e.g. PTBgene, dbPTB)

databases. This uniquely comprehensive platform facilitates rapid exploration and analysis of the evolving processes of pregnancy by synthesizing diverse functional and evolutionary data from pregnancy-associated tissues and phenotypes and enabling intuitive, flexible, and mult-omic meta-analyses.

19. Pressing need to consider evolutionary principles to surmount the innovation deficit in drug discovery

Unnikrishnan Mazhuvancherry and Akhila H S

Innovations in pharmacotherapy drive the engine of the healthcare enterprise. First-in-class new molecules are becoming scarce because of high attrition, early withdrawals, end-stage failures and regulatory hurdles. The current drug discovery paradigm focuses either on minimal innovation via me-too drugs or on highly specific, potent, patentable molecules that bind specifically to molecular targets, validated by advances in molecular biology, genomics and proteomics. Target specificity is vital for killing evolutionarily divergent invaders like pathogens and cancers. However, target validation in chronic illnesses might be an oversimplification of the complex network of molecular mechanisms governing therapeutic effect. Reverse pharmacology addresses lone drug-targets, ignoring the adaptive complexity of multiple signaling pathways, established over evolutionary time-scales; targeting COX2 in isolation back-fired because saving the gut endangered the heart. Target validity is not therapeutic validity; raising HDL cholesterol (via CETP) increased mortality. Phenotypic drug discovery is re-emerging, probably because it yielded many successful multi-target and first-in-class drugs like metformin, with growing applications. Multi-target drugs enjoy better safety and efficacy as demonstrated by the popularity of polypharmacology for complex diseases. Therefore addressing multiple targets by employing a systems approach is more likely to succeed. Many time-tested drugs derived from phytochemicals are pleiotropic because evolutionarily privileged molecular scaffolds of phytochemicals bind multiple proteins, owing to structural diversity (number of aromatic groups, chiral centers, complex ring systems, proportion of heteroatoms) that overwhelms combinatorial compound libraries. Medicinal value of dietary components selected by adaptive mechanisms (E.g. alliesthesia, Baldwin effect) is probably undermined by aggressively promoted regulatory appeal of patentable target-specific drugs. Public health policies have failed to promote lifestyle modifications to counter the aggressive push of standard pharmacotherapeutic guidelines for chronic illnesses with an evolutionary etiology. Evolutionary insights and public health policies can give a meaningful direction to prioritizing safer and effective therapeutic innovations towards treatable conditions.

20. Evolutionary Perspective on Iliopsoas Abscesses

James Mcnary

We present a case of a patient with a bacterial abscess in the psoas major muscle. The iliopsoas complex is a frequent site of intramuscular abscesses; one case series(1) showed that it was the most common (87.8%) site of intramuscular abscesses requiring IR drainage. The human iliopsoas has undergone significant changes owing to the transition from quadripedal to bipedal locomotion (2), placing it in close proximity to the small intestine and thereby creating a nidus for infection via direct extension from the gastrointestinal tract. Interestingly, however, most iliopsoas abscesses occur in the absence of overt GI

infection and our literature review found that the most commonly isolated organism is methicillin-sensitive Staphylococcus aureus (3). Such abscesses are thus presumed to be of hematogenous origin but it remains unclear why the iliopsoas would be such a favored destination for bloodborne bacteria. The iliopsoas has been implicated in back pain related to the modern sedentary lifestyle, as chronic flexion of the muscle results in gradual atrophy and contracture, and one potential explanation for the relative frequency of abscesses would be that contracture of the muscle results in mechanical deformation of the vasculature. It is also possible that such abscesses result from neither direct extension nor hematogenous dissemination but rather some unknown mechanism. More research is needed to determine the etiology and risk factors of iliopsoas abscesses.

21. NOD2 affects microbial resilience after antibiotic treatment in mice

Jacqueline Moltzau Anderson, Maren Paulsen, Simone Lipinski, Robert Häsler, Christian Kautz, Richa Bharti and Philip Rosenstiel

Microbial communities are important for physiological homeostasis in the mammalian gut. To understand how the microbiota interacts with the host's genotype to respond to antibiotics as a selective pressure, it is crucial to determine how stability of community composition is maintained, through resilience and/or the development of genetically fixed resistance.

Concerns related to the use of antibiotics include pathogen resistance, alterations of the microbial composition, and acute and chronic health problems. The increasing rates of autoimmune diseases, such as inflammatory bowel disease, have been hypothesized to be related to the disruption of the interaction within and between the human microbiota and the host.

We select a mouse model deficient in the Crohn's Disease risk gene, NOD2, to investigate the role of this innate immune receptor for microbial resilience after a catastrophic perturbation. We treat C57BL6 (WT) and NOD2 (KO) mice for two weeks with a broad-spectrum antibiotic cocktail and follow fecal microbiota composition for 10 weeks. We determine community composition of the gut microbiota using 16S rDNA phylogenomic analysis (V3-V4 region) and assess the occurrence of selected known resistance genes using qPCR.

Antibiotic administration altered the composition of the microbial gut community in both WT and KO mice, where Escherichia/Shigella was the dominant genus during the 2 week treatment. The resilience phenomenon was observed in both WT and KO, with community profiles re-approaching their original state by day86. However, the KO community composition at day86 was still more similar to the community of day21 than to day0, indicating that the NOD2 genotype impairs the resilience phenomena compared to the WT. Sporadic occurrence of resistance genes from the bacterial phylum Proteobacteria and Firmicutes were observed in both WT and KO individual mice; however, a systematic pattern associated with genotype or time point was not observed with the current set of genes.

22. Clonal interference may delay the development of neutralizing antibody breadth in chronic-stage HIV infection

Nicole Nova and Katia Koelle

The discovery of broadly neutralizing antibodies (BnAbs) targeting human immunodeficiency virus type 1 (HIV-1) has provided new hope for effective HIV vaccines. The potent and polyreactive BnAbs have been found in the chronic stages of HIV-1 infection, but the mechanism behind the development of BnAbs is still poorly understood. Empirical studies suggest that antibody neutralization breadth is evolving and increasing throughout the duration of the infection, resulting in a lineage of different BnAbs that vary in breadth. Here, we introduce a mathematical framework to study the coevolution of Abs and HIV and highlight the 'evolutionary arms race' between the Abs and the virus in a predator-prey setting. We show that the rate of BnAb evolution is not only determined by mutation rates and the passing of time, but also changes in viral diversity. We investigate whether the rate of adaptation of the total Ab population is limited by selection and/or mutation using a population genetics approach including both clonal and multiple-mutations interference. We analyze our model to see if Ab breadth adaptation falls under a strong selection strong mutation (SSSM) regime, or whether it shifts between different mutation-selection regimes. Our results confirm the notion that BnAb evolution is limited by competition with strain-specific Abs. In addition, we also suggest that early BnAbs with smaller breadth delay the development of highly polyreactive BnAbs. Based on recent estimates of Ab adaptation rate, we propose that the evolution of BnAbs and the evolution of breadth within the BnAb subpopulation is primarily limited by selective forces. Finally, we discuss the implications of selection-limited breadth evolution among BnAbs for HIV vaccine development.

23. Body composition changes and diet composition among physically active humans at high altitude temperate and cold environments

Cara Ocobock

A negative energy balance, in which individuals are expending more calories than they are consuming, experienced during high altitude excursions is well documented. High levels of physical activity and physiological acclimatization lead to increased energy expenditure, whereas the decreased appetite at high altitudes is associated with reduced caloric intake. This can create a situation in which individuals have to rely on their own energy stores to fuel this greater metabolic demand resulting in body composition changes. In this study, body fat percentage, fat free mass, total energy expenditure, and energy intake were measured among National Outdoor Leadership School students (N=53). These students took part in 12-16 weeklong courses in the western U.S. backcountry at high altitude (~3500m) temperate and cold climates. Body composition was measured before and after their high altitude excursions, and total energy expenditure and energy intake were measured for 6-11 days while they were at altitude. Subjects in temperate and cold climates consumed nearly 1000 kcal day-1 and 2000 kcal day-1 less than they expended respectively. This resulted in subjects losing a significant amount of body fat and fat free mass. Subjects with a lower initial body fat percentage lost significantly more fat free mass than individuals with a higher initial body fat percentage ($p<0.02$). Increasing dietary protein has been shown to mitigate muscle loss and promote muscle repair in individuals experiencing a negative energy balance. However, the current ration plans rely on a diet consisting of mostly carbohydrates due to the ease of packing, storage, and reduced spoilage. This study demonstrates the need for more individualized provision planning and increasing dietary protein during high altitude excursions to mitigate potential muscle catabolism and reduced physical performance.

24. Accurately inferring imbalanced allele expression using logistic regression models

Kimberly Olney, Line Skotte, Rasmus Nielsen and Melissa Wilson Sayres

Biased allele expression, refers to the imbalanced expression of the two alleles in a diploid genome. Unequal transcription of alleles may occur due to cis-regulatory element variation or allele-specific epigenetic modifications. Allelic imbalance is associated in human diseases such as metabolic disorders and in ovary and breast cancers. However, allelic imbalance may be incorrectly inferred due to technical variation inherent in RNA-Seq data, including read depth, reference mapping bias, and the overdispersion of reads. To correct for technical variation we develop a logistic regression model with a mixed effects approach to combine information regarding biased allele expression from many individuals in a population, and across multiple genes. Simulations show that our method does not suffer from an excess of false-positives when inferring biased allele expression while standard ASE methods (a SNP-wise binomial test and a binomial- based logistic regression) test showed an excess of inflated p-values in the quantile-quantile plots. Further, we conducted additional simulations to predict the power of the method to detect the possible range of biased allele expression under assumptions of variable numbers of SNPs per gene and under variable depth of coverage. We then applied this method to inferring biased allele expression across the genome in 89 lymphoblastoid cell lines samples from a Central European Utah population, and are able to more accurately detect modest degrees of allelic imbalance.

25. Is Parity Protective of Developing Severe Rheumatoid Arthritis?

Tiffany D. Pan, Beth A. Mueller, Carin E. Dugowson, Michael L. Richardson and J. Lee Nelson

Human leukocyte antigen (HLA) diversity is hypothesized to promote pathogen resistance and be maintained by balancing selection. Choosing an HLA-discordant mate, in addition to conferring an immunological benefit for offspring, may also confer some protection against rheumatoid arthritis (RA) for mothers. Exposure to an HLA-disparate fetus in utero is thought to have effects on maternal immune responses that may persist for decades postpartum. Women with RA, an autoimmune disease, often experience amelioration during pregnancy followed by a flare-up postpartum, but the relationship of pregnancy and childbirth to longer-term RA prognosis is unclear. We examined whether parity prior to RA onset was associated with longer-term disease severity. In order to assess maternal-fetal HLA relationships without offspring genotype data, we considered how presence of RA-associated HLA alleles (shared epitope) and time elapsed from birth of the last child to RA onset (latency) influenced the association between parity and RA severity. A cohort study was conducted on 222 women with RA. Stratified categorical analyses were conducted to evaluate the association between parity and 7 RA severity measures based on radiographs, physical exams, and Health Assessment Questionnaires. After adjusting for age at RA onset and age at follow-up, we found limited evidence of altered risk of severe RA with respect to parity; relative risks (RR) ranged from 0.74 (95% confidence interval [CI] 0.48-1.15) for number of affected joints to 1.67 (95% CI 0.99-2.80) for joint space narrowing. In subanalyses considering latency and presence of the shared epitope, the results were also not statistically significant but did suggest potentially increased RA severity with parity among women with no copies of the shared epitope and a recent pregnancy. If parity is associated with disease progression, our results suggest this relationship may be complex and warrants further investigation into the histocompatibility relationships between mother and offspring.

26. (Healthy) Birds of a Feather Flock Together: Disease Vulnerability Moderates Mate Assortment

Randi Proffitt Leyva, Marjorie Prokosch and Sarah Hill

Introduction: Recent research has demonstrated that disease threat increases a preference for mate variety among women most vulnerable to disease (Hill, Prokosch, & DelPriore, 2015). The current research examines the impact of disease threat and vulnerability to disease on positive and negative mate assortment. For women most vulnerable to disease, seeking phenotypically dissimilar mates is perhaps a strategy to diversify the genetic lineage of offspring, thereby increasing the likelihood of inheriting the immune genes necessary to combat pathogens and survive into the next generation.

Method: Females (N= 87) were exposed to either a serious disease threat or home accidents control condition with details of the growing threat in the local environment. Participants reported overall sickness history and preference for minimum acceptable similarity in a mate on various physical, personality, racial/ethnic, and cultural values.

Results: There was a significant interaction between conditions for overall sickness, b = 9.04 (SE = 3.28), t = 2.75, p = .01, semipartial r2 = .09. Follow-up tests revealed that women most vulnerable to disease (+1 SD in Overall Sickness) primed with serious disease threat preferred mates less similar to themselves (negative mate assortment), b = 8.14 (SE = 4.23), t = 1.92, p = .05, semipartial r2 = .04. Additionally, women least vulnerable to disease (-1 SD in Overall Sickness) primed with serious disease threat preferred mates more similar to themselves, b = -8.71 (SE = 4.32), t = -2.02, p = .05, semipartial r2 = .04.

Overall, these results revealed that sickness history for women moderates the relationship between serious disease threat and mate assortment. Women with greatest sickness history (thus, are most vulnerable) preferred dissimilar mates relative to healthier women. Results lend support to the hypothesis that disease vulnerable women may engage in bet-hedging to promote variability in offspring in highly pathogen-dense ecologies.

27. Too Risky a Gamble? Disease threats decrease risk tolerance and risk-taking

Marjorie Prokosch, Jeffrey Gassen, Joshua Ackerman and Sarah Hill

Researchers have long been interested in factors that influence individuals' tolerance for risk. Although frequently characterized as undesirable, some risk-taking is necessary for economic growth and in modern social interactions. Here, we draw from research on the behavioral immune system to examine the role that illness and disease threats play in modulating risk tolerance, testing the hypothesis that disease threats bias human decision-making towards risk aversion. Across multiple studies, we examined the impact of disease cues on individuals' risk tolerance and risk-taking. Results revealed a consistent pattern whereby people were less risky when the threat of disease was high. This shift was found using both self-report and behavioral measures and was eliminated in response to a hand-washing manipulation. The current research provides evidence of a novel conceptual link between environmental pathogen load and risk tolerance, demonstrating a tendency to play it safe when the threat of disease is high.

28. Why evolutionary anthropologists should study cancer

Aaron Sandel

Cancer is a salient part of the modern human experience. While the causes of cancer remain ambiguous, recent advances have clarified certain mechanisms, including underlying genes. Studies over the past decade have also emphasized the relevance of cancer to evolutionary biology. Evolutionary anthropologists, however, despite an increasing interest in evolutionary medicine, have neglected the study of cancer. For example, since its inception, Journal of Human Evolution has published only five studies focused on cancer, three of which were published over 20 years ago. Considerably more articles on cancer have been published in American Journal of Physical Anthropology, but only nine articles have been published with "cancer" or "tumor" in the title, seven of which were published over 20 years ago. I review the importance of studying cancer within evolutionary anthropology. Investigating the genetics and physiology of cancer may elucidate topics in human evolution, such as (1) variation in skin color, (2) the presence of breasts in women, (3) longevity, (4) large brains, (5) high-altitude adaptions, and (6) altruism. For example, the tumor suppressor gene, p53, is implicated in many cases of cancer, but is also relevant for senescence, neurogenesis, cellular metabolism, and oxygen regulation. In addition, evolutionary anthropologists are particularly well situated to provide important insights into the study of cancer by (1) finding evidence of tumors and cancer in historical and ancient populations through paleopathology and ancient DNA analyses, (2) investigating cancer across cultures and species, and, like evolutionary biologists, (3) by taking a life history approach. In sum, cancer may provide insight into questions pertaining to human evolution, and an evolutionary anthropological framework will provide additional perspectives to understand the proximate and ultimate causes of cancer.

29. Measurement Theory and the P-matrix: Ramifications of Variable Choice

Kristen Savell and Benjamin Auerbach

Biomedical advances rely increasingly on an understanding of the interdependence of traits within clinical and evolutionary contexts. Determining which measurements to include in analyses of covariation and coevolution for any given set of traits can be tricky, however. Variable choice may have unintended consequences on conclusions, especially in quantitative genetic analyses that use phenotypic variance-covariance matrices (P-matrices) as an estimation of genotypic variance and covariance. P-matrices are assumed to be proportional to G-matrices within a population, and therefore serve as proxies for interpreting evolutionary change. However, since the multivariate space of a P-matrix changes with the addition or subtraction of variables, P-matrices may be limited by the biases associated with variable choice.

To approach this issue, linear measurements were taken from the tibiae of 60 tamarins. A mean-scaled P-matrix was then subjected to randomly-generated selection gradients to allow for comparison between responses. Matrix construction was evaluated by calculating cosine-similarities between the response vectors of the complete P-matrix and P-matrices that had one measurement or a pair of related measurements removed. Results indicate that the same amount of explanatory information was contained within a single variable—tibial length—as in the complete variance-covariance matrix. Ultimately, quantitative genetic analyses of this variety rely on understanding the structure and apportionment of variance, and so traits that explain most of the variance will swamp the explanatory power of other traits that may be evolutionarily informative. Care must therefore be taken in selecting

traits to include in evolutionary studies using P-matrices, especially when studying human trait covariation and coevolution for biomedical application. If the conclusions of such studies are to be applied in evolutionary medicine, where concepts like tradeoffs are a research focus, we must be diligent that our analytical approaches capture the full extent of genetic relationships among traits.

30. Using kinome profiling to study chemoresistance in pancreatic cancer cells treated with PIM kinase inhibitors

Vandana Singh, T.S. Karim Gilbert, Steve Warner, David Bearss, Lee Graves and Antonio Baines

Pancreatic ductal adenocarcinoma (PDAC) is the most prevalent cancer of the pancreas with a 5-year survival rate of 8%, making it the 4th most common cause of cancer deaths in the United States. One of the challenges related to this cancer is the issue of chemoresistance. Chemoresistance renders most drugs ineffective in the treatment of PDAC, including kinase inhibitors and chemotherapy. PIM (Proviral Integration site for the Moloney murine leukemia virus) kinases are a family of proteins shown to play an important role in the chemoresistance of many cancers, including pancreatic cancer. PIMs act downstream of the JAK-STAT cytokine signaling pathway and phosphorylate substrates involved in numerous cell functions including cell cycle progression and apoptosis. To determine the role of oncogenic PIM kinases on transformed phenotypes of PDAC cells, we tested various PIM kinase inhibitors on the cells. We were able to demonstrate that some of the inhibitors were able to decrease transformed phenotypes such as anchorage-dependent and anchorage-independent growth in the PDAC cells. As confirmation that the kinase inhibitors were selective, we evaluated phosphorylation of downstream targets of PIM kinases such as P-Bad and P-4EBP-1. We observed varying degrees of inhibition of the targets after treatment with the PIM inhibitors. To investigate resistance pathways activated in PDAC cells after treatment with PIM kinase inhibitors, we applied novel multiplexed inhibitor beads (MIBs) mass spectrometry to profile the kinome. We observed numerous kinases that were upregulated in the cells after treatment which we are currently validating as potential targets involved in resistance pathways. Our results suggest that PIM kinases are an important target for cell growth and chemoresistance in pancreatic cancer. Overall, our studies demonstrate that kinome profiling is an effective strategy to identify cellular responses to PIM kinase inhibitors as well as other drugs for treating pancreatic and other cancers.

31. Mitochondrial heteroplasmy in Drosophila

Laura Sligar and David Turissini

Mitochondrial dysfunction is a major of metabolic disorders in humans. Mitochondrial sequences can now be readily characterized by mining existing genome sequence data. It is possible to identify the presence and alternate allele frequencies of mitochondrial heteroplasmy (multiple mitochondrial haplotypes) within a single individual. I use existing Drosophila genome sequences to quantify mitochondrial heteroplasmy patterns within individuals and between species. I have analyzed locations of heteroplasmic SNPs and compare heteroplasmic minor allele frequencies between intergenic, synonymous, and nonsynonymous SNPs. This work was initially funded by a TriCEM graduate fellowship.

32. Deep Sequencing of Influenza A Virus from a Human Challenge Study Yields Insight into the Size of Influenza's Transmission Bottleneck and the Tempo of Within-Host Viral Evolution

Ashley Sobel, Micah McClain, Chris Woods and Katia Koelle

Next-generation sequencing (NGS) yields an unprecedented depth of viral genetic data in infected hosts. Here, we analyze a unique dataset of NGS samples from a human challenge study where volunteers were experimentally infected with egg-passaged influenza H3N2 virus. The dataset comprises samples from the viral inoculum and multiple time-points over the course of infection for each of 7 volunteers. By calculating pairwise genetic distances between viral samples, we first show that egg-passaging of the viral inoculum enriches for several genetic variants, a subset of which have been phenotypically characterized in the literature. Using the frequencies of all identified variants in the inoculum and in volunteer samples, we statistically estimate the transmission bottleneck size to be 6-9 virions. Further analysis shows that some of the variants enriched in the inoculum consistently decreased over the course of infection in the volunteers, suggestive of rapid within-host adaptation towards the reference strain. This observation is consistent with observed decreases in vaccine efficacy in strains carrying egg-adapted genetic variants. Excluding the variants that appear to be under selection when calculating the bottleneck size, our estimate increases from 6-9 virions to 17-30 virions. This discrepancy points towards a loose population bottleneck coupled with rapid within-host adaptation that leads to a selection-driven loss of genetic variation (primarily in the hemagglutinin gene segment). The finding of a loose transmission bottleneck is consistent with findings from several equine and swine influenza studies, although, to the best of our knowledge, has not been previously characterized in human hosts. Our findings of rapid adaptation are also consistent with previously characterized within-host evolutionary dynamics of influenza in swine hosts. Further analyses of these data need to consider the effects of genetic linkage within and possibly between gene segments to disentangle selection from genetic hitchhiking in driving observed variant frequency changes.

33. A comparative study of human and howler monkey Toll-Like Receptor 7 under the selective pressure of yellow fever virus.

Nicole Torosin, Kael Fischer, June Round and Leslie Knapp

Human and non-human primates (NHPs) share many genetic similarities, particularly loci coding for immune responses. We looked at genetic changes in immune genes using a novel comparative approach that focuses on humans and NHPs sharing an environment and pathogenic exposure. Our comparative model was humans and howler monkeys (Alouatta palliata) in Veracruz, Mexico. We studied genetic polymorphism in TLR7, a highly conserved innate immune gene, under the pathogenic pressure of the Yellow Fever Virus (YFV). Research has shown that howler monkeys are much more sensitive to YFV than humans. This may reflect differential abilities to respond to immune challenge. Microbiome composition has also been linked to disease susceptibility; therefore we also examined the microbiomes of humans and howler monkeys. We hypothesized that 1) regional pathogenic selection pressure on TLR7 has led to DNA sequence differences in humans and howler monkeys and 2) microbiome composition is associated with TLR7 genotypes. We collected fecal samples from howler monkeys in three forest fragments surrounding Veracruz, Mexico and from humans in in two nearby villages. Sequence analysis revealed that the coding region of TLR7 has functional nucleotide differences when species are compared. Further analysis is needed to understand whether microbiome composition

differences between the two species, beyond those due to phylogeny, are responsible for YFV susceptibility. In the future, we aim to compare human and howler monkey TLR7 sequences and microbiomes to those living in regions with recent YFV outbreaks and in regions that are not threatened by this pathogen.