4th Annual ISEMPH Meeting

Wed–Sat, August 1-4, 2018
Park City, Utah

ABSTRACTS – SYMPOSIA AND ORAL PRESENTATIONS

SYMPOSIA……

SYMPOSIUM I (THU, AUG 2, 8:45 AM): EVOLUTION AND HEALTH BEHAVIOUR—*Chair: Gillian Pepper*

Host conditional movement influences the evolution of beneficial and harmful microbes – *Athena Aktipis*

Human social interactions are key to solving our adaptive goals, from disease avoidance to affiliation to food acquisition to mating. But our social interactions influence not just our fitness, but also the fitness of the microbes that live in and on us – our microbiota. Previous models have not included host behaviors like conditional movement and the possibility of microbes having positive effects on the fitness of hosts. Here I describe a new model of host-microbe evolution in which microbes can evolve to have both positive and negative effects on host fitness. In this model, microbes also have the capacity to influence host-host contact indirectly through affecting the host phenotype. This model shows that microbes can evolve to be beneficial to hosts even when benefiting the host is costly for the microbes. It also shows that host conditional movement away from sick individuals enhances the evolutionary advantage that beneficial microbes have over harmful ones.

How does repeated or chronic childhood adversity shape social and cognitive abilities? – *Bruce Ellis*

According to the prevailing deficit model, children from high-stress backgrounds are at risk for impairments in learning and behavior, and the intervention goal is to prevent, reduce, or repair the damage. Missing from this deficit approach is an attempt to leverage the unique strengths and abilities that develop in response to high-stress environments. Evolutionary-developmental models emphasize the coherent, functional changes that occur in response to stress over time. Extant research in birds, rodents, and humans suggests that developmental exposures to stress can improve forms of attention, perception, learning, memory, and problem-solving that are ecologically relevant in harsh-unpredictable environments (as per the specialization hypothesis). Many of these skills and abilities, moreover, are primarily manifest in currently stressful contexts where they would provide the greatest fitness-relevant advantages (as per the sensitization hypothesis). This theory and data supports an alternative adaptation-based approach to resilience that converges on a central question: "What are the attention, learning, memory, problem-solving, and decision-making strategies that are promoted by exposures to childhood adversity?" At an applied level, this approach focuses on how we can work with, rather than against, these strengths to promote better intervention outcomes.

Perceptions of control over health, not schooling, are associated with lower treatment uptake in a high mortality population – *Michael Gurven*

Indigenous people worldwide suffer from higher rates of morbidity and mortality than neighboring populations. In addition to having limited access to public health infrastructure, indigenous people may also have priorities and health perceptions that deter them from seeking adequate modern healthcare. Here we propose that living in a harsh, unpredictable and uncontrollable environment may reduce motivation to pursue deliberate, costly behaviors to improve health outcomes. We assess whether variation in Health Locus of Control (HLC), a psychological construct designed to capture self-efficacy with respect to health, explains variation in treatment uptake behavior among Tsimane Amerindians (N=690; age range: 40–89 years; 55.8% female; data collection: 2008–2012), a high mortality and morbidity indigenous population of horticulturalist-foragers in the Bolivian Amazon, Beni Department. First, comparisons with two industrialized populations in Japan (Miyagi prefecture; e0=76.6 years) and the United Kingdom (Caerphilly county borough; e0=81.2 years) confirm that Tsimane (e0=54.1 years) have a more externalized HLC. Next, multilevel level models were used to investigate whether HLC predicts treatment uptake, and mediates the relationship between modernization and seeking treatment. External HLC scores were predictive of treatment outcomes, but the type of externalization matters: Powerful others scores were associated with greater probability of receiving modern treatment (adjusted odds ratio [OR]=1.33), while Chance scores were associated with lower probability of receiving modern treatment (adjusted OR=0.76). We found no effects, however, of Internal HLC or educational capital on treatment uptake. Overall, our findings indicate that health-related decision-making is influenced more by a psychological orientation affecting self-efficacy, shaped in part by perceptions of environmental unpredictability and harshness, than by limited knowledge, education or other indicators of modernization.

The effect of violent victimization on health-risk behaviors in Brazilian adolescents – *Dandara Ramos*

Introduction: Underage drinking and drunkenness, drug use, unprotected sex, and other forms of risky behavior in adolescence have been studied by epidemiologists because they are closely related to increased morbidity and mortality for young people, and therefore represent major public health challenges. In this work, we integrate evolutionary theory and social epidemiology to approach the study of contextual effects on health-risk behaviors (unprotected sex, drunkenness episodes, drugs and tobacco experimentation) among Brazilian adolescents.

Methods: Data from the 2015 Brazilian National Survey of Adolescent Health (PeNSE) was used, and we first analyzed the effects of self-reported violent victimization on health-risk behaviors of 51,192 adolescents aged 11–19 nested in the 26 Brazilian state capitals and the Federal District. We then explored the link between the magnitude of these associations and cues of environmental harshness and unpredictability (youth external mortality and income inequality) and mating competition (sex ratio) on the city level.

Results: Results indicated that self-reported violent victimization is associated with an increased chance of engagement in health-risk behaviors in all Brazilian state capitals, for both males and females, but the magnitude of these associations varies in relation to broader environmental factors, such as the cities' age-specific mortality rates, and specifically for females, income inequality and sex ratio.

Discussion: In addition to introducing a novel theoretical and empirical approach to contextual effects on adolescent health-risk behaviors. From a public health perspective, such findings point to the benefits of intervening not only in adolescent populations directly, but also in their city environments, reinforcing the need to consider synergies between people's life experiences and the conditions where they live, when studying health-risk behaviors in adolescence.

SYMPOSIUM II (THU, AUG 2, 2:15 PM): COMPARATIVE ONCOLOGY—*Co-Chairs: Athena Aktipis and Amy Boddy*

Elephants & Evolutionary Medicine: New perspectives on cancer treatment – *Lisa Abegglen*

Studies of comparative biology have the potential to not only increase our understanding of how different species cope with various threats to health, but also teach us how we can manipulate our own cellular responses to achieve improved outcomes to those same threats. For instance, our collaborative study of cancer across species confirmed that elephants are less likely to die from cancer compared to humans. Due to their large size and long life-span, elephants would actually be predicted to develop high rates of cancer yet previously were observed to have lower cancer rates (a phenomenon known as Peto's Paradox). Detailed analysis of cancer incidence across species revealed that, indeed, cancer incidence does not associate with increasing size or lifespan of the animal, and the elephant stood out as an example of a very large animal with a long life-span and very little cancer. The genome of the African elephant was analyzed to look for genetic clues to explain this cancer resistance. Surprisingly, elephants were discovered to have additional copies of the TP53 tumor suppressor gene. TP53, called the guardian of the genome, is a critical tumor suppressor gene found to be mutated in 50% of all human cancers. Loss of one functional allele of germline TP53 leads to a human cancer predisposition syndrome known as Li-Fraumeni Syndrome (LFS) with more than 90% lifetime risk of developing cancer and multiple primary tumors. The elephant genome contains 20 TP53 genes: 1 conventional gene with introns (EP53-ancestral) and 19 retrogenes that lack introns (EP53-retrogenes: 1-19) versus humans with 1 conventional TP53 gene. Functional studies comparing p53 response in elephant cells versus human cells revealed that this TP53 amplification was associated with increased p53-mediated, DNA damage-induced apoptosis of elephant cells compared to human cells. Following this potential mechanism of cancer resistance in elephants, current work has explored other genomic contributors to cancer resistance in elephants. In addition, we are studying if the human response to DNA damage can be altered to mimic the TP53 response that evolved in elephants. Our recent data suggests that EP53 can enhance and/or restore p53 function in in a wide range of human cancers and trigger p53-mediated cell death. We expressed various EP53 proteins in a variety of cancer cells and compared apoptosis of EP53-expressing cells to negative control protein expressing cells. We observed a significant increase in caspase activity of cancer cells expressing EP53 compared to negative control cells ($p<0.0001$ for all cell lines tested). Our results support further exploration of EP53-based cancer therapeutics, as well as further exploration into the evolution of cancer resistance across species to guide pharmaceutical research and development.

Cellular cheating is everywhere and transmissible cancers might be no exception – *Athena Aktipis*

In this talk I will discuss how cancer is a problem of cheating in multicellular cooperation and how transmissible cancers are a special case of this cheating. During the evolution of multicellularity, cells evolved to cooperate with one another and suppress cellular cheating in order to make multicellular organisms viable, successful and cancer-free. During the evolution of multicellularity, cellular cheating was a problem from within the organism, but also potentially a problem from outside the organism in the form of germ line parasitism and stem cell parasitism. I discuss how this problem of cellular cheating from outside is essentially the problem of transmissible cancer. I end by reviewing how transmissible cancers are not as rare as was previously thought and I discuss how they may have exerted significant selection pressures on life during the evolution of multicellularity.

Comparative Oncology: New insights into an ancient disease – *Amy Boddy*

We currently have a limited understanding of cancer prevalence and mortality across the animal kingdom. While a few reports suggest animals vary in the degree to which they are susceptible to cancer, ranging from relatively cancer free (i.e. the naked mole rat) to cancer prone (i.e. ferrets), there has yet to be a large-scale study to quantify the occurrence of neoplasia. Here we will present data on necropsy reports compiled from four different pathology datasets and estimate cancer prevalence across vertebrates. Consistent with previous estimates the occurrence of neoplasia is higher in mammals (26%), than birds (10%), reptiles (9.5%), and amphibians (4%). I will discuss how

a life history framework can help elucidate this diversity observed in cancer rates across different animal taxa. Our life history analysis focuses on 138 animal species with sequenced genomes, including 77 mammals, 39 species of birds, and 20 species of reptiles. We have compiled life history variables including: body mass, lifespan, litter size for each of the species. This current dataset has body mass ranging from 0.004kg in the green anole to 4,540kg in the African elephant and maximum lifespan ranges from 2yrs in the carmine bee-eater to 80 years in the African elephant. The mouse lemur had the highest incidence of reported of neoplasm (65% of the individuals, n= 35) and alligators had the lowest (1% of individuals, n= 290). In support of Peto's Paradox, we find a negative relationship between cancer incidence and body mass and lifespan. Lastly, I will discuss how life history theory and comparative oncology can help to provide new insights into the nature and prevention of cancer.

An evolutionary perspective on cancer prevalence in non-human primates – *Valerie Harris*

Studying cancer from an evolutionary perspective can lead to important theoretical and applied insights, nevertheless little is known about the rate of cancer occurring in our closest relatives. While tumors have been infrequently reported in nonhuman primates, past reports suggest nonhuman primates, including great apes, get much less cancer than humans. Here we report the incidence of cancer from 2,352 individuals across 40 species, representing 10 Primate families from over 23 years of histopathology and necropsy reports from zoos, sanctuaries and veterinary facilities. In our survey, we found that the overall rate of cancer incidence in Primates is ~18% compared to the overall mammalian incidence rate of 20%. However, we find there is diversity of incidence rates per family, ranging from 53% in Cheirogaleidae (dwarf and mouse lemurs), to 8% in Hylobatidae (gibbons). We suggest a life history theory framework can help elucidate this variation in observed in cancer rates across primates, where long-lived, large-bodied animals invest more energy in somatic maintenance (i.e. cancer defenses) to maintain their cellular body. We then test for an association between cancer incidence and life history traits, including body mass, lifespan, metabolic rate, and age to sexual maturity. Additionally, we isolated and cultured fibroblast cell lines from the Western Lowland gorilla (*Gorilla gorilla gorilla*), Chimpanzee (*Pan troglodytes*), Sumatran orangutan (*Pongo abelii*), and Ring-tailed lemur (*Lemur catta*). Cells were then treated with the growth suppressor doxorubicin in order to assess the cell's apoptotic sensitivity. Our data indicates that larger, long-lived primates have not only increased cancer defense mechanisms compared to smaller, shorter lived primates, but they also have increased sensitivity to apoptosis when exposed to doxorubicin. Combining large-scale cancer incidence records and functional assays can provide useful insights into the dynamics of cancer in all organisms, including humans.

SYMPOSIUM III (THU, AUG 2, 4:30 PM): NOVEL SOLUTIONS TO CHEMOTHERAPEUTIC RESISTANCE—*Chair: Michael Hochberg*

Effective and evolutionarily robust anti-bacterial therapeutics – *Sam Brown*

Infection medicine currently faces two major and growing crises that impact the ability of MDs to treat bacterial infections with our current arsenal of antibiotics. The first is widely recognised – the evolution of antibiotic resistance. The second receives less attention – chronic and life-threatening infections where appropriate antibiotics often fail to resolve infections. By building a multi-scale predictive understanding of microbial dynamics both within and among patients, I aim to develop novel patient-specific conditional strategies that effectively treat patients now *and* into the future.

Therapeutic Application of Phage OMKO1 in Two Cases of Antimicrobial Resistant Pseudomonas Aeruginosa – *Sam Brown*

The increasing prevalence of antimicrobial resistant infections coupled with the lack of viable alternatives has presented the opportunity to re-examine phage therapy as a potential means by which these infections could be managed. We recently described phage OMKO1, a phage observed to force an evolutionary trade-off resulting in re-sensitization to chemical antimicrobials. Here, we present the clinical course and therapeutic application of phage OMKO1 in two divergent cases of antimicrobial resistant *Pseudomonas aeruginosa* infection. These cases suggest that clinical application of this phage can be highly effective at either eradication or antibiotic re-sensitization of *P. aeruginosa* and merit further examination.

A window of opportunity to control the bacterial pathogens by combining antibiotics and phages – *Michael Hochberg*

How can we conserve antibiotic sensitivity and at the same time achieve therapeutic success? Antibiotic resistance as an evolutionary problem that can be solved in a number of ways. Such 'wedges' can be found by looking closer at disease - what I refer to as the 'disease ecosystem'. These wedges can be employed singly or in combination, and I present results from an *in vitro* experimental study of how combining two such wedges – antibiotics and bacteriophage – controls the pathogen *Pseudomonas aeruginosa.* Evolutionary biology explains both the impact on the pathogen population, and the effects of combinations on resistance.

SYMPOSIUM IV (FRI, AUG 3, 8:45 AM): EVOLUTION AND MEDICINE IN LIGHT OF THE MICROBIOME—*Chair: Seth Bordenstein)*

Of mice, men, and monkeys: Using a comparative approach to improve our understanding of the human gut microbiome – *Katherine Amato*

Given the ethical and logistical challenges associated with studying humans, animal models are essential for developing and testing hypotheses in many fields, including microbiome research. While ease of manipulation and short generation times have made germ-free mice a 'go-to' tool for establishing causation in human gut microbiome studies, basic physiological differences between humans and mice should not be overlooked. Complementary work using non-human primates that share more physiological traits with humans is essential. Nevertheless, non-human primates are grossly understudied with regard to the gut microbiome. Systematic comparisons of primate gut microbiomes did not

exist until recently, and it has generally been assumed that great apes, our closest genetic relatives, provide the best model of the human gut microbiome. Here I argue that this is not the case. Using gut microboime data from across the primate phylogeny, I show that Old World monkeys share more gut microbial traits with humans, likely due to similarities in ecology and digestive physiology, and therefore provide a better model for humans. However, key differences still exist between humans and Old World monkeys. Targeting these differences may help us pinpoint microbial mechanisms that drive variation in host phenotypes and, when combined with traditional animal model approaches, ultimately provide a more complete understanding of human-gut microbe interactions.

Microbiomes, evolution, and medicine: What would Darwin think? – *Seth Bordenstein*
Macroscopic organisms are akin to a patina on a planet dominated by microorganisms and viruses. Consequently, large hosts regularly thwart or embrace this vast microbial diversity in stable and/or transient associations. A major challenge in investigating microbiomes is to identify the rules, if any, whereby microbiomes repeatably link to host evolutionary outcomes or health disparities. Here, I will present evidence on these diverse topics, namely (i) how host evolutionary history frequently impacts interspecific microbiome variation and function, (ii) the fragility exhibited by animal hybrids as they succumb to their gut microbiomes, and (iii) the reproducible influences of human ethnicity on gut microbiome diversity and specific microbial taxa, the latter of which may provide hypotheses for examining gut microbes as mediators of health disparities.

The ecological importance of fibre breakdown by microbes in the infant gut – *Jennifer Stearns*
The infant gut is rapidly colonized by microorganisms soon after birth, and the composition of the microbiota is dynamic in the first year of life. Although a stable adult-like gut microbiome may not be established until 1 to 3 years after birth, the infant gut microbiota appears to be an important predictor of health outcomes in later life. Identifying factors that shape the gut microbiome is currently an active area of research and early evidence suggests it is influenced by host genetics and early life exposures, including delivery method, antibiotics, and diet. We have recently found that significant variance in the microbial gut community of 1 year old infants can be explained by ethnicity, even when accounting for breastfeeding, weight gain and other exposures. Since the abundance of lactic acid bacteria was associated with ethnicity and since consumption of dietary fibre differed significantly between Western infants and South Asian infants we wondered how early diet differences might be shaping the gut microbiome and leading to differences during this important dynamic time of child development. Dietary fibre is likely impacting the microbial ecology of the infant gut in a number of ways that have yet to be explored. I will present early data on the diversity in types of fibre breakdown capacity of bacterial isolates from the infant gut using both molecular and culture based methods to study these ecologically relevant traits within the context of the infant gut environment.

SYMPOSIUM V (FRI, AUG 3, 2:00 PM): ADAPTATION AND CRITICAL CARE—*Chair: Joe Alcock*

Evolution and Causation: Informing Research and Therapeutics – *Scott Aberegg*

Searching for dysregulation in sepsis - the emperor has no clothes – *Joe Alcock*
The core conception of sepsis – that it is a dysregulated state - is a powerful and durable idea – that has inspired decades of research into sepsis. But is it true that the body's response to sepsis is dysregulated? To answer that question, I survey the history of trials of experimental sepsis treatments targeting the host response. Sepsis survival is not improved by blocking one or many immune pathways. Similarly, sepsis is resistant to treatment by normalizing one or many physiologic parameters simultaneously. The vast majority of interventions are either ineffective or harmful. With this track record of failure, it is time to consider the null hypothesis – adaptation instead of dysregulation - and possibility that sepsis phenotypes are often functional, adaptive traits. This review discusses the implications of this perspective for the future of sepsis research.

Is This the Dawn of Darwinian Critical Care? – *James Morgan*
The model of a dysregulated state with failure in oxygen delivery leading to lactic acidosis will be challenged and the evolutionary perspective on inflammatory anaemia, fever, hypoxia, and the dangers of fluid therapy and oxygen (hitherto mainstays of sepsis treatment) explored. We will examine the evolutionary concepts of allostasis and immune brinkmanship and their support from the growing body of evidence validating increasingly conservative levels of intervention. Although the paradigm of aggressive physiological normalisation is fading, it is clear we are not optimally adapted for sepsis and the new challenge lies in delineating adaptive, maladaptive and neutral phenomena seen in the acute phase. Achieving this will be crucial in navigating the transition from blind aggressive intervention focusing on short-term physiological goals (oxygen saturation, blood pressure, urine output) to an evidence-based approach mindful of adaptive responses manifesting as physiological abnormality, founded on biologically well-informed research targeting meaningful long-term patient outcomes. The potential of specific insights from evolutionary medicine for future critical care will be introduced. Is this the Dawn of Darwinian Critical Care?

ORAL PRESENTATIONS……

SESSION 1A (THU, AUG 2, 10:30 AM): EARLY LIFE AND MILK—*Chair: Katie Hinde* (Location: Ballroom A)

10:30am	**1A-1**	Fujita, M	An exploratory study of the adaptive anemia hypothesis: Maternal anemia may compromise or enhance breast milk macronutrient levels depending on the type of anemia, the presence of infection, and the milk component

An exploratory study of the adaptive anemia hypothesis: Maternal anemia may compromise or enhance breast milk macronutrient levels depending on the type of anemia, the presence of infection, and the milk component

Masako Fujita (Michigan State University), Nerli Paredes Ruvalcaba (Michigan State University) and Mary Corbitt (Michigan State University)

Background: Maternal anemia has adverse consequences including low birth weight and elevated maternal, perinatal, and child mortality. Recent studies report maternal anemia's association with altered immunological and nutritional components in breast milk. This suggests that compromised breast milk quality may be one pathway linking maternal anemia to child health. To date, no research has investigated this possibility by distinguishing different types of anemia or taking infection/inflammation into account. The present study evaluated the effects of maternal iron-deficiency anemia (IDA), non-iron-deficiency anemia (NIDA), acute infection, and IDA/NIDA accompanying infection on breast milk macronutrients. IDA accompanying infection may represent an adaptive state of activated immune system, inducing the hypoferremia of infection which limits iron in blood circulation that would otherwise support pathogen growth. In contrast, IDA without infection reflects the deficiency state. These states are hypothesized to have different associations with milk nutrients.

Methods: A secondary analysis of cross-sectional data and cryogenically archived milk specimens (n=207) was conducted. Regression models for milk nutrients were evaluated for the effects of maternal IDA/NIDA, subclinical infection, and IDA/NIDA-infection interaction.

Results: After adjusting for covariates, IDA and infection each predicted significantly ($p<.05$) lower milk fat and non-significantly lower lactose. IDA predicted significantly higher total protein while infection predicted non-significantly lower total protein. A significant IDA-infection interaction was present for milk fat; relative to IDA without infection, IDA with infection predicted higher fat. NIDA predicted significantly higher lactose, non-significantly higher protein, and non-significantly lower fat. There was no significant interaction between NIDA and infection.

Conclusions: Whether maternal anemia compromises or enhances milk quality may depend on the type of anemia, the presence of infection, and the milk component. Maternal NIDA may enhance lactose. IDA may enhance total protein. IDA may compromise milk fat; however, IDA accompanying infection may enhance milk fat compared to IDA or infection alone. These findings suggest the possibility that some types of anemia among breastfeeding women may have an adaptive function. Results are tentative given the small sample size. Future research should investigate this possibility.

10:45am	**1A-2**	Morgan, N	What types of life stress have the greatest impact on pregnancy complications?

What types of life stress have the greatest impact on pregnancy complications?

Nathaniel Morgan (University of Utah), Gregory Skedros (University of Utah), Seungmin Kim (University of Utah) and Karen Schliep (University of Utah)

Background: Stress-induced pregnancy complications are thought to represent a significant cause of maternal and perinatal morbidity and mortality. Stress itself is a blanket term for an individual's physiological reactions to unfavorable environmental cues. Current evidence of the association between stress and periconceptual complications focuses primarily on stress as a whole, thus limiting our understanding of how varying types of stress are predictive of adverse outcomes. Our investigation aims to assess the association between specific types of preconception life stress and pregnancy complications.

Methods: Data from the Utah Pregnancy Risk Assessment Monitoring System (UT-PRAMS) 2012–2014 was used to evaluate links between preconception life stressors and the prevalence of hypertensive disorders of pregnancy (HDP) and pre-term labor (PTL) (births <37 weeks gestational age, and very PTL <33 weeks). We categorized 12 specific stressful events into 4 groups: partner, traumatic, financial, and emotional. Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) were estimated using modified Poisson regression, controlling for age, race/ethnicity, BMI, education, smoking, prior high blood pressure, and history of preterm labor.

Results: 4378 mothers completed the survey at median response time of 3.2 months postpartum. 26.6%, 12.2%, 32.2%, and 28.4% reported partner, traumatic, financial, and emotional-related stress. Reporting any of the 4-types of life stress was linked with increased prevalence of HDP (adjusted PR: 1.63 [95% CI: 1.06, 2.50]). The strongest association observed was between financial stress and HDP (aPR: 1.73 [95% CI: 1.15, 2.60]). Financial stress was also the only type of stress significantly associated with an increased prevalence of very PTL (aPR: 1.54 [95% CI: 1.00, 2.35]).

Conclusion: Women reporting financial stress, including job loss, pay reduction, or difficulty paying bills, had an increased prevalence of HDP and very PTL. Not only do these findings suggest a need for mitigating stress for short term gain—to increase maternal/fetal health and wellness, including normal parturition—reductions could also help assuage fetal mortality and morbidity long term. Based on current understandings of transgenerational mortality and morbidity, in relation to in utero stress-linked hormone exposure, reductions in periconceptual maternal stress could equate to reductions in fetal epigenetic markers linked to chronic illnesses, such as, diabetes, CVD, depression, and obesity. Increases in PTL have also been shown to have a direct relationship to hospital based expenditures, creating a negative feedback loop for financial related stress. Reducing financial stress periconceptually could alleviate some of the unnecessary financial burden associated with PTL. This includes the broader systemic burden of insurance premium increases and, potentially, costs for treating stress-linked chronic illness, which in the US alone exceeds two trillion dollars. Known interventions that can moderate the association between financial strain and adverse health outcomes, such as building social capital, may be effective in reducing pregnancy complications among women experiencing financial stress.

11:00am	**1A-3**	Greenwald, A	Evolutionary Insights into Breastfeeding from an Archaeological Hunter-Gatherer Population

Evolutionary Insights into Breastfeeding from an Archaeological Hunter-Gatherer Population

Alexandra Greenwald (Center for Evolution and Medicine, Arizona State University) and Katie Hinde (Center for Evolution and Medicine, Arizona State University)

Our understanding of breastfeeding and weaning practices in ancient human populations is limited. To understand "evolved" lactation dynamics, researchers often extrapolate from modern, short-term studies of non-human primates or extant small-scale societies as analogies for an evolutionary past. Newly developed archaeometric methods, however, can provide fine-grained data at the individual level on breastfeeding and early childhood diet in archaeological populations. I present data on the duration of exclusive breastfeeding, the timing and type of supplemental food introduction, and weaning age from an ancient population of hunter-gatherers using stable isotope measures (δ15N and δ13C) extracted from teeth. These data correlate with bioarchaeological measures of morbidity and ages at death. Taken together, these findings provide information, over a 6,000-year period, on early life and longitudinal health outcomes. This study further substantiates the unique adaptive flexibility of humans and sheds light on maternal and infant health outcomes in the context of social and environmental stress, including climate change, interpersonal violence, and food shortage.

SESSION 1B (THU, AUG 2, 10:30 AM): EVOLUTION AND MENTAL HEALTH—*Chair: Brandon Hidaka* (Location: Ballroom B/C)

10:30am	**1B-1**	Garcia, A	An evolutionary perspective on the links between depression, neuroendocrine-immune interactions, and Type 2 Diabetes risk

An evolutionary perspective on the links between depression, neuroendocrine-immune interactions, and Type 2 Diabetes risk

Angela Garcia (University of California Santa Barbara), Sergio Murillo (Universidad Tecnologica de Honduras, San Pedro Sula), Benjamin Trumble (Arizona State University), Michael Gurven (University of California Santa Barbara) and Aaron Blackwell (University of California Santa Barbara)

The global prevalence of Type 2 Diabetes (T2DM) has nearly doubled in the last 30 years, and is rising most rapidly in low- and middle- income countries. While obesity is a critical driver of T2DM, there are many hypotheses about how social and environmental factors interact with psychosocial stress and inflammation to increase the risk of T2DM. The physiological pathways that unite these seemingly disparate risk factors remain unclear. Using an evolutionary framework that focuses on the evolved function of circadian rhythms of neuroendocrine and immune cells may help us connect these findings to better understand variation in risk and onset of certain metabolic diseases, as well as how social factors like depression influence disease risk. The immune system is one of the most costly and critical traits required for the survival and fitness of any organism. While immune function is crucial, overactive immune responses can lead to autoimmune disorders or even sepsis. As such, natural selection has optimized the immune system to fight infection while reducing the likelihood of hyperactive immune activation and potential for dysregulation. The antiphasic relationship that exists between the circadian rhythms of leukocytes and glucocorticoids optimizes immune response through bidirectional crosstalk between these systems and the signaling of molecules that function to stimulate or suppress the others response, minimizing the risk of dysregulation. We hypothesize that: 1) disruption to the 'normal' antiphasic diurnal profiles of cortisol and leukocytes increases risk for T2DM, and 2) social correlates of T2DM may be linked through their common ability to disrupt the communication between, and regulation of both cortisol and the immune system. We evaluate these hypotheses among Honduran immigrant women (N=123) on the island of Utila, where there are overall high rates of metabolic diseases, but substantial variation in individual risk. Diurnal profiles of salivary cortisol were measured with enzyme-linked immunoassays of saliva samples collected over two days, using four measures per day (0-, 30-, 45-minutes, and 8 hours post waking). Diurnal change in peripheral leukocyte subsets (granulocytes and lymphocytes/monocytes) was measured in morning and evening venous blood draws, using a QBC dry hematology unit. We find that high and blunted cortisol is associated with less change in granulocytes and lymphocytes over the day (b= 0.001, p=0.009 and b= -0.332, p=0.0002). While reduced diurnal variation in granulocytes predicts higher levels of fasting glucose, blunting in both granulocytes and cortisol is a better predictor compared to granulocytes alone, controlling for age and BMI (b=0.103, p=0.026). Lastly, individuals that reported experiencing severe depression symptoms (n=59, 45% of the total sample) had significantly higher fasting glucose (b=0.118, p=0.001) and showed evidence of decreased sensitivity of lymphocytes to cortisol signaling (b= -5.53, p=0.014). Our findings provide evidence that metabolic pathologies may be influenced by dysregulation of neuroendocrine-immune interactions. Finally, severe depressive symptoms may alter the ability of cortisol to regulate leukocytes through effects on glucocorticoid receptor sensitivity, suggesting a pathway by which social factors may be linked to T2DM through influence on neuroendocrine and immune regulation.

10:45am	**1B-2**	Syme, K	When Saying 'Sorry' Isn't Enough: Does some suicidal behavior function to signal an honest apology?

When Saying 'Sorry' Isn't Enough: Does some suicidal behavior function to signal an honest apology?

Kristen Syme (Washington State University) and Edward Hagen (Washington State University).

The present study tested a novel evolutionary model of suicidal behavior (SB) against the ethnographic record. In a previous study, the researchers tested two evolutionary models of SB: the inclusive fitness model (IFM) and the bargaining model (BRM), a game theoretic model based on costly signaling theory that sees SB as an honest signal of need. The researchers operationalized the two models into a set of variables, and two independent coders coded 473 texts extracted from the Probability Sample of the Human Relations Area Files for the variables. While the BRM was well supported by the data, there were recurring themes that did not map on to the original models such as shame and accusations of wrongdoing. The researchers reformulated the BRM, incorporating these variables to create the costly apology model, a sub-type of the BRM that frames SB as an honest signal of apology. Two independent coders recoded the same extracts for these variables. Data analyses lent support to the costly apology model of SB. First, many of the model's variables were moderately represented in extracts and cultures. Secondly, a non-negative matrix factorization showed that the theoretical variables formed distinct clusters, occupying unique components. In sum, SB can function to communicate otherwise private information pertaining to the victim's needs.

11:00am	**1B-3**	Zefferman, M	An evolutionary theory of PTSD and moral injury with evidence from Turkana pastoralist warriors

An evolutionary theory of PTSD and moral injury with evidence from Turkana pastoralist warriors

Matthew Zefferman (Naval Postgraduate School) and Sarah Mathew (Arizona State University)

Is combat-related PTSD as some argue (e.g., Cantor 2009), a culturally-universal collection of symptoms with deep evolutionary roots? Or is it, as some argue (e.g., Junger 2016), unique to soldiers from large-scale industrial societies? To what extent can combat trauma be explained by a genetically evolved fear response and to what extent can it be explained culturally-dependent moral violations? These questions have been difficult to answer because combat stress research has almost entirely been conducted in large-scale industrial societies with similar cultural norms and moral beliefs about war. To better answer these questions I conducted interviews with over 218 pastoral warriors from the Turkana people of northwest Kenya. Warfare is common in the Turkana. Over half of adult male mortality in our study population is due to combat. For each warrior we collected data on combat exposure, their moral beliefs, exposure morally injurious events and PTSD symptom severity using a modified version of PCL-5. We found that the Turkana warriors in our sample had a high frequency and severity of PTSD symptoms. However, compared to the normalized symptom severity of a US military veteran sample, they have lower severity of depressive symptoms. We think these symptoms may be related to moral injury and I will discuss an evolutionary theory of moral injury that relies on mechanisms evolved to avoid the social harm caused by moral violations. I will also discuss various mechanisms in Turkana society that may prevent moral injury and aid in recovery.

11:15am	**1B-4**	Swain Ewald, H	Depression, inflammation and tryptophan restriction: the why and how of it?

Depression, inflammation and tryptophan restriction: the why and how of it?

Holly Swain Ewald (University of Louisville)

Inflammation has been associated with depression and efforts to target treatment accordingly have resulted in some promising as well as disappointing results. Evolution has shaped the immune response to protect against pathogens and minimally damage the individual in the process. Inflammation, therefore is likely to be associated with unresolved environmental insults rather than inherent immune dysregulation. Inflammation associated depression may be a manifestation of the host-pathogen arms race. Tryptophan restriction is a complex immune mediated mechanism for depriving an infectious agent of this essential amino acid. The process produces neuroactive compounds and may also reduce serotonin availability in the host, thus lowering mood. In a recent study (Doyle et al. 2015. Human Nature 26:277) we found that Chlamydia trachomatis, but not other sexually transmitted pathogens, was associated with depression in the patient population. A detailed understanding of tryptophan restriction, its role in the evolutionarily molded protection of the sperm and zygote in the female genital tract, and the mechanism by which Chlamydia trachomatis can circumvent this immune response may shed light on methods for determining causative agents of depression associated inflammation. Targeting inflammatory cytokines, such as tumor necrosis factor alpha, has known dangers. An understanding of the potential role of tryptophan restriction in depression may facilitate identification and prevention of specific pathogens that induce inflammation associated depression and hence safer treatment.

SESSION 2A (THU, AUG 2, 11:30 AM): SELECTION AND ANATOMY—*Chair: Nicole Bender* (Location: Ballroom A)

11:30am	**2A-1**	Bender, N	Increasing variability of body mass and health correlates in Swiss conscripts, a possible role of relaxed natural selection?

Increasing variability of body mass and health correlates in Swiss conscripts, a possible role of relaxed natural selection?

Kaspar Staub (University of Zurich), Maciej Henneberg (The University of Adelaide), Francesco Maria Galassi (University of Zurich), Patrick Eppenberger (University of Zurich), Martin Häusler (University of Zurich), Irina Morozova (University of Zurich), Frank Rühli (University of Zurich) and **Nicole Bender** (University of Zurich).

Background and objectives: The body mass index (BMI) is an established anthropometric index for the development of obesity related conditions. Several causes of the obesity epidemic have been discussed in the literature, such as an imbalance between energy input and output, sleep deprivation, gut microbiome, and epigenetics. Besides environmental factors, genetic causes are considered to be relevant for the obesity epidemics. To date, little attention has been given to the phenomenon of relaxed natural selection in modern human civilizations due to advances in medicine and improved hygiene, leading to an increased survival and a subsequent reduction of differential reproduction of different genotypes. Here, we analysed changes in the distribution of height, weight and BMI over the past 140 years based on data of Swiss conscripts and tested for correlations between anthropometric data and standard blood parameters.

Methods: Height and weight were measured in 59,504 young Swiss males aged 18-19 years during conscription in 1875-79, 1932-36, 1994 and 2010-12. For 65% of conscripts in 2010-12 results of standard blood analysis were available. We calculated descriptive statistics of the distribution of height, weight, and BMI over the four time periods and tested for associations between BMI and metabolic parameters.

Results: Average and median body height, body weight and BMI increased over time. Height did no longer increase between 1994 and 2010-12, while weight and BMI still increased over these two decades. Variability ranges of weight and BMI increased over time, resulting in increasing frequencies below and above the median, while variation of body height remained constant. Elevated levels of metabolic and inflammatory blood parameters were found at both ends of BMI distribution.

Discussion and conclusions: Both overweight and underweight subgroups showed similar changes in inflammation parameters, pointing towards related metabolic deficiencies in both conditions. The increase in BMI variation might reflect phenotypic plasticity as a result of adaptation to changing living conditions and a combination of specific genotypes, types of metabolism, environmental factors, and gene-environmental interactions. In addition to environmental influences, our results indicate a potential role of relaxed natural selection on genes affecting metabolism and body composition. It seems that recent changes in the human gene pool may be contributing to the increasing prevalence of obesity observed worldwide. The decrease in premature mortality during the same time period has led to a relaxation of natural selection, which in turn might have led to an accumulation of harmful mutations. With a relaxed opportunity for natural selection, an increasing number of individuals within the same environment might produce a body mass that either is too low or too high due to suboptimal physiological regulation of the energy balance and nutrient metabolism.

11:45am	**2A-2**	Boyd, K	Dental, Facial and Respiratory Development in Pre-industrial H. sapiens: how anthropology can inform modern orthodontic diagnosis and treatment

Dental, Facial and Respiratory Development in Pre-industrial H. sapiens: how anthropology can inform modern orthodontic diagnosis and treatment

Kevin Boyd, DDS, MSc (Lurie Children's Hospital, Chicago; The University of Pennsylvania, Museum of Anthropology, Philadelphia)

Observation of skeletal specimens from the University of Pennsylvania's Museum of Anthropology seem to suggest that most *H. sapiens* living around that time of the Industrial Revolution (early-mid 19th-Century) had well-developed boney airways and adjacent jaws that were large enough to easily accommodate well-aligned anterior and posterior dentitions, inclusive of their wisdom teeth. Anthropologists have long reported that after their nearly 250,000 years of being *anatomically modern*, human jaw and facial volumes first began diminishing around the time of the advent of agriculture in the Middle East some 10-12,000 years ago. However, given evidence showing that markedly narrowed jaws and crooked teeth, commonly known as human malocclusion (HM), did not begin to appreciably appear in the skeletal record until around the mid/late-17th-Century, seemingly coincident with events peripheral to The Enlightenment, Scientific and Industrial Revolutions. HM seems most accurately described as an *epigenetically-influenced* trait (i.e. genetic-environmental) as opposed to being a primarily *genetically-determined* phenotype. A connection appears to exist between the prevalence of HM and lifelong dietary feeding behaviors, especially during the first years of infancy and early childhood. As many HM phenotypes are known to be comorbid with respiratory problems such as Obstructive Sleep Apnea (OSA), it seems reasonable to hypothesize that resolution of HM in early childhood might also help prevent and resolve comorbid health disparities that are associated with compromised breathing. Case studies will be presented as evidence in support of this hypothesis.

12:00pm	**2A-3**	Hanzal, E	A few basic assumptions about the evolution of continence

A few basic assumptions about the evolution of continence

Engelbert Hanzal (Medical University of Vienna)

Introduction: Urinary and fecal incontinence range among the most prevalent medical conditions in humans, displaying a pronounced gender difference, often affecting the quality of life of the afflicted quite severely [1,2]. Risk factors involve aging, pregnancy, childbirth, and obesity [3]. In a very basic sense, continence in humans can be seen as the ability to dispose of urine and feces in a specified space and at the "right" time. But how might continence or its precursors have evolved?

The process of delivering copies of genes to the next generation needs energy, driving a complex series of biochemical reactions ultimately producing compounds that aid in successful reproduction, but also those not useful or even harmful to an organism that it needs to get rid of. Even in single-cell life, waste products of metabolism can get stored in vesicles (storage function) that move to the cells' periphery, where by merging with the outer cell membrane waste products can be expelled (excretory function) [4].

If this process of excretion is random, waste will accumulate evenly throughout the organism's outside environment until it gets broken down chemically with time, to eventually yield useful precursors of metabolism again. Therefore, within this time-frame (that needs to be specified for each habitat), life-forms with non-random excretory function will give rise to an uneven spatial distribution of waste products in their environment yielding areas of high and low waste concentrations. Theoretically, an environment that provides a higher concentration of useful compounds for the procreation of an organism should constitute a positive selective force for non-random excretion.

Assumtions/hypotheses: H 1: All - but perhaps the most primitive - life-forms have the ability to non-randomly dispose of waste products of metabolism. H 2: Reproduction rates will be higher in areas with lower waste concentration. H 3: A trait of non-random excretion in a life form is a selective force in evolution.

Discussion: While the proximate mechanisms of excretion have been studied thoroughly, the aspect of non-random excretion (aka continence) appears to have received relatively little attention in the life sciences, including medicine so far. Psychologically this makes sense since according to the above hypotheses every organism including humans, has a vital interest to stay away from excretions and we have evolved expensive sensorimotor and cognitive (disgust) mechanisms to avoid those. This concept may well extend as far as to the avoidance of scientific research into this problem. However, to be continent involves the intactness of so many costly biological functions, which points to the importance this trait might have. To study the evolution of excretion and waste management in biological systems more deeply would offer insights into many more proximate and ultimate causes of the important healthcare problem of urinary and fecal incontinence and considering waste products in a given habitat, their distribution and the consequences on evolution could add yet another interesting aspect to evolutionary thinking.

Literature: 1. Obstet Gynecol. 2014 Jan;123(1):141-8 2. J Urol 2010 Sep;184(3):1022 3. JAMA 2008 Sep 17;300(11):1311
4. Current science 1998;75(10):1062

12:15pm	**2A-4**	Uhl, E	Osteoarthritis: Insights from evolution, tensegrity and comparative pathology

Osteoarthritis: Insights from evolution, tensegrity and comparative pathology

Elizabeth Uhl (University of Georgia) and Michelle Osborn (Louisiana State University)

Osteoarthritis (aka: degenerative joint disease, DJD) is the most common disease affecting man and animals. It has been believed that DJD results from structural and functional failure of the joints through a process of inflammation and 'wear and tear' in which damage exceeds repair. Recently, the primary importance of aberrant mechanical forces in the pathogenesis of DJD has been recognized. Anti-inflammatory drugs generally provide only temporary relief, while exercise based therapies are more effective and can make drug and surgical intervention unnecessary. An accurate understanding of how the body works and why the lesions develop is necessary to realize the full potential of mechanical therapies, and is best provided by an evolutionary and comparative perspective. Models depicting the body as a machine are not accurate as they do not provide adequate explanations for the functional anatomy of bones, muscles and joints, and cannot explain the evolution of the various forms of the vertebrate body. A rigid, robot-like, compression-based body structure with hinge-like joints has a narrow functional range and a limited capacity to be modified to survive in different environments. In contrast a body structured through tensegrity (integrity by tension) has a seamless integration of structure and function

from the molecular, cellular, tissue and organ levels to whole body, can function in a variety of environments and is more likely to remain functional when modified by genetic changes. Tensegrity explains the functional anatomy of bones and muscles, the importance of connective tissue (which has generally been ignored in dissections) and the irregular shapes of joints. Joints structured through tensegrity allow mechanical forces to be transmitted and dispersed throughout the surrounding connective tissues and counteracted by muscular contractions rather than transmitted as compression across a joint space. A review of the pathology of DJD across species indicates that the lesions can be explained by a failure of tensegrity. The initial lesions indicate tension-induced damage in the connective tissues supporting the joint (i.e.: stretched collagen and fibro-osseous reinforcement). As these tissues fail, the joint space narrows and the bones come in contact with each other, resulting in the transfer of damaging compressive forces to the articular cartilage and underlying bone. Insights from evolution, tensegrity and pathology can: (1) explain why the joints most commonly affected by DJD vary across species; (2) explain how environmental/occupational factors affect the location of DJD through their impacts on joint tensegrity; and (3) predict that DJD therapies focused on restoring joint tensegrity will be effective.

SESSION 2B (THU, AUG 2, 11:30 AM): LIFE HISTORY—*Chair: Andrea Graham* (Location: Ballroom B/C)

11:30am	**2B-1**	Jasienska, G	Trade-offs between reproduction and health: women with high parity have poorer health in post-reproductive age

Trade-offs between reproduction and health: women with high parity have poorer health in post-reproductive age

Reproduction requires substantial energy and causes changes to maternal physiology. Life history theory predicts that resources invested in reproduction trade-off against investment in maintenance. It is less clear, however, if reproduction has long-term negative consequences for maternal health.

Health consequences of reproduction were studied among 415 post-reproductive women from rural Polish population with parity of 1 to 13 children (mean 4.1). A composite index of health was designed to include 16 measured variables characterizing cardiovascular health, lipid profile, inflammation, physical strength, cognitive decline, obesity, anemia and diabetes. Eleven variables were coded 1 (if their values were within clinically established norms) or 0 (outside of norms). Five variables were coded with respect to their population medians. The component variables contributed equally (6.25%) to the total score. This index was found to be consistent with the 5-level self-reported health scores (a mortality predictor used in epidemiology) and also shows the expected pattern of significant age-related decline (of about 0.4% per year, or from 0.59 in the 45-55 years of age category to 0.47 in the category 75+ years).

Women's reproductive investment, expressed as the number of children, correlated with a decline in the index of health ($p=0.0004$, with negative age effects accounted for). The index declined at the rate of -0.01, or about 2% per each child born. The number of sons born to a mother had a significant detrimental effect on her health status ($p=0.0038$); the number of daughters had a similar effect ($p=0.0305$). Age at first and last reproduction, and inter-birth intervals did not have any effects on the health index. It suggests that, independent of the number of children, the timing and pace of reproduction by themselves do not have a long-term impact on maternal health.

11:45am	**2B-2**	Frumkin, A	The cost of reproduction in women: Reproductive effort and oxidative stress in premenopausal and postmenopausal American women

The cost of reproduction in women: Reproductive effort and oxidative stress in premenopausal and postmenopausal American women[9.5]

OBJECTIVES: Life history theory predicts a trade-off between female investment in reproduction and somatic maintenance, which can result in accelerated senescence. Oxidative stress has been shown to be a causal physiological mechanism for accelerated aging and a possible contributor to this trade-off. We aimed to test the hypothesis for the existence of significant associations between measures of reproductive effort and the level of oxidative stress biomarkers in premenopausal and postmenopausal American women.

METHODS: Serum samples and questionnaire data were collected from 63 premenopausal and postmenopausal women (mean age 53.4 years), controls in the Connecticut Thyroid Health Study, between May 2010 and December 2013. Samples were analyzed for levels of 8-OHdG and Cu/Zn-SOD using immunoassay method.

RESULTS: Levels of oxidative damage (8-OHdG) but not oxidative defense (Cu/Zn-SOD) were negatively associated with parity and number of sons in premenopausal women ($r = -0.52$ for parity, $r = -0.52$ for number of sons, $P < .01$). Together, measures of reproductive effort, women's BMI, age, and menopausal status explained around 15% of variance in level of 8-OHdG. No association between reproductive effort characteristics and oxidative damage was found for postmenopausal women.

CONCLUSIONS: We found no evidence of a trade-off between somatic maintenance as measured by 8-OHdG and reproductive effort in women from this American population. On the contrary, higher gravidity and parity in premenopausal women was associated with lower damage to cellular DNA caused by oxidative stress. These results highlight the importance of population variation and environmental conditions when testing the occurrence of life-history trade-offs.

12:00pm	**2B-3**	Koepke, N	The obstetrical dilemma – evidence from historical Swiss data

The obstetrical dilemma – evidence from historical Swiss data

Obstructed labour is a leading cause of maternal and neonatal death and morbidity. It mainly results from a misfit between fetal head size and maternal pelvis. Traditionally attributed to a trade-off between selection for large-brained neonates and a biomechanically efficient, narrow pelvis for bipedal locomotion, this obstetrical dilemma has recently been questioned in various ways. One alternative hypothesis is the ecological model. It posits that cephalo-pelvic disproportions might only have exacerbated relatively recently, when maternal stature and pelvic dimensions decreased as a result of more insecure food availability. Thus, rather than long-term evolutionary processes affecting the risk of cephalo-pelvic disproportion, short-term intergenerational effects might be most critical.

Here, we analyse a data set of c.3000 singleton births in adult mothers from Switzerland to better understand the multifaceted aspects of interrelated maternal and offspring growth patterns. The data were compiled from the archives of the maternal hospital in Basel, Switzerland, that recorded head circumference, length and weight of the newborn, type of head presentation and position, birth complications, parity, as well as maternal stature, external pelvic dimensions and information on the socio-economic strata of both parents, among others. We focus on the birth cohorts between 1896 and 1945. This allows us to analyse the effects of the different crises during the first half of the 20th century and to consider the potential mediating impact of medical achievements on the birth outcome. We examine two major short-term factors that affect the offspring's body growth and potentially intensify the obstetrical dilemma: (a) direct effects such as environmental circumstances during the fetal development determined by current living conditions of the expectant mother, and (b) indirect effects, i.e., the living conditions during the growth period until adulthood of the expectant mother that are crucial for maternal height and pelvic dimensions and thus set the basic frame for pregnancy and birth outcome. These dynamics during the skeletal growth period of the future mothers complexly interact with the offspring's size and thus impact the obstetrical dilemma.

Particularly, our data allow examining the issue of short maternal stature that has variously found to be related to difficult delivery outcome although it is disputed to which extent maternal height is actually associated with pelvic dimensions and birth difficulties. We also discuss whether maternal body frame affects the overall growth of the fetus per se, or only restricts sub-measures of perinatal size due to a lower plasticity of newborn head circumference. Thus, these large historical data sets are fundamental for understanding the constraints of maternal pelvic dimensions on fetal growth and perinatal outcome on the one hand, and the potential buffering in newborn head circumference on the other hand.

12:15pm	**2B-4**	Ryan, C	Genome-wide DNA-methylation varies with reproductive status and parity and supports costs of reproduction in a cohort of young Filipino women

Genome-wide DNA-methylation varies with reproductive status and parity and supports costs of reproduction in a cohort of young Filipino women

Background: Evolutionary theory predicts that reproduction entails costs that detract from somatic maintenance, accelerating biological aging. Despite evidence for costs of reproduction (CoR) in human and non-human animals, little is known about the mechanisms through which such costs are expected to accrue. Human pregnancy involves extensive hormonal, metabolic, and immunological shifts, which are likely integral to any long-term impacts on somatic maintenance and senescence. Recently, we reported a positive relationship between parity and two separate measures of cellular aging - shortened telomere length and accelerated 'epigenetic age' – in our cohort study in the Philippines.

Methods: Here, we build upon these findings by exploring genome-wide DNA-methylation (DNAm) among 394 young (20-22 years old) women in four categories of reproductive status: nulliparous, pregnant, breastfeeding, and parous (but not reproductive). Among parous women we also consider relationships with parity. We use data from the Cebu Longitudinal Health and Nutrition Survey, a 35-year longitudinal dataset with complete reproductive histories, as well as extensive social, genetic, and phenotypic measures. DNAm was measured using a subset of 110,631 variable sites from the Infinium Human Methylation 450k Beadchip array. Genome-wide DNAm association comparisons of reproductive status were combined with measures of age, socioeconomic factors, and genetic variation, and followed by gene set enrichment using biological processes from gene ontology (GO).

Results: After false discovery correction, 769 cytosine-guanine dyads (CpGs) were differentially methylated among pregnant compared to nulliparous women. The majority of these (730) were down- or hypo-methylated. Differences were enriched in pathways associated with T cell activation, and our data support a shift from acquired to innate immunity during pregnancy. In contrast, breastfeeding women exhibited a greater number (1087) of differentially methylated CpGs compared to nulliparous women, the majority of which (727) were hypermethylated. Most differences in DNAm between nulliparous and currently reproductive women were no longer present in parous (but not currently reproductive) women, suggesting that many of the differences in DNAm present during pregnancy and breastfeeding are transient, and return to pre-reproductive levels. However, there were similarities in DNAm between currently breastfeeding women and women who had already weaned their child, suggesting that some changes in DNAm during breastfeeding are persistent. Consistent with this observation, we also found evidence for cumulative changes in DNAm and cell composition with parity.

Discussion: Although cross-sectional, our results point to a role of DNAm and immunosenescence in the CoR among women, and suggest that these costs may manifest, in part, through changes in immune regulation that accumulate over multiple pregnancies. We consider these findings in light of epidemiological patterns of cardiovascular and autoimmune disease, and theorize about the physiological and ecological contexts that may moderate these costs.

SESSION 3A (THU, AUG 2, 3:45 PM): CANCER—*Chair: Amy Boddy* (Location: Ballroom A)

3:45pm	**3A-1**	Buetow, K	Networks of interacting germline and somatic variants drive tumor etiology, progression, and response

Networks of interacting germline and somatic variants drive tumor etiology, progression, and response

Evolutionary processes altering molecular networks drive susceptibility, development, and outcome of cancer. These operate through inherited and de novo variation in both the host and tumor. Using novel biologic network model-based analytic tools developed by our group, we have observed interactions between pathways associated with susceptibility and somatic changes. In studies of human hepatocellular carcinoma (HCC) – the 2nd leading cause of global cancer mortality and increasing incidence in the developed and developing world, we have been able to identify pathways associated with germline susceptibility. Pathways associated with immune processes (Antigen Presentation and Processing, TCR signaling, Interferon gamma Signaling), growth control (PI3K-Akt Signaling, MAPK-Signaling), Calcium Signaling, and Lipid Metabolism are observed. Interestingly, these pathways connect to form a single, integrated master network. Our analysis of variation in the transcriptome of normal liver, uninvolved liver from cancer patients, and HCC tumors identifies pathways involved in oncogenesis. The susceptibility pathways significantly non-randomly overlap with oncogenesis pathways. More provocatively, the observed master susceptibility network is commonly a target of somatic mutation in HCC tumors. Examination of the observed non-synonymous acquired somatic DNA variants of genes in the master susceptibility pathway shows significant over-representation.

4:00pm	**3A-2**	Hamilton, P	Cancer stem cell characteristics and immune surveillance across cancers

Cancer stem cell characteristics and immune surveillance across cancers

Evolution underpins the genesis and progression of cancer. The pressures that drive this evolution within the tumor microenvironment (TME) remain poorly understood, but it is increasingly clear that genetic and phenotypic heterogeneity in cancers and selection by the host immune system are important in sculpting the TME. Although the stem cell-like characteristics of cancers are known to be important to patient outcome and can affect anti-cancer immunity in some contexts, their importance across cancers is unclear. Here, we report pervasive negative associations between cancer stemness and anti-tumor immunity across >8000 cancers in The Cancer Genome Atlas, suggesting stemness is an important determinant of anti-tumor immunity. Corroborating this, high-stemness cancer cell lines suppress immune signaling pathways, demonstrating cell-intrinsic immune escape mechanisms associated with stemness. Moreover, high-stemness cancers show increased intratumoral heterogeneity, implicating stemness in the evolution of clonally-diverse solid cancers. Investigating the relationship between stemness, immunity, and intratumoral heterogeneity in a cohort of high-grade ovarian cancer patients for which we have multi-region genome sequencing, gene expression, and IHC-based immune cell profiling, we find that stemness associates with distinct patterns of suppressed immune cell infiltration and higher intratumoral heterogeneity within and across patients. Collectively, these results reveal that the convergence of cancers on a high-stemness phenotype has important intersections with the immunology, clonal heterogeneity, and evolvability of cancer.

4:15pm	**3A-3**	Organ, C	Analyzing Cellular Traits with Developmental Phylogenetics

Analyzing Cellular Traits with Developmental Phylogenetics

The trillions of cells in the human body are developmental descendants from a single fertilized egg. The tissues that arise during this process share many traits in common, from density to gene expression. The degree to which cellular traits are similar often depends on how much developmental history the cells share. That is, tissue-level data are not statistically independent owing to their shared developmental history. Independence is a critical assumption for common statistical analyses. To date, studies of tissue-level traits have not accounted for developmental non-independence, which is a major unidentified problem in the field. There are, however, richly developed tools for studying the evolution of traits among species called phylogenetic comparative methods. Here we develop a phylogenetic developmental tree based on human fate map data. We apply phylogenetic comparative methods to assess how much tissue-level trait data vary according to their developmental history. Specifically, we model the interplay of lifetime cancer risk with stem cell division rate while accounting for developmental non-independence. We show that some traits, like stem cell division rate, are highly structured by their developmental history. In such cases developmental history must be accounted for, otherwise, spurious conclusions may be reached. This approach could be widely used in fields ranging from oncology to developmental biology.

SESSION 3B (THU, AUG 2, 3:45 PM): REGULATION & HOMEOSTASIS—*Chair: James Morgan* (Location: Ballroom B/C)

3:45pm	**3B-1**	Perlman, R	An Evolutionary View of Physiological Control Mechanisms

An Evolutionary View of Physiological Control Mechanism

The maintenance of homeostasis and the response to both endogenous and exogenous stresses are important parts of our evolved life history strategies. Using examples from the regulation body temperature, blood pressure, and blood glucose, I will consider how natural selection has shaped our physiological control mechanisms to maintain homeostasis in the face of challenges such as starvation, trauma, and disease. Discussions of physiological regulatory mechanisms have largely focused on negative feedback mechanisms, mechanisms that sense deviations of a regulated variable from a range around a "set point" and act to restore that variable toward its desired value. Negative feedback mechanisms are conceptually simple and are presumably easy to evolve; in any event, we do have a wealth of them. But negative feedback mechanisms have limitations as well as strengths. They don't become active until a perturbation has already occurred, they take time to counteract that perturbation, and, most importantly, negative feedback mechanisms cannot completely counteract deviations. The time course of a negative feedback response depends on the physiological and biochemical mechanisms it involves: neural or endocrine, and changes in the activity of pre-existing proteins, synthesis of new proteins, or the production of new cells and cellular structures. The degree to which negative feedback mechanisms can correct a deviation from a set point is a function of the gain of the feedback loop. High gain provides a greater corrective response to a disturbance, but gain is limited by energetic costs and the risk of producing oscillations. Feedforward control mechanisms complement negative feedback processes; feedforward mechanisms act in anticipation of stresses and so prevent deviations from set point ranges. Feedforward mechanisms are especially important in response to eating and to physical activity. But these mechanisms may not correctly predict the magnitude of the pending disturbance and so may cause regulated variables to overshoot their targets. Both negative feedback and feedforward mechanisms may involve changes in behavior that work together with physiological changes. A narrow Cartesian view of the body as a machine that is separate from the mind has caused us to minimize or neglect the role of behavior, and of our active involvement with our environments, in homeostasis. Probably because they are defended by a host of regulatory mechanisms, set points tend to be well buffered during evolution. With a few exceptions such as the unusually high blood pressure of giraffes, body temperature, blood pressure, and blood glucose are remarkably constant among placental mammals. Set points are maintained at levels that provide safety factors, such that relatively large deviations can be tolerated without untoward consequences. Moreover, set points and the strengths of homeostatic mechanisms are not necessarily fixed but may themselves adapt. Because different control mechanisms have different strengths and weaknesses, we have evolved a myriad of complementary and overlapping mechanisms, both negative feedback and feedforward, which differ in their sensitivity to perturbations, speed of response, gain, and the plasticity of their set points.

4:00pm	**3B-2**	Nijhout, F	Homeostasis, cryptic genetic variation and predisposition to disease

Homeostasis, cryptic genetic variation and predisposition to disease

Many biological systems, from gene networks to metabolism and whole body physiology, are governed by homeostatic mechanisms that keep variation of critical functions within a fairly narrow range. Because homeostatic mechanisms buffer traits against environmental and genetic variation, they allow the accumulation of cryptic genetic variation. Homeostatic mechanisms are never perfect and can be destabilized by mutations in genes that alter the kinetics of the underlying mechanism, and also by environmental factors that push the system out of the homeostatic regime. When this happens, the effects of deleterious genes are no longer buffered and the system can move to a disease state. Homeostatic mechanisms therefore enhance fitness, and continue to evolve. Understanding how these mechanisms function can help us to understand the nature of predisposition to disease, and helps explain why so many deleterious genes persist in human populations, often at high frequencies.

4:15pm	**3B-3**	LeGrand, E	Immune Cell Metabolism: Examining Natural Selection's Design

Immune Cell Metabolism: Examining Natural Selection's Design

Immune cell metabolism as it relates to function has recently gained prominence. A paradigm in the immunometabolism field is that immune cells are optimized by natural selection for metabolic efficiency. Nevertheless, it remains unclear what the selective advantage is for the preferential use of energetically inefficient aerobic glycolysis by effector immune cells compared with oxidative phosphorylation. Since tumor cells and many infectious pathogens also rely on glycolysis and consequently have high glucose needs, there has been concern that competition for glucose and other nutrients may impair immune cell functionality. A related paradigm is that immune cells' high uptake of glucose and other nutrients is required to supply their substantial nutrient needs in host defense.

In contrast to these paradigms, we propose that effector immune cell function evolved to efficiently control potential pathogens rather than to optimize metabolic efficiency. Additionally we do not accept that high uptake of nutrients necessarily reflects the nutritional needs of effector immune cells. Rather, we propose that, in addition to their typically accepted functions, effector immune cells function to deprive pathogens (including tumor cells) of oxygen, glucose, and other nutrients while simultaneously using the increased metabolic waste (reactive oxygen species, lactic acid, heat) as additional stressors to harm the pathogens.

If we were to design an immune system where effector cells battling pathogens routinely find themselves in a hostile local environment, we would include the following features: 1) immune cells would arrive prepared to fight and would bring along needed nutrients where possible, and 2) they would be adapted for taking up nutrients despite scarcity. Additionally, 3) immune cells would be able to take in more nutrients than they actually need, so as to deprive the pathogens of nutrients. Even better, 4) excess nutrients would be converted to harmful waste products, so as to further harm the pathogens. Since effector immune cells must work in stressful locations that they helped create, 5) we would want them to be most effective in conditions that are slightly stressful (e.g., slight hypoxia, slight acidity, and slight heat). It should be noted that growth and synthesis are processes particularly vulnerable to stress, and that pathogens generally must replicate at the inflammatory site to be pathogenic. Given this universal vulnerability of growth and synthesis to stress, 6) we would have immune cells proliferate and develop at low-stress sites distant from infected sites (e.g., bone marrow, lymph nodes, and spleen). Furthermore, 7) we would design means of not only of preventing the spread of pathogens, but of containing the localized stressors with the pathogens. Finally, 8) we would seek to support the localized stress on the pathogens with additional systemic measures. Not surprisingly, we find each of these features has evolved in real immune systems. We propose that what appears to be inefficient and wasteful metabolism of effector immune cells is intentionally wasteful, and that this creation of non-specific stress to preferentially harm the pathogens is an evolved immune function.

SESSION 4A (FRI, AUG 3, 10:15 AM): MICROBIOME—*Chair: Kevin Boyd* (Location: Ballroom A)

10:15am	**4A-1**	Ozga, A	Dental calculus microbiome variation across foraging-farming and metropolitan populations

Dental calculus microbiome variation across foraging-farming and metropolitan populations

In recent years, research in the field of microbiomes has flourished; with studies focusing on its diversity in humans and its impacts on human health. An abundance of this research has been devoted specifically to the gut microbiome, which is globally diverse and dependent on host geography and diet. The microbiome of the human oral cavity is much less studied despite the fact that it is considered just as, if not more diverse than the human gut. Oral microbiota in humans have been directly correlated with health states including cancer, irritable bowel disorder, and cardiovascular disease (CVD). However, most of this research focuses on saliva, rather than dental calculus (calcified plaque) which hardens during the life of the host and provides a long-term profile of bacterial occupation within the mouth. There has yet to be a baseline established for what the calculus microbiome in both healthy and diseased human mouths. Studies of human plaque found links between certain bacterial species and periodontal disease as measured by the presence or extent of caries (cavities) and tooth loss. Previous microbiome research with the Tsimane found significant differences in the taxonomic profiles of the mothers that aided in food premastication for their infant and the child themselves, but unfortunately did not find any significant correlations between pathogen types and tooth loss/caries. This preliminary research utilizes 25 dental calculus from the Tsimane Health and Life History project, which is focused on the long-term health, growth, aging of these lowland Bolivian hunter horticulturalists. Roughly half of these individuals investigated will fall into the poor oral health range (as designated by tooth loss and caries) while the rest will fall into the fair oral health spectrum. These samples will be compared to calculus from 25 metropolitan individuals collected from the Midwestern College of Dental Medicine in Arizona. After phenol chloroform extractions, a portion of the 16S rRNA gene (variable region 4 of the ribosomal RNA subunit) will be PCR amplified and sequenced on an Illumina MiSeq. The results will be analyzed using QIIME, which allows for taxonomic OTU picking, phyla and genera breakdowns, and R which generates PCA plots in order to assess between group differences and create comparisons to larger 16S rRNA datasets. In particular, this research seeks to: a) establish a baseline calculus microbiome in living populations and b) assess the associations between calculus buildup and caries/tooth loss in a population with high rates of periodontal disease, but low rates of atherosclerosis. We hope these results will act as pilot data for a larger study investigating detailed oral health states between indigenous and metropolitan communities across the Americas.

10:30am	**4A-2**	Ojong, J	Iron-driven host-microbiota coadaptation: an influence factor in Mycobacterium tuberculosis infection?

Iron-driven host-microbiota coadaptation: an influence factor in Mycobacterium tuberculosis infection?

Iron is an indispensable micronutrient for growth, differentiation and survival of both, the eukaryotic host and bacteria, pathogenic and commensal ones. We hypothesize that iron availability can shape host-microbiota coevolution, which in turn, can modulate the susceptibility to infection by Mycobacterium tuberculosis (Mtb). The iron regulatory proteins, IRP1 and IRP2 determine cellular iron availability through post transcriptional modulation of iron transport and iron storage protein expression.

To investigate the influence of iron availability on Mtb infection, wildtype (wt), Irp1-/- and Irp2-/- mice were infected via aerosol route with a virulent (H37Rv) strain of Mtb at day 0. Colony forming unit (CFU) assays revealed increased mycobacterial burden in the lungs and spleens of Irp2-/- mice in comparism to wt mice. Similarly, Irp2-/- bone marrow-derived macrophages (BMMOs) were more permissive to Mtb infection in vitro than wt and Irp1-/- BMMOs.

Prussian blue staining revealed cell specific iron overload in alveolar macrophages (aMO) of both, non-infected and Mtb infected Irp2-/- mice at day 63 post infection (p.i.). However, iron deposits were observed in aMOs of all mouse strains studied, wt, Irp1-/-, and Irp2-/- mice at days 28 and 63 p.i. Prussian blue positive iron overloaded Kupffer cells in Irp2-/- livers were observed at day 63 p.i., in perivascular infiltrates around the central vein and sinusoids, as opposed to little-to-no iron accumulation in Kupffer cells of wt and Irp1-/- mice.

The influence of iron availability on commensal communities is currently studied by 16S rRNA analysis from lung-, trachea-, and gut tissue of Irp1-/- and Irp2-/- mice compared to their respective wt littermates. These data will provide the basis for microbial community ecological and interaction analysis between host control of iron availability, microbiota, and Mtb infection.

Following the concept of evolutionary medicine, we aim to understand how iron can drive host-microbiota coadaptation and how this might influence susceptibility to Mtb infection.

10:45am	**4A-3**	Horvath, J	Investigating recovery of the skin microbiota after surgery

Investigating recovery of the skin microbiota after surgery

Skin microbes, microscopic organisms including bacteria, Archaea, and fungi, contribute to the overall health and wellness of animals, and have been shown to influence the wound healing process. It is not yet understood how the microbes play a role in wound healing, but a better understanding would allow potential new treatments to emerge using microbes themselves, and/or microbial products. We are sampling microbes from the skin of dogs undergoing routine soft tissue or orthopedic surgery to investigate how skin microbe composition changes after surgery to determine which microbes are important to this process. Skin bacterial samples were analyzed from five dogs across 11 time points spanning six weeks. Dogs were swabbed at both a surgical site (abdominal) and a control site (stifle/knee) to use each dog as its own control for bacterial composition. Bacterial DNA was isolated and amplified using the V4 region of the 16S rRNA with high throughput sequencing conducted on an Illumina MiSeq. Data were analyzed with Illumina's Basespace and QIIME, and visualized with Calypso. At the Phylum level, the bacterial composition of the dog's in this study is similar what has been found in previous human and dog microbiome studies, identifying taxa from Firmicutes, Proteobacteria, Actinobacteria, and Bacteroidetes. The bacterial diversity (based on Shannon Index) is similar between control and surgical site samples, but control samples (knee) have approximately twice the richness across the six weeks of the study. Additional sample processing is underway and will provide a larger sample size to assess compositional changes across all dogs in the study. Our study will investigate the ecology and evolution of microbiota community structure to identify if and how the community composition impacts wound healing. The findings will be directly relevant to improving veterinary health through understanding recovery of wounds after surgery, which is also very applicable to human health.

11:00am	**4A-4**	Brown, D G	Gut symbionts influence CNS immunity during a virally induced demyelinating disease

Gut symbionts influence CNS immunity during a virally induced demyelinating disease

Multiple sclerosis (MS) is an increasingly prevalent autoimmune disease characterized by the destruction of the myelin sheaths that promote signal conduction in neuronal axons. While the etiology of MS is unknown, central nervous system (CNS) viral infection and increased hygiene are two factors thought to increase susceptibility. Using a murine hepatitis virus model of MS, we hypothesized that colonization with symbiotic microbes could prime the immune system to better limit CNS viral infections, decreasing subsequent CNS pathologies. Germ-free (GF) and lifelong antibiotic treated (bABX) mice were less able to clear virus and developed a worsened demyelinating disease when compared to specific pathogen free (SPF) controls. We found that microglia (CNS-resident immune cells) from GF mice have decreased ability to present antigen to T cells during infection, resulting in less viral-specific T cells. Notably, feeding GF mice TLR2 and TLR4 agonists decreased morbidity. Furthermore, microglia from TLR4-/- mice displayed lower levels of MHCII and have a worsened response in this model. These data indicate that symbiotic microbes are beneficial in a virally-induced model of MS and suggest that microbial products benefit the host by priming the immune system to respond to viral triggers of autoimmunity. The protective role of the microbiota in this model of autoimmune MS is consistent with a central prediction of the hygiene hypothesis.

SESSION 4B (FRI, AUG 3, 10:15 AM): EV MED EDUCATION—*Chair: Djuke Veldhuis* (Location: Ballroom B/C)

10:15am	**4B-1**	Anderson, D	Development and field testing of a health sciences version of the Conceptual Inventory of Natural Selection

Development and field testing of a health sciences version of the Conceptual Inventory of Natural Selection

Taking an evolutionary perspective towards human health requires that students understand natural selection as a major mechanism of evolutionary change. However, some college programs require these students to take Anatomy & Physiology to fulfill life science requirements rather than a general biology course, so they develop little to no understanding of evolutionary theory. Even if they do take biology, they may be unlikely to transfer that knowledge to understanding human biology. With the increase in knowledge of how natural selection has impacted human health, as well as how important it is in understanding issues such as the development of antibiotic resistance, it is essential that young nurses, doctors, physical therapists, and other health professionals understand this topic well.

In order to study this issue, a well-designed, easy-to-use assessment tool valid for use with college students is needed so that college students' understanding of natural selection can be measured. This information can then be used to develop and test classroom interventions to improve understanding.

The 20-tiem, multiple-choice Conceptual Inventory of Natural Selection (CINS) was published in 2002 as a research and teaching tool for assessing college students' understanding of natural selection (Anderson, Fisher & Norman, 2002). The CINS requires students to apply their understanding to three extensively-researched examples of natural selection. Each question includes one correct answer and three incorrect answers with embedded alternative conceptions commonly held by students. The questions address the necessary ecological, genetic, and differential survival/reproduction concepts. A major revision of the CINS were completed in 2013 (Evans & Anderson, 2013) to create an improved high school/college version, as well as a version validated for use with middle school students. The validation process included student interviews and extensive classroom testing.

The purpose of the current study was to develop and field test a version of the CINS for early-stage health science students (nursing, kinesiology, pre-med, etc.) by changing the question contexts from lizards, guppies, and finches to examples of medical importance such as antibiotic resistant bacteria and medically-related human traits shaped by natural selection. While the CINS cannot be used to assess detailed and in depth understanding of how evolutionary biology works (that will be up to other researchers), the Health Science version of the CINS should be a useful tool for to assess the basics. During the presentation, an overview of the development of the instrument will be provided, then sample questions will be discussed, and various ways to use the CINS in a classroom setting will be described.

Anderson, D.L., Fisher, K.M., & Norman, G.J. (2002). Development and evaluation of the Conceptual Inventory of Natural Selection. Journal of Research in Science Teaching, 39, 953-978.
Evans, P. & Anderson, D.L. (April 2013). The Conceptual Inventory of Natural Selection a decade later: Development and pilot testing of a middle school version leads to a revised college/high school version. Paper presented at annual meeting of the National Association for Research in Science Teaching (NARST) 2013, Rio Grande, Puerto Rico, April 6-9, 2013

10:30am	**4B-2**	Nesse, R	EvMedEd

EvMedEd

Courses on evolutionary medicine are available now at most major research universities, thanks to growing interest in the field supported by several new textbooks, a new journal, and ISEMPH. However, few resources are available for adding evolutionary medicine content to other courses, and fewer yet are available to serve the needs of health professionals. That is not quite accurate; vast resources are available online, but there has been no way to find them, to determine which ones are authoritative and valuable, and to match specific resources to the needs of learners in different settings.

To address this need, EvMedEd provides an open access searchable, sortable, curated database of online teaching and learning resources for evolutionary medicine. It includes links to books, articles, videos, podcasts, websites, and syllabuses. In addition, it provides suggested learning objectives, lesson plans, teaching modules, and guides to resources on specific topics.

EvMedEd now includes over 1000 resources, guides to a handful of topics, and several lesson plans. We are looking for ways to encourage contributions from the evolution and medicine community that will expand the list of resources, and augment and improve the provided pedagogical materials. The objective is for any teacher or learner to be able to quickly find well-organized up-to-date guides to authoritative and interesting content on all relevant topics, ready to insert into courses at any level. In particular, EvMedEd aims to provide brief ready-to-go modules that can be added to curricula for health professionals. The editors and development team hope EvMedEd will also encourage creation of more new online open access resources that can be organized into free online courses at several levels.

10:45am	**4B-3**	Grunspan, D	The State of Evolutionary Medicine in Undergraduate Education at American Universities

The State of Evolutionary Medicine in Undergraduate Education at American Universities

Evolutionary medicine is a growing field with relevance for medical professionals. Increasing its presence in undergraduate education is an important step for creating future medical professionals who are able to apply evolutionary thinking to medicine. As part of a larger goal to increase the presence of evolutionary medicine in undergraduate education, we examined the current state of evolutionary medicine in undergraduate education.

To understand the current state of evolutionary medicine in undergraduate education, we searched university course catalogs for courses that included some aspect of evolutionary applications to health and disease. We identified courses that either were entirely focused on evolutionary medicine, included evolutionary medicine as a sub-topic of the course, or focused on a specific application of evolution to health or disease. We then sent a survey to instructors of those courses entirely focused on evolutionary medicine to better understand what is being taught, why instructors started teaching evolutionary medicine, and what challenges they face in teaching.

In total, 89 evolutionary medicine courses were identified, almost exclusively at research intensive universities. Of these courses, 70 instructors were identified and recruited to take a survey about their class experiences – 77% of these instructors responded. We report on the findings from this survey, including the learning goals, difficulties, and approaches to teaching evolutionary medicine.

11:00am	**4B-4**	Burt, N	The Unwilling Student: Teaching Evolutionary Medicine to the Museum Public

The Unwilling Student: Teaching Evolutionary Medicine to the Museum Public

Museums have a unique relationship with the public, who are both patrons paying for a desired experience as well as learners seeking expert instruction. The relationship between curator and museum visitor is more complicated than the traditional student/teacher interaction for the following reasons 1) visitors can be any age from children to retirees, 2) the relationship is short in duration, often a hour or less, and 3) the visitor may leave at any time or decide not to engage with no repercussions. Given the specifics of this unique relationship, how can we hope to educate, challenge, or even cause a life-changing shift in the visitor newly confronted with complex scientific ideas such as evolutionary medicine or bioethics?

I approach the subject as a Curator of Human Health and Evolutionary Medicine, who is engaging with the public around my own research in biological anthropology as well as the wider field of human health and variation. My encounters with the public range from positive and productive to hostile and unfruitful. The public perception of the evolution and the associated bioethics can be a massive hurdle in engagement and education. The aim of this presentation is to discuss what has and has not worked for public engagement around human health and evolution at the Cleveland Museum of Natural History. I will be comparing different examples from my own work teaching drop-in educational events, formal classes, invited presentations for lay audiences, and simply walking past people in the exhibit halls on the way to coffee. This presentation and discussion is an initial step toward pedagogy of evolutionary medicine teaching in museums.

SESSION 5A (FRI, AUG 3, 11:15 AM): RESISTANCE EVOLUTION—*Chair: James Gurney* (Location: Ballroom A)

11:15am	**5A-1**	Barlow, M	Growth rate assays reveal fitness consequences of β-lactamases

Growth rate assays reveal fitness consequences of β-lactamases

Clinical resistance determination is critical to monitor the spread of antibiotic resistance, but is limited by its sensitivity. Here we show that the results of growth rate assays correlate well with clinical resistance determination, while providing the sensitivity required for direct input into mathematical models. Additionally, by measuring the growth rates of sequenced clinical isolates obtained from Dignity Health's Mercy Medical Center, we detect the fitness effects of individual resistance genes on bacteria as they are exposed to different antibiotics. Specifically, we report two novel findings: (1) that the CTX-M-15 gene increases fitness in the presence of the three cephalosporins; (2) that TEM-1 decreased fitness in the presence of these three cephalosporins. The OXA-1 gene had no effect. These subtle effects on fitness could explain the increasing presence of CTX-M-15 and OXA-1 in ESBL clinical isolates across the world.

11:30am	**5A-2**	Paaijmans, K	Turning back the clock: Why we should stop using insecticides on bednets to fight malaria

Turning back the clock: Why we should stop using insecticides on bednets to fight malaria

Long-lasting insecticidal nets (LLINs) remain a cornerstone of malaria control and elimination programs and have been shown to successfully reduce malaria transmission over the past two decades. However, mosquito resistance to pyrethroids (currently the only chemical class approved for use in/on nets) is now widespread throughout Africa and is threatening malaria control efforts. As such, the insecticides on bednets may no longer significantly contribute to the elimination goals, and may actually harm other vector control tools that use the same chemistries. Here we propose a rather controversial approach: Taking the insecticide out of the long lasting net to manage insecticide resistance.

11:45am	**5A-3**	Thomas, M	Iron-related fitness epistasis is antagonistic to the evolution of silver resistance in Escherichia coli

Iron-related fitness epistasis is antagonistic to the evolution of silver resistance in Escherichia coli

Fitness epistasis (or genetic background effect) can have powerful influences on the evolutionary trajectory of populations. Here we examine the influence of a prior resistance to ionic iron (Fe2+/Fe3+) on the capacity for E. coli to evolve silver resistance. Five replicate populations of Fe2+-resistant and Fe3+-resistant E. coli were cultured for > 80 days in 20 micrograms/L of ionic silver. This low concentration was chosen because both Fe2+/Fe3+ showed diminished resistance to Ag+ relative to both Ag+-selected and controls (grown in standard DMB medium w/o Fe or Ag). After 80 days of selection in Ag+, no increase in Ag+-resistance was observed in either the AgFe2+ (silver selection w/Fe2+ background) or AgFe3+ (silver selection w/Fe3+ background) replicates. Furthermore, the observed correlated resistances to traditional antibiotics (e.g. ampicillin, rifampicin) as well as to gallium, displayed in the iron-resistant ancestors was lost. Whole genome sequencing of the AgFe2+- and AgFe3+-selected replicates demonstrated that the iron/metal resistant mutations observed in the Fe2+/Fe3+-resistant ancestors (e.g. fecA, rho, fur, murC, dnaK, tolC, and nusA) were all lost. Also no anti-silver mutations were observed (e.g. cusS, ompR) in the AgFe replicates. These results suggest that the AgFe replicates were undergoing reverse selection relative to Fe2+/Fe3+-resistance, but could not be cultured at concentrations of Ag+ required for selection to drive Ag+-resistance. Early replicates cultured at concentrations (~ 75—100 micrograms/L) that allowed rapid evolution of Ag+ resistance consistently went extinct. We suggest that this is evidence that Fe2+/Fe3+ genetic background is antagonistic to the evolution of silver resistance.

12:00pm	**5A-4**	Huijben, S	The evolution of drug resistance in different immunological contexts

The evolution of drug resistance in different immunological contexts

The rise and spread of drug resistant malaria parasites is one of the major challenges for malaria control, and indeed will be a huge obstacle for malaria eradication. Successful drug treatment is dependent on both the killing effect of the drug and the killing effect of the immune system. In addition, the immune system is known to play an important role in within-host competition between parasites, which in turn has been shown to be a key part of resistance evolution. Moreover, there are the historical observations that resistance initially occurs in area of low transmission intensity and hence low level of antimalarial immunity. It is thus hypothesized that the immune system is a critical factor in the emergence and spread of drug resistant mutants. Using data of clinical trial on IPTp use in pregnant women in Benin, Gabon, Kenya and Mozambique, we present the occurrence of resistant mutants in a variety of immune contexts, from HIV infections to breadth of immune response by antibody levels, and show that resistant mutants are indeed more frequently observed in low immune environments. We subsequently hypothesize how vaccination could lead to an increased cost of resistance and be used as a novel tool for drug resistance management.

SESSION 5B (FRI, AUG 3, 11:15 AM): METABOLISM—*Chair: Benjamin Trumble* (Location: Ballroom B/C)

11:15am	**5B-1**	Pontzer, H	Why is Exercise Essential? Constrained Energy Expenditure and the Mechanisms of Metabolic Health

Why is Exercise Essential? Constrained Energy Expenditure and the Mechanisms of Metabolic Health

Metabolic studies over the past decade, across a broad range of lifestyles and species, have challenged the traditional view in public health and evolutionary biology that daily energy expenditure increases in a linear, dose-dependent manner with daily physical activity. Instead, daily energy expenditure in humans and other animals appears to be maintained within a narrow, evolved, physiological range, with the body adapting to variation in activity to keep expenditure in check. This Constrained Model of energy expenditure holds broad implications for understanding metabolic health and ecological energetics. Here, I review the evidence of metabolic constraint and adaptation across human populations with different daily physical activity. I then I test one prediction of the Constrained Model, that increased physical activity will decrease energy investment in other physiological tasks. Recent work in humans has demonstrated a wide range of potential signaling mechanisms through which musculoskeletal activity might downregulate activity in other systems. I reviewed the published literature on metabolic response to long-term (e.g., months or years) endurance exercise in recreational and elite athletes, focusing on 1) global mediators of metabolic rate (thyroid hormones, norepinephrine, cortisol), 2) reproductive system activity (estrogen, testosterone), and maintenance activity (cytokines). As predicted by the Constrained Model, endurance exercise is associated with decreased hormone levels compared to age- and sex-matched non-exercising adults. Thyroid and norepinephrine levels decrease with prolonged exercise, and the effect is more pronounced with caloric restriction. Cortisol levels increase during and immediately after exercise, but cortisol awakening response is diminished in endurance athletes. Similarly, testosterone levels increase during exercise, but the effect is blunted in endurance athletes. Further, resting levels of testosterone (males) and estrogen (females) are lower in endurance athletes, and occasionally associated with clinical hypogonadism. Cytokine levels increase immediately after exercise, but long-term endurance exercise is associated with lower inflammatory cytokines and lymphopenia. I discuss life-history and health implications of these trade-offs between physical activity, reproduction, and maintenance. High levels of daily physical activity such as those that characterize hunter-gatherer and other small-scale societies may have suppressive effects on growth, reproductive investment, and immune response, particularly if food availability is limited. Conversely, the downregulation reproductive and immune activity (inflammation) may be and important and underappreciated mechanism underlying the well-established health benefits of exercise and daily physical activity in developed populations.

11:30am	**5B-2**	Corbett, S	The Relative Immunity of Europids to Type 2 Diabetes Modelling the Fitness of Insulin Sensitivity across the Demographic and Nutritional Transition

The Relative Immunity of Europids to Type 2 Diabetes Modelling the Fitness of Insulin Sensitivity across the Demographic and Nutritional Transition

The lower incidence and prevalence of Type 2 diabetes in people of European descent, or Europids, compared to almost all other populations, is a consistent finding in inter-ethnic comparisons of diabetes occurrence.

In 2003 Jared Diamond advanced the startling hypothesis that the cause was an epidemic of diabetes mortality in Europe in the eighteenth century which reduced the frequency of diabetes genes in the European population. This putative epidemic was alleged to have been driven by nutritional improvements accompanying the Industrial and Agricultural Revolutions, which occurred 2-300 years earlier in Europe than elsewhere.

Whilst we agree with critics of this hypothesis that post-reproductive mortality from diabetes is unlikely to effect rapid evolutionary change, we believe that this hypothesis deserves closer examination for three reasons. Firstly, the changes in fertility, mortality, nutrition and lifespan linked to the Agricultural and Industrial revolutions are without precedent in the entire history of our species and have the potential to drive rapid evolutionary change. Secondly insulin resistance and sensitivity, viewed as a continuous metabolic trait, has many of the characteristics which make it a good candidate for rapid evolution in the last 300 years – high levels of genetic variation, a genetic architecture involving many genes of small effect and most importantly, the trait impacts directly on on vital rates, particularly fertility. And thirdly the implications of this model are profound, because it suggests that the current global epidemic of diabetes may recede due to strong purifying selection against the diabetic phenotype.

We have modelled the differential effects of insulin sensitivity and resistance on three life history traits across the demographic transition in England and Wales between 1535 and 2013 - the duration of lactational amenorrhoea and intra-uterine foetal death and miscarriage in pre-industrial populations, and obesity related ovulatory infertility in contemporary populations. Using the Euler-Lotka equation we have modelled changes in fitness across this 300 year period, enabling an estimate of the intensity of purifying selection against an ancestral, insulin resistant phenotype. We conclude that reductions in gene frequency commensurate with observed differences in prevalence and incidence of Type 2 diabetes between Europid and non-Europid populations are plausible. The results suggest that the global epidemic of this condition may be ameliorated by rapid selection.

11:45am	**5B-3**	Nunez-De La Mora, A	Non-diabetic low fasting glucose levels in women and children living in poverty in a food insecure rural setting: a sign of silent hunger and an overlooked precursor of adverse metabolic syndrome risk?

Non-diabetic low fasting glucose levels in women and children living in poverty in a food insecure rural setting: a sign of silent hunger and an overlooked precursor of adverse metabolic syndrome risk?

Despite decades of social development policies at the federal and local level, over half the rural population in Mexico experience multi-dimensional poverty, and up to 44% suffer from any level of food insecurity. Furthermore, these rural communities (75% of which are small-scale farmers) are in the midst of an unprecedented nutritional, epidemiological and social transition as their traditional subsistence economies are eroded by a combination of ecological, demographic and socioeconomic factors, forcing its members to supplement their diets with market purchased foods bought with income from remittances and government cash-transfer programmes. Irregular and scant incomes result in suboptimal food choices and behavioural strategies with potential adverse consequences for growth, development and health. The nutritional and physiological consequences of food insecurity are poorly documented; however, there is evidence for associations between meal frequency consumption patterns and early metabolic syndrome risk. The aim of this study was to assess the relationship of food insecurity to fasting serum glucose levels and anthropometric indices in women and children from Ocotepec, an archetypal rural community in Veracruz, Eastern Mexico living in conditions of extreme poverty and food insecurity. Single fasting serum levels of glucose were measured in 56 parous women aged 20-74 years old, and 112 children of both sexes aged 2-18 years old. Anthropometric data (height, weight, mid upper-am circumference and waist-to-hip ratio (WHR) (in women only)) were obtained at time of collection and food security was assessed through various direct and indirect indicators. Preliminary results indicate a clear pattern of dual malnutrition with high prevalence of WHR > 0.85 (94.8%), overweight (36.2%) and obesity (46.5%) in women in all age groups and a high prevalence of mild (22.9%) and moderate (5.72%) stunting in children already evident by age 2 yrs. Low fasting plasma glucose levels (< 65 mg/dL adults; <60 children 3-15 yrs old) are prevalent in both, women (70.7%) and children (71.4%) independent of age and nutritional status. Quantitative and qualitative data on food intake, dietary diversity, daily eating patterns and perceived food security strongly suggest that a large proportion of individuals in Ocotepec do not have sufficient food to meet their basic daily nutritional needs. High prevalence of fasting non-diabetic hypoglycaemia, consistent with protracted periods of no or very low food intake, may be interpreted as a biological indicator of the silent hunger experienced by the study population. We take an evolutionary perspective to advance some hypotheses of how a chronic hypoglycemic state in early life may translate into adverse metabolic architectures and health in later life.

12:00pm	**5B-4**	Urlacher, S	Childhood energy expenditure in evolutionary medicine perspective: Direct measures of energy use among Amazonian forager-horticulturalists

Childhood energy expenditure in evolutionary medicine perspective: Direct measures of energy use among Amazonian forager-horticulturalists

The way in which organisms use energy (i.e., calories) is a fundamental aspect of phenotype that lies at the center of many evolutionary (e.g., life history theory) and epidemiological (e.g., nutritional transition) models for understanding variation in human health and fitness. Nonetheless, research directly measuring human free-living energy expenditure is scant. This shortcoming is most notable for small-scale populations characterized by socio-environmental conditions – including limited nutrition, high rates of infectious disease, and physically active lifestyles – that resemble those present throughout most of the history of our genus. No previous research has investigated direct measures of energy expenditure among children in such contexts, restricting understanding of energy use during a derived life stage that is unique to humans and is critical in establishing lifetime trajectories of cardiometabolic health. To address this issue, we measured total energy expenditure (TEE; via doubly labeled water urinary stable isotope analysis) and resting energy expenditure (REE; via triplicate-repeated fasted respirometry) from Amazonian forager-horticulturalist Shuar children (N = 44, age 4-11 years) over a 14-day study period. Conservative analysis indicates that Shuar energy expenditure is greater than estimated from standard age- and weight-based prediction equations for both TEE (mean +289 kcal/day vs. WHO prediction, $p < 0.001$) and REE (mean +271 kcal/day vs. Schofield prediction, $p < 0.001$). Using a comparative sample of US and UK children (N = 41) we next performed more robust analyses accounting for individual-level differences in fat-free mass (FFM). Multivariate regression models controlling for age, sex, and FFM demonstrate dramatically elevated Shuar REE compared to industrialized references (mean +172 kcal/day, $p < 0.001$). However, despite greater REE, Shuar TEE was indistinguishable from that of US/UK children ($p = 0.109$). Consequently, estimated mean physical activity level (TEE/REE) and activity energy expenditure values for the Shuar were 0.20 units and 270 kcal/day lower than for references, respectively (both $p < 0.001$). Our discussion highlights three major implications of these findings: 1) The widely performed prediction of child TEE and REE using measures of body weight appears to considerably underestimate daily energy requirements among non-industrialized populations at risk for malnutrition; 2) Child REE is chronically elevated in at least some small-scale societies, likely as a result of persistent, low-level immune function that is often not accounted for in energy expenditure models; 3) Child TEE may be constrained within a relatively narrow range cross-culturally, suggesting that energetic tradeoffs between competing individual components of energy use are common and that variation in lifestyle and pathogen burden may not be consistently reflected in overall energy expenditure. Directly incorporating these outcomes into models of human life history evolution, the developmental origins of health and disease, and the pathways underlying the epidemiological transition should be a primary target of future research.

SESSION 6A (FRI, AUG 3, 4:00 PM): HOT TOPICS—*Chair: Melissa Wilson Sayres* (Location: Ballroom A)

4:00pm	**6A-1**	Ilardo, M	Sea Nomads: A novel system for the study of acute hypoxia

Sea Nomads: A novel system for the study of acute hypoxia

The 'Sea Nomads' of Southeast Asia have lived a marine-dependent lifestyle for over 1000 years. Their marine hunter-gatherer existence depends notably on the food they collect through free diving. They are renowned for their extraordinary abilities, diving over 70 meters with nothing more than weights and wooden goggles. The unique lifestyle of the Sea Nomads relies on a number of cultural traits and technical innovations. However, this lifestyle is also facilitated by physiological and genetic adaptations to diving. These adaptations have important implications for the study of acute hypoxia.

4:20pm	**6A-2**	Martin, A	Genetic risk prediction across diverse populations

Genetic risk prediction across diverse populations

The vast majority of GWAS are performed in individuals of European descent; their applicability to other populations varies with genetic divergence, differences in LD and allele frequencies, and genetic architecture. Demographic models provide a critical lens into complex trait studies, including the transferability of genetic risk prediction to understudied populations. Previously, we simulated an out-of-Africa model to show that genetic risk predicted using European summary statistics transfers poorly to non-European populations. Here, we empirically evaluate genetic risk prediction across populations using results from the Psychiatric Genetics Consortium. We find that East Asian schizophrenia risk is better predicted by summary statistics from smaller East Asian cohorts (13k cases and 16k controls) than from ~3-fold larger European cohorts (37k cases and 113k controls, liability $R2 = .029$ vs $.022$). To improve cross-population genetic risk prediction, we develop a novel statistical method to improve prediction accuracy across populations when GWAS summary statistics are available from multiple populations. Our method computes the covariance of effect size estimates in each population weighted by LD structure in each respective population to more closely approximate causal effect sizes used in prediction. Even under neutral evolution (i.e. no heterogeneity of effect by population), our work cautions that findings from large-scale GWAS may have limited transferability across populations with standard approaches, highlighting the need to include more diverse individuals in medical genomics.

SESSION 6B (FRI, AUG 3, 4:00 PM): EVOLUTION AND BEHAVIOR—*Chair: Gillian Pepper* (Location: Ballroom B/C)

4:00pm	**6B-1**	Sarafin, R	Who's really in charge here? Manipulation of human behavior by sexually transmitted organisms

Who's really in charge here? Manipulation of human behavior by sexually transmitted organisms

The hypothesis that parasites may manipulate host behavior for their own end is not new, yet few studies have examined human behavior from this viewpoint. This review seeks to explore the possibility of behavioral manipulation by sexually transmitted organism (STOs) to increase their own transmission rates. The theoretical evidence for such a claim comes from disparate literatures. Firstly, the behavioral immune system posits that human behavior and personalities are plastic; given this plasticity, is it possible that STOs are co-opting our machinery for their own ends? Secondly, some STOs appear capable of manipulating our immune system to prevent infection clearing, which researchers have theorized to be an important first step in behavioral manipulation. Lastly, there are theoretical reasons to think that STOs, more so than many human pathogens, would have evolved to manipulate our behaviors. Once we assume this premise, we can delve into further theoreticals: which STOs manipulate our behavior? Which behavioral/personality traits are prime for manipulation? What are the proximate mechanisms by which this may occur? And lastly, where does our research go from here?

4:15pm	**6B-2**	Doyle, C	Depression and Infection among reproductive age women

Depression and Infection among reproductive age women

Although depression has been of great interest to the health sciences, its causes remain uncertain. Chlamydia trachomatis infection has been suggested as a cause of depression that could act through inflammation or other immunological responses (Maes 2008, Miller et al. 2009, Canli 2014, Doyle et al. 2015). If C. trachomatis caused depression through inflammation, one would expect that other pro-inflammatory pathogens would also do so. This expectation would apply particularly to Neisseria gonorrhoeae, because it has a similar pathology to C. trachomatis. To address whether infection or generalized inflammation plays a role in depression, we conducted a study using data from the Kentucky Women's Health Registry (KWHR) at the University of Kentucky. Data collected included self-reports of depression and depressive symptoms, sexually transmitted infections, menstrual histories and demographic and behavioral variables. Among 1510 normally menstruating women of reproductive age, 74% (n=1121) reported suffering from depression. Bivariate analyses showed a statistically significant association between rates of depression and a positive report of infections with C. trachomatis ($p = 0.0164$), N. gonorrhoeae ($p=0.049$), T. vaginalis ($p=0.0002$), human papillomavirus (HPV) ($p=0.0136$) and herpes simplex virus (HSV) ($p=0.013$). However, multivariate analyses, which can control for interactions between variables, showed that the only pathogen that was significantly associated with depression was C. trachomatis ($p=0.039$).

Conclusions. The results of the multivariate tests accord with the hypothesis that the significant bivariate associations of sexually transmitted pathogens with depression may reflect correlations but not causation. The lack of an association between depression and other inflammation-inducing pathogens argues in favor of an alternative causal pathway for C. trachomatis such as chronic tryptophan restriction via the indoleamine 2,3-dioxygenase (IDO) pathway. Tryptophan restriction, which the body invokes as a generalized defense against infection (Hrboticky et al 1989; Xiao et al 2004), also leads to low levels of serotonin and low mood (Akers and Tan 2006). This defense may be chronically stimulated by C. trachomatis because this bacterium synthesizes its own tryptophan (Aiyar et al. 2014) and can persist in the presence of tryptophan restriction. This supports the hypothesis that infections could be responsible for associations between inflammation and infection, but challenges the presumption that associations of depression with infection and inflammation support the hypothesis that infection-induced inflammation is the mechanism by which pathogens contribute to depression.

4:30pm	**6B-3**	Anderson, A	A Review of the Evidence for Adaptive Anemia

A Review of the Evidence for Adaptive Anemia

Unlike other non-genetic anemias, anemia of inflammation may serve an adaptive function. Iron is an essential nutrient for humans and their pathogens, and there is an ongoing arms race for iron control. Multiple mechanisms of mammalian iron metabolism work independently to lower iron availability to invading pathogens, while pathogens have evolved a range of iron acquisition strategies that target different aspects of host iron metabolism. Hospital studies have shown that blood transfusion may worsen outcomes for patients with mild to moderate anemia. However, several theories of adaptive anemia based on an understanding of host-pathogen iron competition show mixed support in epidemiological studies. This review provides an overview of mammalian iron metabolism, antagonistic iron-related adaptations of host and pathogens, and in vivo evidence for adaptive anemia.

SESSION 7A (SAT, AUG 4, 8:45 AM): MICROBIAL EVOLUTION—*Chair: Misty Thomas* (Location: Ballroom A)

8:45am	**7A-1**	Rorick, M	Evidence of niche partitioning within the antigenic genes of the malaria parasite P. falciparum and implications for malaria vaccine design

Evidence of niche partitioning within the antigenic genes of the malaria parasite P. falciparum and implications for malaria vaccine design

The most deadly malaria parasite in humans, Plasmodium falciparum, induces a strong antibody response that is effective at clearing infection in non-immune individuals. These antibodies are mainly directed against P. falciparum erythrocyte membrane protein 1 (PfEMP1). This protein would be an ideal vaccine target if it were not for its extensive sequence diversity. We consider whether PfEMP1 can be simplified and understood from the perspectives of theoretical evolution and ecology. We sample PfEMP1 sequences from a highly endemic community in Ghana, and observe thousands of distinct PfEMP1 variants. We simplify this diversity by deconstructing it into its constituent, recombining parts. We use a Bayesian model to identify functional groups of recombinant parts based on patterns of co-occurrence. We then map all of the PfEMP1 variants onto a set of functional types that is two orders of magnitude less diverse. We observe that common functional types are non-randomly distinct from one another, indicating that intermediate PfEMP1 variants may be selected against due to functional redundancy. We also test for selection against intermediates at a higher level of biological organization—that of PfEMP1 genomic repertoires. In the context of a highly endemic parasite population, like the one studied here, there is strong intraspecific competition for host immune space. Both the theory of niche partitioning from community ecology and strain theory from epidemiology predict that under such conditions antigenic repertoires should be structured into discordant strains. We find that on average isolates have less PfEMP1 repertoire overlap than expected randomly. Furthermore, the linkage network of PfEMP1 variants reveals a pattern of non-random modularity unique to the antigenic genes, and not explainable by neutral forces such as host population heterogeneity, geospatial population structure or recombination constraints among distinct antigenic types. These findings are consistent with a role for immune selection in structuring PfEMP1 diversity into discordant strains. An understanding of the evolutionary dynamics and constraints shaping PfEMP1 diversity in nature could make it possible to target this primary natural antigen through a multivalent vaccine. Despite decades of intensive research there is otherwise little prospect for a malaria vaccine with high efficacy at preventing disease. We therefore believe that a PfEMP1-based vaccine should be considered alongside other malaria interventions in the effort to achieve elimination.

9:00am	**7A-2**	Gurney, J	Efficacy and evolutionary robustness of a phage-antibiotic combination therapy

Efficacy and evolutionary robustness of a phage-antibiotic combination therapy

Phage therapy has the potential to treat currently intractable infections. However, the evolutionary robustness of phage therapy is currently unclear. We examined a potential therapeutic phage in a clinically relevant environment, to assess efficacy and evolutionary robustness.

Pseudomonas aeruginosa (PA) a major opportunistic pathogen. In people with Cystic Fibrosis it is the leading cause of mortality worldwide, due to chronic lung infections. Despite constant antibiotic treatment, polymicrobial competition, highly activated host immune defenses and physical therapy, PA infections become chronic and are virtually impossible to eradicate with conventional therapeutic approaches.

The phage OMKO1 infects PA via a major mechanism of antibiotic resistance (the mexXY efflux system) and has shown positive results in two compassionate release cases. OMKO1 forces PA into a 'catch-22' - with efflux on it can be killed by phage and with efflux off it can be killed by antibiotics.

We show that in simple *in vitro* and *in vivo* (waxmoth larvae) environments, combined OMKO1 and antibiotic treatment can simultaneously reduce antibiotic resistance, bacterial titre and host mortality. Currently we are examining the short term (initial treatment) impacts and longer term (evolutionary and co-evolutionary) dynamics of the combination treatment in a synthetic sputum medium that recapitulates the biochemistry and physical structure of the CF lung environment, using a range of PA isolates and clinical communities. Initial results suggest that under clinically relevant antibiotic dosing, a single therapeutic dose of OMKO1 can persist and co-evolve with PA, with the introduction of antibiotics shifting co-evolutionary dynamics from arms race to fluctuating selection. We conclude with a survey of the clinical relevance of our results.

9:15am	**7A-3**	Cooper, V	Why evolution in biofilm-associated infections generates greater diversity and yet may be predictable

Why evolution in biofilm-associated infections generates greater diversity and yet may be predictable

Opportunists such as Burkholderia and Pseudomonas have extremely low genome-wide mutation rates and among the largest effective population sizes of any organism measured. These two properties provide clear evidence that the power of natural selection to refine any trait important for fitness in Bcc is almost unimaginably strong. Consequently, the inherent capacity of these bacteria to grow on a variety of biotic surfaces in aggregates or larger biofilms is likely governed by well-coordinated regulatory circuits. A powerful approach to discover these circuits is the genomewide surveillance of evolution in action under conditions that select strongly for biofilm production, and hence alterations in these pathways. Theory predicts that the structured environment of biofilms facilitates the simultaneous rise of multiple adaptive lineages, which could reveal different adaptations or parallelism in the same pathways. Here, we report results from many laboratory evolution experiments and longitudinal surveys of isolates from patients with cystic fibrosis (CF) that reveal repeated adaptive mutations in two interrelated systems: rpfF/rpfR in Burkholderia and wsp in both Burkholderia and Pseudomonas, which increase attachment and aggregation by regulating polymer and lectin production. Evolved nonsynonymous mutations in different protein domains of these clusters generate different biofilm phenotypes and thus inform the function of these pathways. Remarkably, mutations affecting the same protein residues evolve repeatedly in independent experiments, yet these sites are not hypermutable, which demonstrates extraordinarily strong selection for the adaptive traits generated by these mutations. This parallelism is remarkable because genomewide knockout screens have identified many more genes that affect biofilm traits. The key insight is that evolutionary dynamics in biofilms are superpowered to select for the very best new mutations that produce superior attachment or stress avoidance, often by disrupting negative regulators of pleiotropic circuits in optimal ways. Ultimately, such mutations should be very rare in nature, where the conserved "wild-type" allele represents the regulator that maintains an optimal range of function.

9:30am	**7A-4**	Dichosa, A	Developing targeted alpha-radiotherapies to combat antimicrobial resistance in bacterial pathogens

Developing targeted alpha-radiotherapies to combat antimicrobial resistance in bacterial pathogens

"Antibiotics are becoming ineffective" – WHO, Dec 2014. The rapid rise of antimicrobial resistance (AMR) in bacterial pathogens, including multi-drug and extensively-drug resistant pathogens (aka, "superbugs") poses a serious threat to our nation's public health and economy, while the introduction of AMR into potential biothreat agents threatens our nation's security. The diversity of antibiotic resistance mechanisms employed by bacterial pathogens is not matched by the currently available tools employed to defeat them. Depending upon the infection, commonly used antimicrobial treatments combine topical and oral treatments, and tend to be broad spectrum: none are specific for particular microorganisms and may not be useful in the treatment of some invasive infections. Clearly, developing revolutionary, novel, and effective antimicrobial therapeutics is warranted to overcome the emerging threat of superbugs.

To potentially overcome all evolved or acquired mechanisms of AMR and deliver a therapeutic agent against a bacterial pathogen, we will adapt current anti-cancer radiotherapy modalities that exploit the targeting specificity of antibodies paired with the known energy decay of certain radionuclides. As proof of concept, our objective is to target alpha-emitting therapeutic radionuclides to the surface of an evolved, multi-drug resistant surrogate strain of *Yersinia pestis*, the causative agent of plague. We expect that our developed radiotherapy, upon binding a superbug target, results in surface damage or destruction of the pathogen, while leaving nearby healthy host tissue/cells relatively unperturbed due to high linear energy transfer of alpha particles. The immediate benefit of this strategy is that pathogens with AMR will succumb to radiation treatments since, as with few exceptions, bacteria do not possess natural mechanisms to rapidly evolve resistance to radiation exposure. If successfully demonstrating targeted kill against a Gram negative pathogen, we believe that targeted radiotherapies against pathogens represents a paradigm shift over current antibiotic treatments.

SESSION 7B (SAT, AUG 4, 8:45 AM): HOST PATHOGEN EVOLUTION—*Chair: Michelle Blyth* (Location: Ballroom B/C)

8:45am	**7B-1**	Nunn, C	Vector-Borne Disease Risk in Human Altered Host-Vector Communities: A Network-Based Simulation Study

Vector-Borne Disease Risk in Human Altered Host-Vector Communities: A Network-Based Simulation Study

Anthropogenic disturbance has strong impacts on diversity and phylogenetic composition of communities. These changes can dramatically change species interactions, and thus may alter disease dynamics for human populations. Using a theoretical model, we investigated how phylogeny and extinction influences network structural characteristics relevant to disease transmission in disturbed environments. We modelled a multi-host, multi-vector community as a bipartite ecological network, where nodes represent host and vector species and edges represent connections among them, and simulated vector preferences and threat status on host and parasite phylogenies. We then simulated loss of hosts through human activities, including phylogenetically clustered loss of hosts, to investigate how changes in host ecological communities influence network structure. We compared effects of phylogeny and extinction to those of host specificity, with increasing specificity expected to predictably increase modularity. The simulations revealed that host extinctions often increase modularity of ecological networks, suggesting that one effect of disturbance may be to reduce cross-species transmission of vector-borne disease, thus decreasing disease prevalence in more disturbed communities. Although effects were mixed, increasing the proportion of species that went extinct tended to increase modularity, while phylogenetic signal in vector preferences and host traits increased modularity. Additional simulations confirmed that increased modularity on bipartite networks tended to reduce disease prevalence.

9:00am	**7B-2**	Torosin, N	The evolution of TLR7 and TLR8 in yellow fever virus endemic areas

The evolution of TLR7 and TLR8 in yellow fever virus endemic areas

In Misiones, Argentina, the howler monkey populations (Alouatta guariba clamitans) and (Alouatta caraya) were devastated first in 1965, and then in 2008-2009 by Yellow Fever Virus (YFV). Howler monkeys are the most susceptible to YFV of all primates and die within a week after infection. To better comprehend the relationship between immune function and genetic variation, we have employed a novel approach comparing TLR7 and TLR8 immune evolution in a non-human primate species, howler monkeys, to humans sharing the same pathogenic pressure and environment in rural Argentina. A field campaign in 2017 yielded samples from Alouatta individuals in three categories: those alive prior to the outbreak, those that died from the virus, and those that survived the outbreak, along with their progeny. Using these data, along with genetic data collected from Alouatta palliata mexicana, and published primate immune gene sequences, we found preliminary evidence that the purifying selection is significantly stronger in the howler monkey clades compared to other New and Old World primate species and humans. We also examined allele frequencies of innate immune genes TLR7 and TLR8 from pre- and post-YFV outbreak howler individuals. Finally, using human genotype data from regions with historical YFV exposure, we are testing for positive selection in TLR7 and TLR8. We will compare post-YFV TLR7 and TLR8 alleles in the howler monkeys to human TLR7 and TLR8 to evaluate potential variants important in YFV susceptibility.

9:15am	**7B-3**	Emery Thompson, M	Epidemiology of respiratory disease in wild chimpanzees

Epidemiology of respiratory disease in wild chimpanzees

Given their close evolutionary relationship to humans, great apes are highly vulnerable to human diseases. Respiratory viruses of human origin have caused high-mortality respiratory outbreaks in wild ape populations across Africa. While the etiology of these infections has received considerable attention, little is known about their epidemiology. We examined long-term patterns of morbidity and mortality from respiratory infections in the Kanyawara community of wild chimpanzees in Kibale National Park, Uganda. Respiratory disease was the leading known cause of mortality over a thirty-year period, accounting for over 25% of deaths. We used a series of GLMMs to investigate the individual and temporal predicators of respiratory signs over a 22-year period. Respiratory signs, chiefly comprising productive coughing and sneezing, occurred at a median rate of 3.7% chimpanzees per month (range 0-89.7%), with 17 outbreaks affecting at least 20% of chimpanzees at a time. Diarrhea and respiratory signs had a strong pattern of comorbidity, particularly in young chimpanzees. In female chimpanzees, the frequency of respiratory signs increased with age but was unaffected by social rank or reproductive status. In male chimpanzees, respiratory signs were elevated during the period of peripubertal maturation (10-20 years), as well as in those over 40 years. Adult males were most likely to be sick if they were young and low-ranking, or old and high-ranking. We found a strong seasonal pattern, with respiratory signs peaking the month of March, but this was not readily explained by climate, dietary quality, group sizes, or various measures of human contact. Most strikingly, rates of chimpanzee respiratory signs did not track respiratory disease in the nearby human village. Our results suggest that respiratory disease, which elicits conspicuous signs, has strong potential as a model for individual immunocompetence in chimpanzees. However, our analysis provides relatively few clues as to the temporal factors that predict introduction to and transmission among the chimpanzees. This comprehensive study indicates some important differences between chimpanzee and human respiratory epidemiology. Human respiratory illnesses most commonly affect infants and juveniles, kill the very young and very old, and exhibit seasonally predictable patterns linked with climate. By contrast, respiratory disease has killed several young adult chimpanzees presumed to be in otherwise good health. Immature individuals were the least likely to exhibit signs of illness, despite high rates of social contact by juveniles. Finally, chimpanzee outbreaks do not follow a reliable temporal epidemiological profile and may be the result of stochastic exposure events.

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9:30am	**7B-4**	Green, M	The Origins of the Black Death: A Consilient Approach from Phylogenetics and History

The Origins of the Black Death: A Consilient Approach from Phylogenetics and History

The Black Death (1346-1353) is rightly considered the largest pandemic in human history. New work in paleogenetics in the 2000s and 2010s established definitively that *Yersinia pestis* was the causal agent of the pandemic, and work on modern isolates of *Y. pestis* has allowed increasing precision in the construction of a global phylogeny for the organism. From an origin in northern Eurasia about 28,000 years ago, around the time of the Last Glacial Maximum, *Y. pestis* has had an unbroken history of transmission, producing strains involved in outbreaks from the Bronze Age to the present day. As the recent outbreak in Madascar demonstrated, plague, which is already present on all inhabited continents save Australia, remains a potential cause of significant human disease. Both climate change and antibiotic resistance may upset the current state of control over the disease, thus posing a potential threat to global health.

The mechanisms that have caused this disease of rodents to erupt into human pandemics remain unclear. What happened to the organism in the 13th and 14th centuries, leading up to the Black Death, remains the greatest unsolved puzzle in epidemiological history. Phylogenetics has established that *Y. pestis's* suddenly diverged into four new branches, a polytomy geneticists have called "the Big Bang." These new lineages seem to have been involved in a series of outbreaks in eastern, central, and western Eurasia, as well as possible penetration into sub-Saharan Africa.

Only six genomes of *Y. pestis* have thus far been recovered from the 14th century, and none from the 13th century. These have been insufficient either to localize the site of the polytomy geographically, or pinpoint its chronology. However, the geographical distribution of surviving plague strains, combined with the documentary historical record from Mongol Eurasia in the 13th and 14th centuries, permits identification of the likely location, and the cultural and environmental circumstances, of the late medieval polytomy and the events that may have led to parallel pandemic outbreaks in both China and western Eurasia. By taking a consilient approach to biological and cultural data, this paper will suggest both a methodological model for reconstructing epidemiological history, and the value of a scalar approach to evolutionary genetics which traces both pathogens and human simultaneously.

SESSION 8A (SAT, AUG 4, 9:50 AM): IMMUNITY—*Chair: Stephen Corbett* (Location: Ballroom A)

09:50am	**8A-1**	Graham, A	Late life on the double-edged sword: Antibodies among Taiwanese elderly

Late life on the double-edged sword: Antibodies among Taiwanese elderly

Antibodies can confer resistance to important human pathogens such as malaria, pneumococci, dengue and influenza. Yet antibodies can also cause autoimmune diseases like lupus when they attack host tissue (e.g., as self-reactive "autoantibodies" can) or accrue at such high densities that they damage organs. Data from wild sheep suggest that hosts prone to autoimmunity exhibit greater infection resistance and survival than hosts lacking autoantibodies. While these data are suggestive, the relative contributions of autoantibodies and virus-specific antibodies to human health and survival are unknown. Here, we address that gap, drawing upon biomarkers and data from a longitudinal study of older Taiwanese (Social Environment and Biomarkers of Aging Study, SEBAS), from an island-wide population-representative sample of people who were aged 54 and older in 2000. We studied 639 individuals who participated in both rounds of blood collection, in 2000 and 2006. We measured plasma concentrations of autoantibodies as well as antibodies specific to 4 influenza A viruses that circulated widely in Taiwan 1957-2005 (including 2 pandemic viruses), antibodies specific to 2 prevalent herpesviruses, and several inflammatory molecules. We first assessed relationships among all of the biomarkers, and repeatability of measurements within biomarker types over time, using generalized linear models. We then used Cox proportional hazards analyses to assess associations of survival with autoantibodies, virus-specific antibodies, and inflammatory markers, while also accounting for effects of host sex. We found negative associations of herpesviruses and inflammatory cytokines with late-life influenza memory in this sample. Herpes-associated immunosenescence, previously reported in Scandinavian cohorts, thus also appears to affect elderly Taiwanese. Independent of such immunosenescence, we find that autoantibodies are positive predictors of both influenza resistance and survival over a 10-year follow-up period. Our findings suggest that individuals experience a trade-off: susceptibility to autoimmune diseases OR acute viral infections, but not both. Such a trade-off could help to explain the persistence of genes conferring susceptibility to autoimmune diseases like lupus in human populations.

10:05am	**8A-2**	Wiessner, P	Not all Elevations in Late Night Salivary Cortisol Are Pathological

Not all Elevations In Late Night Salivary Cortisol Are Pathological

The amount of cortisol present in biological fluids, such as blood, urine, and saliva shows a pronounced circadian variation with the highest levels upon awakening and the lowest levels occurring in the late evening. Superimposed on the circadian cortisol rhythm, acute elevations in cortisol occur with stress, exercise, and meals and chronic elevations are observed in a number of diseases such as Cushing's syndrome, depression, and alcoholism. The concentration of cortisol in saliva reflects the amount of non-protein bound and physiologically active cortisol in serum. Measurement of late night salivary cortisol is a standard method to screen for pathological elevations in cortisol and values greater than 0.11 mcg/dL are used to identify patients for whom additional evaluation is needed.

We undertook a study of cortisol concentrations in subsistence populations to understand the physiology of the pituitary adrenal axis in hunter-gatherer and subsistence agricultural populations, the Kalahari Bushmen and the Enga of Papua New Guinea. The study focused on the effects of ritual behavior on the stress response. Saliva samples were collected upon awakening, in the midday, and in the late evening on days in which there were no ritual activities and on days during which ritual activities took place e.g. political rallies, evening celebrations and healing dances. Salivary cortisol was measured in a 75 microliter aliquot of fresh saliva using a point-of-care immunochromatographic cortisol assay. This assay measures cortisol in the range 0.03 – 1.5 mcg/dL with a intra and interassay c.v. < 10% and 20% respectively and is specific for cortisol. Samples were collected from groups of individuals at discrete time points throughout the day, stored at 7 oC. , and assayed within 24 hours of sample collection. Salivary cortisol performance standards were assayed daily.

The results showed that circadian cortisol concentrations and rhythms in these small-scale subsistence-based communities are equivalent to those observed in industrialized populations. However, late night salivary cortisol concentrations in both New Guinea and Kalahari groups showed significantly elevated cortisol concentrations while members of the group were in a positive social setting involving ritual and celebration. Late-night salivary cortisol levels greater 0.11 mcg/dL were routinely found.

These findings indicate that non-stressful social behavior can elevate late-night salivary cortisol, and these results require further investigation.

10:20am	**8A-3**	Trumble, B	The exposome in the evolution of human inflammatory responses: from dust to diesel

The exposome in the evolution of human inflammatory responses: from dust to diesel

Air pollution is associated with 15 million excess or premature deaths per year, with the death toll expected to nearly double by 2050. Globally, airborne toxins are a major focus in characterizing the exposome, a comprehensive analysis of external and internal toxins across human lifespan. Mass exposures to cigarettes and fossil fuel pollution are novel in human history.

We describe the human exposome history in five phases, with cumulative impact for which we postulate genetic adaptation. Phase I: during the acquisition of long-stride walking and running on savannas, early human ancestors inhaled increasing amounts of crustal dust, fecal aerosols, and spores. Scavenging of carrion also introduced new parasites and pathogens. Phase II: With expanding use of domestic fire, early Homo experienced novel toxins from smoke and advanced glycation end-products from cooking. Phase III-IV into the neolithic, H sapiens had expanded pathogen exposure from domestic animals and dense communities. Since 1800 (Phase V), further novel toxins were experienced through the industrial revolution, combustion engines, and tobacco.

The inflammatory responses to airborne toxins from cigarettes and fossil fuels are shared with the pathophysiological of chronic diseases currently associated with air pollution. We hypothesize that adaptation to ancient airborne toxins may be recognized in modern genetic variations, possibly including the genotypes of cigarette survivors who reached their ninth decade in apparent health. Evolutionary inquiry of the human exposome points to unexplored domains of inflammatory processes in the evolution of lung and brain that may inform on the future of human health and longevity during global warming.

10:35am	**8A-4**	Mattison, S	Kinship ecology and sex differences in C-reactive protein among matrilineal and patrilineal Mosuo of Southwest China

Kinship ecology and sex differences in C-reactive protein among matrilineal and patrilineal Mosuo of Southwest China

As a basic foundation of human social organization, kinship systems structure a range of important social processes in human populations that impact gender roles, lifestyles, and health. By now it is well-known that gender roles typical in matriliny and patriliny can generate different costs and benefits for males and females through patterns of decision-making, resource allocation, control over productive and reproductive strategies, and access to kin support networks. However, evolutionary theorists have yet to articulate how the behavioral and socioecological circumstances of kinship systems may translate into different health outcomes for men and women at a biological level. In this paper, we use blood-spot C-reactive protein (CRP) levels collected from matrilineal and patrilineal Mosuo populations to investigate how chronic stress and accumulated allostatic load may reflect the physiological effects of gender dynamics in different kinship systems. We hypothesize that men and women will experience lower allostatic burden and reduced risk of chronic inflammation in the kinship system where they are heads of household, dominant inheritors, and where post-marital residence keeps them close to consanguineal kin. In support of this hypothesis, we find that females are at greater risk of high CRP under patriliny, while males are at greater risk of high CRP under matriliny. This study is the first to incorporate biomarkers to directly examine the physiological effects of kinship and gender inequality on differential health outcomes for men and women.

SESSION 8B (SAT, AUG 4, 9:50 AM): GENOMICS AND COMPLEXITY—*Chair: Brandon Hidaka* (Location: Ballroom B/C)

09:50am	**8B-1**	Duello, T	Concepts of 'Race' in Genetics Clinical Trials: A Systematic Review of Literature Since the Human Genome Project

Concepts of 'Race' in Genetics Clinical Trials: A Systematic Review of Literature Since the Human Genome Project

In 1986 the NIH established a policy on the inclusion of women in medical research as it was well established physiology differed by gender. Thus, all studies of men could not be generalized to women. In 1993 the NIH expanded these guidelines to the inclusion of both women and minorities as subjects in clinical research. In 1997 the Office of Management and Budget reissued OMB Directive 15, which states that data on race and ethnicity should not be interpreted as being scientific or anthropological in nature. Subsequently, the Human Genome Project established in 2003 that there is no genetic basis for race. Nonetheless, there is a great deal of confusion in the biomedical literature surrounding the use of race.

In May 2017 the Entrez-PubMed biomedical literature database was queried using African continental ancestry, genetics, and clinical trials as search terms for articles published since 2003. A total of 185 full length journal articles were identified addressing human genetics, all of which were published in peer-reviewed journals. Eighteen journal articles reported studies of race/ethnicity as a social category examining health behavior, risk assessment, cancer screening, and clinicl tiral recruitment, and retention, 60 studied medical outcomes in biological studies of racial/ethnic populations, and 107 studied the genetics of racial/ethnic populations. Preview software was used to search pdf files of all publications in the latter category for keywords relevant to evolution: evolution, genetic drift, natural selection, Founder effect, mutations, admixture, genetic variation, ancestry informative markers, and ancestry proportion. In addition, each paper was reviewed by two authors to determine if/how race was defined and its use in genetic studies.

A wide range of criteria was used to define study populations as African American/black/African descent in the 107 genetic studies: self/surrogate-reported race (29), self-reported race with 4 grandparents who self-identify as of African descent (3), self-reported race combined with ancestry proportion to address population stratification (6), or ancestry proportion alone (1). The remainder did not clarify whether they believed 'race' to be a genetic category or a proxy for a genetic category/disease incidence.

Only 8 of the genetic studies addressed or alluded to the impact of genetic drift, natural selection, or the Founder Effect on the reported human genetic variation with an additional 20 discussing mutations.

Given 1) the limitations of ancestry informative markers based on evolutionarily recent populations, 2) extensive genetic variation on the African continent, 3) the extensive genetic mixing between those of African descent and other 'races', 4) the addition of recent African immigrants to the African American population, and 5) the fact that admixture may range from 1 to 99 percent, it is not possible for these studies to be reproduced, unless the exact same study populations are used. If we only have an approximation of genetic ancestry, then we have only approximated science. At a bare minimum, this analysis indicates the need for editorial standards requiring investigators to state the rationale for the use of 'race' as a genetic category and the limitations of the data generated.

10:05am	**8B-2**	Bergstrom, C	Burning money: competition generates inefficiencies in the grant proposal system for scientific funding

Burning money: competition generates inefficiencies in the grant proposal system for scientific funding

A large fraction of scientific research funding is allocated through a system of grant proposals and awards. We use the economic theory of contests to analyze the scientific efficiency of this process. Investigators participate in contests to write high-quality proposals. Funding agencies use these contests not as a mechanism for extracting work from participants, but rather as a screening mechanism intended to reveal the most promising research projects. As a first approximation, the work that investigators do in proposal preparation provides no extrinsic value to the funder. We find that the effort researchers that expend in preparing proposals may be comparable to the total scientific value of the additional funding, The problem may be exacerbated as the fraction of funded proposals drops and when investigators derive non-scientific utility from fund their funding successes (in the forms of e.g., hiring, promotion, tenure, or reputation). We suggest that partial lotteries for funding may ameliorate the problem by reducing the intensity of competition and the extra-scientific benefits associated with funding success. Alternatively, funders could use the contest structure to extract useful work by rewarding scholars for their past successes.

10:20am	**8B-3**	Chevalier, R	Champion of American science and public health, William H. Welch was a pioneer in Darwinian medicine

Champion of American science and public health, William H. Welch was a pioneer in Darwinian medicine

Less than 40 years after Darwin published On the Origin of Species, pathologist William H. Welch (1850-1934), first dean of Johns Hopkins University School of Medicine, wrote an essay titled Adaptation in Pathological Processes (1897). After receiving his MD in New York, Welch traveled to Germany to train with eminent pathologist Julius Cohnheim, and became an early convert to Darwinism. In Adaptation in Pathological Processes he claims that variation, natural selection, and heredity are factors that underlie pathological adaptations. The terms "evolution" or "evolutionary" and "fitness" are repeated 12 times, and "natural selection" is repeated 6 times in the text. Aware of ultimate as well as proximate explanations for disease, Welch regrets that "the only question open to scientific investigation is 'How?' and never 'Why?'." Distinguishing between physiological and evolutionary adaptation, he notes, "Natural selection may be operative in securing protective adjustments … [that] help us to explain the marked imperfections of most pathological adaptations as contrasted with the perfection of physiological adjustments." He acknowledges the concept of evolutionary tradeoff: "Introduction into the workings of the organism of some better mechanisms to compensate the morbid conditions might be at the sacrifice of more important physiological attributes of the body." He formulates the concept of evolutionary mismatch: "While we must believe that variation and natural selection combined with heredity have been important factors in the development and maintenance of adjustments to normal conditions of environment, it is difficult to see how they could have intervened in any direct way in behalf of most pathological adaptations." Finally, he highlights the importance of variation in the differential vulnerability of individuals to infection with a pathogenic microorganism, resulting in either no symptoms, recovery, or death.

Welch's evolutionary approach to medicine was not shared by most of his contemporaries. Throughout the past century, Western medicine emulated Sir William Osler (1849-1919), professor of medicine at Johns Hopkins, and quintessential clinician. He regarded the patient as a "classic case" with disordered homeostasis. In addition to Welch and Osler, surgeon William Halsted (1852-1922), and obstetrician Howard Kelly (1858-1943) constituted the "Big Four" founding physicians of Johns Hopkins. Far from an evolutionist, Kelly was a proselytizing Christian fundamentalist, whereas Halsted proclaimed of his patient that "God cured him; I assisted." In the early 20th century there was a wide range of opinion among Americans regarding Darwinism. Of the Big Four, Welch was clearly the physician with the most training in biology, and emphasized the need for basic science to inform medical practice. Limitations to Osler's approach have been exposed by global epidemics of metabolic syndrome and diabetes, antibiotic resistance, and cancer in aging populations. Since the publication of Welch's Adaptation in Pathological Processes, an evolutionary approach to medicine had been largely ignored for nearly a century until George Williams and Randolph Nesse published The Dawn of Darwinian Medicine in 1991. Progress in molecular genetics, epigenetics, and evolutionary biology have added powerful tools to advance the new discipline of evolutionary medicine, providing another dimension to the legacy of William Welch.

10:35am	**8B-4**	Laubichler, M	Complexity and evolution as the basis for evolutionary medicine

Complexity and evolution as the basis for evolutionary medicine

It is widely recognized that diseases are complex phenomena and indeed most mechanistic explanation of disease phenotypes include at least an implicit understanding of complex systems. Barabasi and his colleagues have recently suggested a theoretical framework—network medicine—that merges complex systems theory explicitly with the study of disease and therapeutics. However, this approach thus far lacks any serious consideration of evolutionary principles or evolutionary history.

At the same time the majority of evolutionary approaches to disease and medicine are grounded in a version of evolutionary theory that by and large is still Neo-Darwinian, ie focused mainly on (mal-)adaptive dynamics and phylogeny and inherently atomistic in nature. What is needed is to bring those two perspectives together in a more integrated framework that merges complex systems and evolutionary theory and sees phenotypic evolution as a process of transformation of nested complex networks.

In this talk I will sketch the main elements of such an evolutionary systems theory and apply it to a number of issues in evolutionary medicine.

Specifically, I will focus on following challenges in understanding phenotypic evolution, including the evolution of disease phenotypes:
(1) Analyzing robustness and evolvability as complementary properties of evolving complex systems
(2) Evolutionary theory needs to explain both stability and change
(3) Stability is the main challenge for current evolutionary theory
(4) Understanding the links between robustness and evolvability explains the systemic vulnerabilities of complex systems
(5) Stability and evolvability can be explained and studied from the perspective of developmental/extended evolution