Question from Lorenz Hauser: *Climate change is likely to impose strong selection pressures on wild populations, potentially leading to genetic adaptations ameliorating climate effects.*

*a. Provide a review of examples of genetic changes in wild populations*

*b. Discuss the rate of such genetic changes in relation to the rate of climate change*

*c. Discuss the potential and shortcomings of approaches to studying genetic changes in wild populations.*

Extensive climate change is predicted to occur over the course of this century, altering habitats and promoting change in natural populations. The Intergovernmental Panel on Climate Change (IPCC) predicts an increase in global mean temperature of 1.8-40C by the end of the 21st century and a sea level rise of 0.18-0.59 m (IPCC 2007). Past, current, and future emissions of greenhouse gases, especially CO2, will contribute to ocean acidification of 0.14-0.35 units (IPCC 2007). For natural populations that have evolved to thrive in certain environments, these global climate changes will present novel selection pressures to which they may or may not be able to adapt. Climate change has the potential to act as a “hard” selection pressure, causing rapid selection for stress-tolerant genotypes (Reusch & Wood 2007). Of course, a population can only respond to this selection pressure if it has a variable trait, a form of which will help it survive in its new environment. If there is a variable trait to be selected for, there will also need to be rapid evolution of that trait to occur simultaneously with ecological dynamics while also altering those same dynamics towards the population’s favor (Hairston et al. 2005). The following provides a review of genetic changes in wild populations in response to changes in the environment, an analysis of the relationship between the rates of genetic and climate changes, and the benefits and shortcomings of using wild populations to study genetic change.

Any consistent change in the environment will place a selection pressure on local populations, resulting in acclimatization, adaptation, or extinction. There are limits to acclimatization since, for the most part, it represents phenotypic plasticity and no real genetic change. A population needs to undergo microevolution to respond to climate change since cues for plastic responses may become uncoupled from the environment and the complicated organism-environment interaction may incur selection on multiple life history traits at once (Visser 2008). Global climate change will be long-term and pervasive and many populations will need to adapt to survive. Selection acts on phenotypic traits, which are the interface between an organism and its environment. In order for selection to work, there needs to be sufficient variability in a trait (Graur & Li 2000). With consistent selection pressure and trait variability, adaptation can occur through the shift in phenotype distribution over generation caused by a change in genotype (microevolution) or phenotypic plasticity (Visser 2008). If the selection pressure is stabilizing on the selected trait, then adaptation can occur; if it is directional selection then the phenotype can occur without a change in genotype (Visser 2008; Gienapp et al. 2008). If an evolutionary or plastic response to the environmental change is impossible, then physiology can change but the population will go extinct locally (Chown et al. 2010). In order to interpret a population’s response as being a direct result of climate change, there needs to be evidence of selection on a trait, the selection needs to be caused by or linked to climate change, and change in the genetics underlying the trait (Gienapp et al. 2008). The rate and extent of adaptation to climate change depends on the magnitude and rate of climate change, the variety of ecological variables individual genotypes encompass, the distribution and genetic variation of relevant traits, gene flow, demographic flux of populations, and changing interspecific competition based on different responses to climate change (Davis et al. 2005). Constraints to adaptation arise from lack of trait variability, inbreeding due to bottlenecked populations, and correlations among traits (Gienapp et al. 2008; Davis et al. 2005). The mechanisms behind adaptation to climate change are much more complex than a simple selection-adaptation relationship. Future evolution potential depends upon a population’s evolutionary history and how much variation has been maintained in traits that may not yet be important for survival. Long-term evolutionary studies, local adaptation to environmental pollution, and climatic events provide evidence for the potential of a variety of species to adapt to novel environments.

A wide range of studies has already been accomplished that provide support for predictions of the effects of future climate change on genetic changes in populations. The studies reviewed below are drawn from a number of taxa and ecosystems, but they all demonstrate evidence of how climate change at different scales can affect wild populations. The IPCC defines climate change as any change, natural or anthropogenic, over time that can be identified by changes in mean or variability (IPCC 2007). I apply this definition to include adaptive radiation in *Daphnia pulex* (habitat change), pollution events in east coast rivers, and more traditional climate change such as ocean warming, seasonal shifts, and El Niño events. Each of these studies gives insight into the genetic signatures of adaption to a new environmental regime and sometimes the actual adaptive mechanism that allowed for exploitation of a newly changed habitat.

The genome of *Daphnia pulex* provides evidence of the adaptive mechanisms of exploiting an aquatic habitat and how an organism can thrive in a wide variety of environmental regimes. Nine gene families have expanded independently in *Daphnia* spp. and other aquatic lineages, including for photoreceptive and photoresponsive mechanisms (Colbourne et al. 2011). The adaptive expansion of these particular gene families was most likely in response to a more complex light regime in an aquatic habitat. *Daphnia* also exhibits very high rates of gene duplication, but 47% of these paralogs are non-allelic, supporting evidence for concerted evolution on protein coding sequences (Colbourne et al. 2011). Some paralogs with low sequence divergence even show differential gene expression in different environmental conditions, hinting at the mechanism behind these functionally diverging genes (Colbourne et al. 2011). As genes duplicate they are co-opted for new functions, potentially in a broader range of environmental conditions. Colbourne et al. (2011) posited that the functionally divergent gene duplicates are maintained via preservation by entrainment, where interaction with other suites of genes maintains a novel function for a newly duplicated gene. Of course, *Daphnia* had evolutionary time (in its typical definition) to evolve these mechanisms of habitat exploitation, but its ability to adapt to a wide range of habitats may make it a more robust species in the face of future climate change.

Old World anchovies, *Engraulis* spp., inhabit coastal upwelled environments off of Europe, Japan, South Africa, and Australia. Changes in historic climate regimes have led to a variety of population distribution shifts and extirpations in this group (Grant & Bowen 2006). Climate change during the Pleistocene, characterized by changes in temperature and sea level, affected population demography in both the southern and northern hemispheres (Grant & Bowen 2006). Anchovies in Europe, Japan, and Australia all have much higher haplotype and nucleotide diversities than the South African population. Relationships between haplotypes indicate that South Africa and Australia probably experienced local extirpations during climate regime shifts and were recolonized by northern hemisphere anchovies (Grant & Bowen 2006). The northern hemisphere populations have access to longer coastlines, providing suitable habitat for range shifts during climate change; South Africa and Australia do not have coastlines along which the anchovies could have migrated. In this case, related species (potentially historic sub-species) inhabited a variety of habitats and the northern hemisphere populations were able to move to suitable waters to avoid a harsh climate. Southern hemisphere species/populations were not able to avoid the adverse conditions and were not able to adapt to the dramatically changing environment and went locally extinct until conditions allowed recolonization. It is possible that such a scenario could occur in future climate change, but there would need to be suitable habitat for refugia left in part of the species’ range and habitable conditions would need to return at some point in the future for recolonization to happen.

On a shorter time scale, genetic change can occur in response to discrete environmental changes when alleles for adaptation to that change are already present in the population. Both killifish (*Fundulus heteroclitus*) and tomcod (*Microgradus tomcod*) have adapted to highly polluted environments in a span of 50-100 years (Whitehead et al. 2010; Wirgin et al. 2011). *F. heteroclitus* have developed pollution tolerance to polychlorinated biphenyls (PCBs) in heavily polluted estuaries on the Atlantic coast. Killifish that are native to non-polluted estuaries do not demonstrate the same tolerance to PCBs. Fish from both types of population were reared in the lab and their respective F2 generations were exposed to varying amounts of PCBs (Whitehead et al. 2010). Offspring from the tolerant population showed much greater pollution tolerance than those from the sensitive population, demonstrating that the tolerant phenotype is heritable. The sensitive population up-regulated genes in the aryl hydrocarbon receptor (AHR) pathway in a dose-dependent response to PCBs, whereas a similar up-regulation was not seen in the tolerant population, except at aberrant phenotypes for high doses (Whitehead et al. 2010). Similar mechanisms are at play in a population of tomcod in the Hudson River (HR). Between 1947 and 1976, GE facilities released 590,000 kg of PCBs into the river. In a comparison of the AHR alleles between HR and two reference rivers, four out of five polymorphisms are fixed in the HR population (two synonymous, one nonsynonymous, and one 6-nucleotide deletion; Wirgin et al. 2011). The other AHR allele seen in the reference populations is only seen in heterozygotes in the HR tomcod. There is also no evidence of a genetic bottleneck in the HR population based on mtDNA sequence (Wirgin et al. 2011). The adaptive mechanism that makes the HR allele more suitable for a polluted habitat is that it has a binding affinity for toxicants that is five times lower than the other allele (Wirgin et al. 2011). Both of these studies show evidence of rapid genetic change in wild populations when faced with a strong and consistent selection pressure. The analysis in Wirgin et al. (2011) gives stronger support for the adaptive mechanisms and population history behind the adaptation, but it is probably safe to assume that a similar situation occurred for the killifish. The allele for PCB tolerance was already present in both tomcod and killifish, as evidenced by its current occurrence at low frequencies in other tomcod populations (Wirgin et al. 2011). As their natal estuaries became more polluted, only the relative fitness of the tolerant individuals dramatically increased. In tomcod, a population bottleneck may have been avoided since gene flow still seems to occur with other nearby populations that have low frequencies of the tolerant allele (Wirgin et al. 2011).

Genetic changes in response to climate shifts in temperature have already occurred in marine and terrestrial populations in response to El Niño events and the ongoing process of global climate change. The classic example of Darwin’s finches, *Geospiza* spp., on the Galápagos islands hints at the trade-off between adaptation and population size that may affect populations in future climate scenarios. When a favorable trait for a new climate regime is only apparent in a small percentage of a population, then selection will cause a dramatic decrease in population size and possibly a genetic bottleneck. The El Niño of 1982-1983 changed the food availability on Daphne Major, selecting for finches that could forage on the newly available types of seeds (Grant & Grant 1993). *G. scandens*, a specialist on cactus seeds, which became rare after 1983, dropped dramatically in abundance. *G. fortis* is more of a generalist, but it also suffered some decreases in population size since only small birds were able to thrive – there were no large seeds for the larger birds (Grant & Grant 1993). In *Geospiza*, beak traits are highly heritable and the smaller *G. fortis* were able to reproduce and exploit the new resource regime. In a quantification of evolutionary changes versus ecological changes, Hairston et al. (2005) determined that in Darwin’s finches, evolutionary change occurred 2.2 times faster than ecological change.

Sometimes environmental changes already lie within the tolerance limits of an extant population. The American red squirrel, *Tamiasciurus hudsonicus*, in the southwestern Yukon, Canada has experienced climate warming of spring temperature 20C over the past 27 years. The population of squirrels has advanced the timing of breeding by 18 days over that time (Réale et al. 2003). A large part of this shift is due to plasticity in *T. hudsonicus*’ response to increased resource availability, but a significant portion is microevolution in response to selection for earlier breeders (Réale et al. 2003). *T. hudsonicus* has both the phenotypic and genetic variability necessary to effect this phenological shift and adapt to climate change. Another opportunist in recently warmed environments is the barrens-forming urchin, *Centrostephanus rodgersii*. The urchin has been expanding from its native habitat near Australia poleward as waters warm and become more habitable. Gene diversity in the expansion zone is approximately equivalent to that in the source population and there is no evidence of a founder or bottleneck effect (Banks et al. 2010). *C. rodgersii* appears to be robust to and even profit from ocean warming and it may do well in acidified waters since echinoderms appear to be relatively amenable to decreased pH (Dupont et al. 2010). In this case of organism-environment interaction, there is a release of selection pressure previously imposed by the cooler southern waters and the urchin is able to expand its range into new territory.

In the examples given above, the rate of genetic change closely mirrors the rate of climate change, although there is a bias in the review since populations not studied could be extirpated. In the case of killifish, tomcod, Darwin’s finches, and squirrels the genetic and phenotypic variability were already present in the populations at low frequencies before they were faced with the selection pressures of environmental change. Anchovies also had variability in their range capabilities that allowed for long-term (thousands of years) maintenance of populations that span both hemispheres. Herbaceous species introduced to North America and Europe show genetic differentiation and clinal variation in response to climate change over time periods of decades to a century (Davis et al. 2005). The pitcher plant mosquito effected a genetic change in its critical photoperiod in response to environmental change over five years (Bradshaw & Holzapfel 2001). Thus, the scale of adaptation matches well with the scale of change. It is clear from these examples that this broad range of taxa possess variability in some form that allows them to adapt to the challenges that they have so far faced. Change in phenotype (R) is determined by selection pressure (s) and heritability (h2) so that R= h2 \* s (Falconer & Mackay 1996). In all cases, the adaptive traits were at a high enough frequency and had great enough heritability in each population so that individuals were able to reproduce successfully after the onset of the environmental change. The selection pressure was also very strong, necessitating a phenotypic shift.

In cases where a new phenotype must evolve because it is not yet present in the population, there would be a greater lag in evolution of a better-adapted phenotype behind the environmental change. Also, when there is decreased genetic variance in a population there is a greater lag between the mean phenotype and the optimum phenotype under the specific environmental conditions (Bürger & Lynch 1995). This lag increases the selection pressure, thus decreasing effective population size and further decreasing genetic variance through drift. Without mutation to rescue the lagging mean phenotype, the population will likely go extinct (Bürger & Lynch 1995). Irrespective of amount of genetic and phenotypic variability, a population can respond evolutionarily to low variability in environmental change for a long time, however, when the change is fast and highly variable, it greatly increases the likelihood of extinction (Bürger & Lynch 1995). In rapid climate change there is also the risk of countergradient variation, where, due to removal of environmental constraints on the pre-change phenotype, a population can appear to be under selection (Conover & Schultz 1995; Gienapp et al. 2008). In this scenario, phenotype can be diverging without any underlying genetic change so no adaptation to environmental conditions happens (Gienapp et al. 2008). In cases of successful adaptation to rapid environmental change, the population needs the capability to quickly increase the allele frequency for the selected trait, probably within one to two generations. A risk to this rapid selection is that hitchhiking of genes deleterious for another trait could occur (Gillespie 2004). Whether the hitchhiking trait is currently important or will become important once the population is faced with a subsequent environmental change, it could lead to extirpation. To keep pace with climate change, a population needs to have a number of genetic and phenotypic resources before the change occurs. The beneficial trait needs to be present to a certain degree in the population and heritable; the environmental change needs to have low variance; the trait under selection cannot be linked to adverse phenotypes; and strong enough selection needs to be acting so that the new phenotype replaces others quickly.

There are a number of benefits and shortcomings to studying genetic change in wild populations, but generally the benefit is that the population is responding to its natural environment on a relevant timescale and the shortcoming is the lack of control over the study system. Within a population’s natural setting, all observations are relevant to the organism’s biology and evolutionary history. There are multiple co-occurring stressors, the effects of which are sometimes difficult to separate, but which are more relevant to the studied population than a single stressor in a lab. In studying adaptation to an environmental change, that change will be necessarily important within the study system and ecologically relevant. It is also possible to observe true acclimatization and adaptation over realistic timescales for the study organism, although frequently longer generation times make this difficult. A wild population study also allows the researcher the chance to work within the structure and natural variability of the population. Once an organism is domesticated or raised in the lab, it is no longer in its natural environment to which it is evolutionarily adapted. In studying gene expression across a natural cline of *Fundulus* spp. fish, it was possible to discern which genes were differentially expressed in each population, giving evidence for mechanisms of local adaptation (Oleksiak et al. 2008). A similar experiment would be impossible on a non-wild population, demonstrating the insight into evolutionary processes that can be gleaned from natural populations.

As ideal as it seems to study a natural population’s response to environmental change in its native habitat, there are a number of inherent difficulties in working in such an uncontrolled environment. It is much harder to study multiple generations of wild animals, especially when the heritability of a certain trait is under question. Frequently, the heritability of a trait in a wild population can be too low to detect in a short-term study (Visser 2008). In a population of great tits, phenotypic response to environmental change masked the effects of microevolution altogether (Gienapp et al. 2006). It is also frequently difficult to know the evolutionary and ecological history of a natural population. Immigration occurs between wild populations and immigrants may have experienced different selection pressures, thus changing the average population response to local pressure (Gienapp et al. 2008). Teasing apart acclimatization (phenotypic plasticity) and adaptation is also difficult in a wild population and requires studies over generations of a pedigree (Visser 2008). The inherent variability in wild populations can occlude the presence or frequency of the adaptive trait of interest. For example, in killifish along a geographic cline from Maine to Georgia that spans a 12.50C difference, there were greater differences in intrapopulation gene expression than interpopulation expression (Whitehead & Crawford 2006). Along this same vein, countergradient changes in phenotype and genotype during environmental selection can mask the effects of microevolution (Merilä et al. 2001). Selection and heritability can also be misestimated due to parallel changes in the environment and evolution (Gienapp et al. 2008). Finally, results of selection can be confounded by spatial or temporal autocorrelations of environmental effects among relatives (Gienapp et al. 2008). In general, the complexities of the organism-environment interaction and of the genome make field experiments on wild populations difficult to fully interpret. It can be difficult to discern what the mechanism of the physiological and genetic responses are and how various genes interact with each other.

The assessment of genetic change in response to climate change can be accomplished in wild populations where conclusions are more evolutionarily and ecologically meaningful. The wild-based studies should be supplemented by laboratory research that provides solid supporting evidence for the evolutionary principles in question. For example, it would be difficult to determine the lack of correlation between the evolution of gene sequence and gene expression across 7 strains/lineages of any other organism than yeast (Tirosh & Barkai 2008). The full characterization of the yeast genome, known differences between strains, and a controlled environment facilitated this study. Although the same lack of association was noted in wild ecotypes of lake whitefish (Jeukens et al. 2010). The conclusions in Jeukens et al. (2010) lend evolutionary significance to the findings in yeast. As the effects of climate change become more and more apparent, a plethora of natural study systems will be available for observing and recording the effects on genetic change. Of course, if the environmental change proves to be beyond the adaptive capacity of the population, there will be limited opportunity to understand the interplay between environmental change, selection and adaptation.

Emma, you have a lot of information here. I particularly liked the case studies you presented. However, this could have been organized a bit better. Generally, it’s a good idea for a multipart question to have subquestions as headings. Here, it is difficult to work out what you are addressing where. For example, the first few paragraphs before case studies seem to use buzzwords without clear definition what they are and without clear connection. Towards the end of the case studies, it gets a bit confused again: I don’t understand what the squirrels have to do with sea urchins – they are different taxa, but more importantly there seem to be different mechanisms at work, without a clear comparison.

This is for organization, which can’t be completely separated from content, but I try. You did cover a lot of information, but I was expecting a more through treatment of approaches, at least a clear separation of molecular and quantitative genetic approaches and some discussion how genetic changes (as opposed to purely phenotypic change) can be shown in wild populations. If I look at the three parts of the question:

A: examples: that’s very good – you missed a bit of the literature, but you covered most aspects

B: rates: you make a very good point about observational bias, and you discuss the rates, so that’s good. Some discussion of how rates could be measured would be good – you compare ecological and genetic change quantitatively in finces, without defining either. But that’s good.

C: potential and shortcomings – as mentioned above, that aspect is a bit disappointing, but I am hoping this is in the other question….

**References**

Banks, S.C., S.D. Ling, C.R. Johnson, M. P. Piggott, J.E. Williamson, and L.B. Beheregegaray. 2010. Genetic structure of a recent climate change-driven range extension. *Molecular Ecology*. 19: 2011-2024.

Bradshaw, W.E., and C.M. Holzapfel. 2001. Genetic shift in photoperiodic response correlated with global warming. *PNAS*. 98(25):14509-14511.

Bürger & Lynch. 1995. Evolution and extinction in a changing environment: a quantitative-genetic analysis. *Evolution*. 49(1): 151-163.

Chown, S.L., A.A. Hoffmann, T.N. Kristensen, M.J. Angilletta Jr., N.C. Stenseth, and C. Pertoldi. 2010. Adapting to climate change: a perspective from evolutionary physiology. *Clim. Res.* 43: 3-15.

Colbourne, J.K., M.E. Pfrender, D. Gilbert, W.K. Thomas, A. Tucker, T.H. Oakley, S. Tokishita, A. Aerts, G.J. Arnold, M.K. Basu, D.J. Bauer, C.E. Caceres, L. Carmel, C. Casola, J.-H. Choi, J.C. Detter, Q. Dong, S. Dusheyko, B.D. Eads, T. Frohlich, K.A. Geiler-Samerotte, D. Gerlach, P. Hatcher, S. Jogdeo, J. Krijgsveld, E. V. Kriventseva, D. Kultz, C. Laforsch, E. Lindquist, J. Lopez, J.R. Manak, J. Muller, J. Pangilinan, R.P. Patwardhan, S. Pitluck, E.J. Pritham, A. Rechtsteiner, M. Rho, I.B. Rogozin, O. Sakarya, A. Salamov, S. Schaack, H. Shapiro, Y. Shiga, C. Skalitzky, Z. Smith, A. Souvorov, W. Sung, Z. Tang, D. Tsuchiya, H. Tu, H. Vos, M. Wang, Y.I. Wolf, H. Yamagata, T. Yamada, Y. Ye, J.R. Shaw, J. Andrews, T.J. Crease, H. Tang, S.M. Lucas, H.M Robertson, P. Bork, E.V. Koonin, E.M.Zdobnov, I.V. Grigoriev, M. Lynch, and J.L. Boore. 2011. The Ecoresponsive genome of *Daphnia pulex*. *Science*. 331(6017): 555-561.

Conover, D.O. and E.T. Schultz. 1995. Phenotypic similarity and the evolutionary significance of countergradient variation. *TREE*. 10(6): 248-252.

Davis, M.B., R.G. Shaw, and J.R. Etterson. 2005. Evolutionary responses to changing climate. *Ecology*. 86: 1704-1714.

Dupont, S., O. Ortega-Martínez, and M. Thorndyke. 2010. Impact of near-future ocean acidification on echinoderms. *Ecotoxicology*. 19(3): 449-462.

Falconer, D.S., and T.F. Mackay. 1996. *Introduction to Quantitative Genetics*. Longman, NY.

Gienapp, P., E. Postma, and M.E. Visser. 2006. Why breeding time has not responded to selection for earlier breeding in a songbird population. *Evolution*. 60: 2381-2388.

Gienapp, P., C. Tplitsky, J.S. Alho, A. Mills, and J. Merilä. 2008. Climate change and evolution: disentangling environmental and genetic responses. *Molecular Ecology*. 17: 167-178.

Gillespie, J.H. 2004. Population Genetics: A Concise Guide. Second Edition. The Johns Hopkins University Press, Baltimore, MD.

Grant, W.S. and B.W. Bowen 2006. Living in a tilted world: climate change and geography limit speciation in Old World anchovies (*Engraulis*; Engraulidae). *Biological Journal of the Linnean Society*. 88: 673-689.

Grant, B.R. and P.R. Grant. 1993. Evolution of Darwin’s finches caused by a rare climatic event. *Proceedings: Biological Sciences*. 251(1331): 111-117.

Graur, D. and W.-H. Li. 2000. Fundamentals of Molecular Evolution, Second Edition. Sinauer Associates, Inc., Sunderland, MA.

Hairston, N.G., S.P. Ellner, M.A. Geber, T. Yoshida, and J.A. Fox. 2005. Rapid evolution and the convergence of ecological and evolutionary time. 8(10): 1114-1127.

IPCC 2007. Contribution of Working Groups I, II, and III to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. R.K. Pachauri and A. Reisinger (Eds). IPCC, Geneva, Switzerland. pp 104.

Jeukens. J., S. Renaut, J. St.-Cyr, A.W. Nolte, and L. Bernatchez. 2010. The transcriptomics of sympatric dwarf and normal lake whitefish (*Coregonus clupeaformis* spp., Salmonidae) divergence as revealed by next-generation sequencing. *Molecular Ecology*. 18(24): 5389-5403.

Merilä, J., L.E.B. Kruuk, and B.C. Sheldon. 2001. Cryptic evolution in a wild bird population. *Letters to Nature*. 412: 76-79.

Oleksiak, M.F., G.A. Churchill, and D.L. Crawford. 2008. Variation in gene expression within and among natural populations. *Nature Genetics*. 32: 261-266.

Réale, D., A.G. McADam, S. Boutin, and D. Berteaux. 2003. Genetic and plastic responses of a northern mammal to climate change. *Proc.R.Soc.Lond.B.* 270(1515): 591-596.

Reusch, T.B.H. and T.E. Wood. 2007. Molecular ecology of global change. *Molecular Ecology*. 16: 3973-3992.

Visser, M.E. 2008. Keeping up with a warming world; assessing the rate of adaptation to climate change. *Proc. R. Soc. B.* 275(1635): 649-659.

Tirosh, I. and N. Barkai. 2008. Evolution of gene sequence and gene expression are not correlated in yeast. *Trends in Genetics*. 24(3): 109-113.

Whitehead, A., and D.L. Crawford. 2006. Neutral and adaptive variation in gene expression. *PNAS*. 103(14): 5425-5430.

Whitehead, A., D.A. Triant, D. Champlin, and D. Nacci. 2010. Comparative transcriptomics implicates mechanisms of evolved pollution tolerance in a killifish population. *Molecular Ecology*. 19(23): 5186-5203.

Wirgin, I., N.K. Roy, M. Loftus, R.C. Chambers, D.G. Franks, and M.E. Hahn. 2011. Mechanistic basis of resistance to PCBs in Atlantic tomcod from the Hudson River. *Science*. Doi: 10.11126/science.1197296.