Candidate's Statement – J. Andrew Whitehead

1. Research Activities

1.1 Overview

My research program seeks to understand the mechanisms through which animals integrate cues from, respond to, and are shaped by the external environment. We examine responses to stress that occur over physiological timescales (acclimation responses) and over evolutionary timescales (adaptive responses). We integrate genome expression profiling, population genetics/genomics and phylogenetics, and physiology, to study how individuals and species respond to and adapt to environmental stress. Stressors of interest include those that are natural (temperature, salinity) or of human origin (pollutants).

I was an Assistant Professor at Louisiana State University starting in 2005, where I was promoted to Associate Professor just before accepting my current job at UC Davis. Since starting as an Assistant Professor I have secured five grants from the NSF, one grant from the NIH, and several additional grants from other sources, summing to nearly $3 million. Of these, two grants are currently active – one NSF grant was transferred from LSU to UC Davis, and one NIH R01 was awarded to me after starting at UC Davis. I have served as PI on all of these grants except for one as Co-PI (from the Gulf of Mexico Research Initiative). I have authored 31 publications. Since starting as Assistant Professor in 2005 my group has published 22 research articles and reviews and 1 book chapter, 8 of which have been published since starting at UC Davis (in 2012). These publications have been cited over 1,000 times (~850 times since 2008) and my h-index is 16 according to Google Scholar (http://scholar.google.com/citations?user=UiH9RSAAAAAJ). My group is currently pursuing 3 broad research themes, as follows.

1.2 Comparative Genomics of Physiological Plasticity

Physiological plasticity (or flexibility) that enables acclimation to variable environments is a key trait that contributes to persistence of wildlife in rapidly changing human-altered environments. The physiological pathways, the genes, and the regulatory architectures that support such plasticity are not well understood. We use evolutionary contrasts, comparative physiology, and comparative genomics to illuminate these pathways, genes, and architectures. We use and have developed the comparative killifish model system to address these questions because of the extraordinary physiological flexibility of some of these fish, and because of the variation in flexibility to be found within and among species (references 9 and 14). We have made several key discoveries. First, within the killifish genus *Fundulus* we discovered that osmotic flexibility has been lost multiple times in independent evolutionary events, that loss of flexibility does not reverse, and that alternate physiologies can evolve quickly (reference 14). Second, we have found that osmotic physiologies have evolved recently among populations of the Atlantic killifish distributed along natural salinity gradients (reference 18). These studies have helped establish killifish as a powerful micro- and macro-evolutionary model for studying physiological evolution. Third, multiple studies have demonstrated that it is not the well-known effectors of osmotic acclimation, but rather the lesser-known immediate-early

responses, that appear important in contributing to evolved population differences (references 18, 19, 23, and 29). Fourth, we found that the genomic and physiological mechanisms that are associated with adaptive fine-tuning within species also contribute to divergence at macroevolutionary scales as species diversify across osmotic niches (reference 29, plus a manuscript that has been accepted for publication in *Evolution*). Fifth, we discovered a core gene set that enables osmotic plasticity, whose expression is canalized by natural selection operating along a steep salinity gradient to preserve the canalization of extreme osmotic plasticity (manuscript in review).

Ongoing studies seek to define the conditions under which non-native osmotic environments incur fitness costs. Additional studies exploit hybrid zones, and use high-throughput sequencing and population genomics analyses, combined with genotype-phenotype mapping experiments, to discover genetic determinants of osmotic plasticity.

These studies have been supported by funding from the NSF (EF-0723771, Whitehead PI). They have produced 9 publications in journals including *BMC Evolutionary Biology* (reference 13), *Evolution* (reference 14), *The Journal of Experimental Biology* (references 22 and 23), *Journal of Heredity* (reference 19), *Molecular Ecology* (references 10, 20, and 29), and *PNAS* (reference 18).

1.3 The Genomic Basis of Repeatedly Evolved Extreme Pollution Tolerance

Humans have rapidly and sometimes dramatically altered environmental conditions worldwide, and are thus a potent evolutionary force. The ecological and demographic conditions that promote adaptation, and the genetic variation that enables adaptation to rapidly changing environments, are poorly understood. Natural populations of the Atlantic killifish have repeatedly evolved extreme tolerance to persistent environmental pollutants. We seek to discover the mechanisms and genes that enable this adaptation. We have made three key discoveries. First, profound desensitization of the entire aryl-hydrocarbon receptor signaling pathway is the derived mechanism that supports extreme pollution tolerance (reference 15). Second, this mechanism is common to each of the populations that have independently evolved tolerance (reference 21). Third, pollutant-activated genes from these evolutionary studies are predictive of the genomic response to contamination from the Deepwater Horizon oil spill (reference 27).

A current 5-institution collaborative NSF grant (DEB-1265282, Whitehead lead PI) has enabled sequencing of the killifish genome. Furthermore, we are sequencing 400 additional genomes: 50 genomes from each of 4 tolerant and 4 sensitive populations, such that genome-wide scans for fingerprints of recent natural selection can discover in detail the genetic changes that supported such extreme, rapid, convergent adaptation to 20th century pollutants. These studies have produced 4 publications in journals including *Journal of Heredity* (reference 12), *Molecular Ecology* (reference 15), *PNAS* (reference 27), and *Proceedings of the Royal Society B* (reference 21).

1.4 Ecotoxicology of the Deepwater Horizon oil spill

The Deepwater Horizon drilling disaster caused the largest marine oil spill in history, yet the ecological consequences are unknown. Immediately after the disaster, my group initiated experiments (initially funded off of our personal credit cards) to test for in situ impacts of oil that was to contaminate sensitive and important marsh habitats. We discovered genomic and physiological signatures of exposure to contaminating oil that are

predictive of toxicity (references 25 and 27). Field observations have been confirmed by laboratory studies (reference 28 and manuscript in revision), and additional studies show that fish embryos are particularly sensitive to developmental impairment caused by the types of exposures experienced in the field (reference 28).

These studies provide a valuable and unique resource for the damage assessment process. They are valuable insofar as field data demonstrate a clear impact and cause-effect relationship with contaminating oil, field observations have been confirmed by laboratory studies, and effects are likely to be ecologically important. These studies are unique insofar as no other field studies (to our knowledge) have provided clear temporal, spatial, and mechanistic evidence to connect oil spill exposure to important health impacts in resident species. A recently funded NIH grant (1R01ES021934-01, Whitehead lead-PI) seeks to discover early-life molecular markers following exposures to low levels of oil that are predictive of impaired health in adults. These studies also explore the importance of genetic variation in buffering sensitivity to oil spill toxicants, and the trans-generational impacts of exposures to oil spills. These studies have produced 4 publications, including in *BMC Genomics* (reference 25), *Environmental Science and Technology* (reference 28), *Integrative and Comparative Biology* (reference 30), and *PNAS* (reference 27).

1.5 Future Research Directions

My group is leading NSF-funded efforts to develop killifish genomic resources to facilitate advanced comparative and functional genomics research for our group, and for the broader research community. This genome serves as a key resource for future genetic mapping, RNAseq, comparative genomics, and population genomics studies. We are developing the killifish to be a premier model in environmental biology (reference 9).

Several avenues of research are extending our understanding of the mechanisms that underlie physiological plasticity, and the patterns and processes through which plasticity evolves. We are planning experiments to identify whether reproductive success is affected by genetic background and by the salinity within which development unfolds. These experiments will help identify the nature of fitness costs for life in non-native osmotic environments. In order to further dissect the genetic basis of physiological plasticity, we are exploiting two parallel hybrid zones within *F. heteroclitus*, where a resilient group has naturally interbred with a less resilient group. We plan to use genome-scale methods to generate thousands of markers that we can use to map many phenotypes including metabolic rate, metabolic scope, upper and lower thermal tolerance limits, hypoxia tolerance, and osmotic tolerance, in hundreds of hybrid animals. This work is in collaboration with colleagues at University of British Columbia (Canada).

Our group is leading ongoing international collaborations with multiple institutions (Indiana U., Washington U. School of Medicine, U. of Miami, Woods Hole Oceanographic Institution, US Environmental Protection Agency, Mount Desert Island Biological Laboratory, U. of Birmingham UK) to discover the genetic variants responsible for recently evolved adaptive pollution tolerance in killifish. We are starting sequencing of 400 genomes from a total of 4 tolerant and 4 sensitive populations, and using population genomics analyses to discover variants exhibiting signatures of selection, and combining these data with genotype-phenotype linkage analysis. This dataset will be unprecedented in scope and scale, especially for a non-traditional model organism.

We were recently awarded an R01 from the NIH to further our oil spill research. Our aims are to test for oil spill effects at various sensitive stages of the vertebrate life cycle including effects that span generations, to characterize the spatial and temporal extent of vertebrate risk from the spill, and to test for the influence of individual and population genetic variation on sensitivity to oil pollution. These data will offer insight into risk and mechanisms of oil spill impacts in a vertebrate model, offer biomarkers predictive or reflective of impaired biological processes, and accelerate the discovery of genetic and physiological risk factors. For this work we are continuing important collaborations with colleagues at LSU, and forming new collaborations with colleagues at NOAA, Florida State U., and Woods Hole Oceanographic Institution.

My group is considering developing a series of new model organisms for climate change research, particularly for studying ocean acidification. Our idea is to examine existing variation in populations of various marine species that currently inhabit niches that vary in ocean acidity, with the expectation that tolerance to acidic conditions already exists in some populations, particularly in areas of historic low pH – such as Pacific coastal habitats near Bodega Marine lab. The ultimate goal of such studies is to discover genetic variants that are pre-adapted to future environments that may help considerably with mitigation and conservation efforts.

2. Teaching Activities

I consider the education of an informed citizenry as one of my most important missions. My main research interests in evolution, climate change, and environmental pollution, are fields that are not well understood, or are woefully misunderstood, but the American public. Proper education in these fields is crucially important for the near-term and long-term prosperity and integrity of our society. I have taught Evolution in the past, and at UC Davis I teach Ecotoxicology (including climate change) and Aquatic Toxicology, and am actively developing a new course about the impacts of humans on evolutionary processes, and a new course in Ecological Genomics. Though more senior faculty currently teach large enrollment classes in my department, I have taught several guest lectures and am keen to contribute to these courses in the near future. I of course seek to instill an understanding of, and appreciation for, these particular topics in my students, but perhaps more importantly I use these classes as a vehicle to teach and instill a basic understanding of the scientific process. I want students to understand science not as a collection of facts, but as an active, creative, and rigorous process. As such, I discuss scientific questions in the context of testable hypotheses, and make much use of data and data interpretation. I also make much use of active learning tools, including student feedback "clickers" to enhance active engagement, "think-pair-share" activities, debates, group work, and case studies. I require students to do much writing, as I consider excellent written communication skills crucial for almost any career in science. I provide much constructive criticism on assignments, and allow for revisions, just as professional scientists benefit from peer evaluations and the opportunities for improving our work that ensue. The heavy writing requirements in my classes usually attracts criticism on student evaluations, but I receive just as many compliments. Importantly, I sometimes witness huge improvements in writing quality in progressive assignments, which offers self-validation of my teaching model, despite typically average or slightly above-average student evaluation scores. Though students sometimes complain that my courses are too much work, I do pay close

attention to student evaluations that offer constructive criticisms. As such, my teaching styles and approaches continue to evolve, as does my efficacy and impact as an educator.

3. Advising Activities

I consider the training of graduate and undergraduate students in all aspects of the scientific endeavor as a core component of my mission. I seek inclusivity across genders and racial groups. I have graduated 1 Ph.D. student, 1 master's student and 1 postdoctoral researcher (all female). I currently have 5 Ph.D. students, 1 undergraduate student researcher, and 1 postdoc active in my lab (3 male, 4 female, 1 Asian-American). I have mentored many undergraduate students in my research lab, whose duties have spanned field research, laboratory research, and laboratory animal care, including minorities (two African-American students, one Indian-American student). African-American student Princess Ojiaku was a student trainee in my lab; she went on to earn an MS in Biology from North Carolina Central University, and is currently enrolled in the Neuroscience PhD and Master's of International Public Affairs programs at the University of Wisconsin-Madison. As part of the killifish genome project, my group organized and led an international bioinformatics workshop that included nearly 60 participants, and that paid for the travel and participation fees of 24 students and postdoctoral researchers, as part of an inclusive community-building exercise. African-American student Walter Guillory was an active member of my lab for two years, and was fully supported to participate in the bioinformatics workshop. He is currently applying to medical schools while finishing his undergraduate degree. I also secured an NSF RUI supplement to support the genomics training of a visiting scientist in my lab this past summer, which I combined with the training of an LSU graduate student from Columbia.

4. Service Activities

I served on multiple successful faculty recruitment committees and advisory committees while at LSU. At UC Davis I currently serve on my departmental IT committee and teaching committee, and the PTX graduate group membership committee within which we have vetted seven applicants in the past year. I am an active participant in the PTX and Ecology Graduate Groups for which I participated in graduate student application review and interviews in 2013, and was recently accepted as a member of the Population Biology Graduate Group. I have served as a reviewer for 55 research proposals for national and international agencies in the United States, Canada, France, Belgium, and Croatia, and have served on two grant review panels at the NSF (2008 and 2012). I have reviewed 75 manuscripts for journals spanning diverse disciplines (e.g., environmental toxicology, evolutionary biology, comparative physiology, molecular biology) and served on three editorial boards. Our studies on the Gulf oil spill garnered much scientific and media attention, and provided an extraordinary opportunity for broad outreach and education, where I communicated the importance of our findings, and of environmental science research in general, to huge audiences in Canada, Europe, and the United States, through diverse media (print, online, radio, video). Our oil work was also communicated to lawmakers; after coaching Senator Bill Nelson on the meaning of our work, he presented our findings on the floor of the senate during his arguments about the important role of science in the aftermath of the spill. This research was also highlighted in the NSF's 2013 report to congress, and in a 2013 report by the European Commission.