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EDITORIAL

Editorial: evolutionary medicine special issue

For a long time, biologists focused on accruing data without having a general framework in which to interpret their results. A suitable analogy would be the way that one might use observation to discern the details of how pieces move on a chessboard without knowing the object of the game. In chess, once the object of the game is understood, the patterns of movement, and how they fit together in sequence, suddenly become much clearer. This appreciation of the reasons behind the patterns brings with it a level of understanding that is not possible through detailed examination of each piece's movement in isolation.

Analogous understanding is possible in biology. The great insights of Charles Darwin gave biologists the 'object of the game': evolutionary biology provides an extremely powerful organizational framework in which to make sense of a bewildering array of observations. Evolutionary principles have allowed biologists to understand why biological patterns occur in the way that they do, and scientists now regularly use these principles to enormous advantage in many contexts.

Despite its power, the principles of evolutionary biology remain conspicuously absent in much of medical science. Most modern physicians receive comprehensive training in several of the life sciences including anatomy, physiology, immunology, microbiology, biochemistry, and genetics, but seldom do they receive much training in evolutionary biology. At first glance, this is perhaps understandable. Given the long list of subjects that must be mastered by medical students, it might seem impractical to ask for more. It is quite likely, however, that infusing medical science with principles from evolutionary biology will have the same positive effect that it has had in other areas of life science. Not only does evolution provide a unifying framework from which to understand the occurrence of disease and illness, but it can also suggest novel approaches to treatment as well. It therefore seems reasonable to expect that a modest investment in evolutionary training by medical scientists could yield considerable returns. This special issue of *Evolutionary Applications* is devoted to advancing this cause.

There are a number of other useful sources of information on evolutionary medicine, as well as a variety of scientific activities that are planned. The Evolution and Medicine Review (evmedreview.com) provides news and commentary on current developments in the field, and the Evolution & Medicine Network (evolutionandmedicine.org) lists books, meetings, courses, and other resources for those interested in orienting themselves to this rapidly emerging field. Randy Nesse, who co-authored the book that founded the field, is one of the guiding lights for both efforts. And shortly after this issue goes to press, the National Academy of Sciences (USA) will host a Sackler Symposium on Evolution in Health and Medicine (http://www.nasonline.org/site/PageServer?pagename=Sackler_Evolution_Health_Medicine). Thus, this special issue is one of the many efforts that recognize the value of evolutionary insights into medical issues. That evolutionary thought should now be receiving some recognition as helpful in medicine reflects the growing recognition that its insights can save lives and reduce suffering by suggesting important alternative explanations, and reducing the potential for unpleasant surprises.

This special issue

The articles in this special issue are a collection of both primary research papers and syntheses that illustrate the utility of taking an evolutionary perspective on topics relevant to human health and disease. Despite the relative infancy of evolutionary medicine, researchers have already applied evolutionary insights to a wide array of medical issues. Those addressed here include the evolution of pathogens and infectious diseases, the evolution and spread of drug resistance in pathogen populations, the evolutionary biology of cancer, human genetics and evolution, and the evolutionary biology of immune responses.

With their long experience in the evolution of host–parasite interactions, evolutionary biologists contribute naturally to medicine through the study of infectious diseases, where they have developed both a wealth of ideas and some powerful model systems. The first paper by Reece et al. (2009) provides an excellent example: the authors develop evolutionary explanations for patterns of pathogenesis in malaria and how they are expected to respond to environmental factors. They also review some exciting recent experimental results that test these predictions using a mouse model system. Joseph et al. (2009) present primary research results from an elegant evolutionary model system of bacteria and phage, demonstrating that bacteria infected with phage can become more susceptible to further infection. Although these initial results come from an experimental system quite removed from human health, they are intriguing because they show that closely related pathogens can differ markedly in their susceptibility to co-infection. This is significant because theoretical considerations show that the extent of co-infection can greatly affect the evolutionary dynamics of pathogens and thereby our ability to control disease. The third contribution on infectious diseases, by Brown et al. (2009), reviews ideas about how bacterial pathogens compete with one another within a host. Competition can occur via classical alleleopathy, through phage-mediated killing, and through differential susceptibility to host defenses. The authors make an interesting suggestion for how the significance of these reactions can be understood within an evolutionary theory of social interactions.

Another area of medical research in which evolutionary biology has much to offer is the emergence and spread of drug resistance in pathogens. This has clearly become an issue of central concern in modern medicine. Unfortunately, even when medical practitioners recognize the spread of resistance as an evolutionary problem, they seldom consider how an understanding of evolutionary biology might be of further use. But the evolution of drug resistance goes far beyond the simple observation that drug resistance evolves. For example, we can use evolutionary knowledge to design drug treatment protocols that slow the spread of drug resistance and perhaps even design interventions that use evolutionary change to our advantage.

Two contributions to this special issue examine the evolutionary biology of drug resistance in detail. Read and Huijben (2009) provide a trenchant overview of the evolution of drug resistance in malaria. They highlight several fallacies in current thinking on drug use and go on to describe several very interesting, and still unanswered, evolutionary questions. They make the provocative suggestion that current drug use protocols are dangerously suboptimal from an evolutionary standpoint. In a similar vein, Pongtavornpinyo et al. (2009) present original research on the appearance of drug resistance mutants in malaria using mathematical models. By depicting the malaria life cycle in detail, their models provide compellingly simple expressions for the probability of resistant mutants arising in different stages of the life cycle. One important conclusion is that, in the presence of drug use, the mutants that are selected for resistance will most likely arise during the blood stage portion of the life cycle.

An area of rapidly increasing interest in evolutionary medicine is the application of evolutionary principles to the biology of cancer. Evolutionary change by natural selection occurs whenever there is heritable variation among individuals in reproductive capacity: precisely the properties of individual cells within many cancerous tumours in humans. Thus, it is increasingly thought that many facets of cancer biology, including incidence, progression, metastasis, and the emergence of resistance to treatment, can be better understood by focusing on the evolution of cell populations within an individual. Pepper et al. (2009) provide a very nice summary of the state of play together with intriguing ideas for future research. As they point out in their article, taking an evolutionary perspective could yield both ideas for novel and more lasting treatments, as well as basic insights that emerge from applying current ideas in evolutionary biology (e.g., phylogenetics).

There are many important and devastating illnesses in humans in addition to infectious diseases and cancer, and many of these are influenced by a significant genetic component. Here again an evolutionary perspective is natural and helpful. The genetic composition of the current human gene pool, including those genes that are implicated in human illness, has arisen via descent with modification from that of ancestors. Understanding this evolutionary process can reveal the origins of genetic disorders and some of the reasons for their existence. Modern techniques in molecular biology, including the sequencing of the human genome (along with that of other species) have greatly increased our ability to discover the underlying genetics of such diseases.

Here, Heyer and Quintana-Murci (2009) provide an excellent overview of how genetic techniques can detect the effects of natural selection in the human genome. They illustrate these approaches both for human adaptation to historical environmental conditions and for understanding the genes underlying some important human diseases. Crespi et al. (2009) then provide a comprehensive examination of the genetics underlying certain neuro-developmental disorders in humans. They focus on the cognitive and behavioural consequences of copy number variation in genes, and use association studies, along with analyses aimed at detecting selection in the human genome, to understand the causes of such disorders. The authors make the very interesting suggestion that copy number variation gives rise to phenotypic variation along an autistic-psychotic spectrum. Varki et al. (2009) then present an interesting perspective on the evolutionary biology of heart disease. Instead of looking within humans, the authors exploit the evolutionary relationship between humans and chimpanzees to better understand the causes of heart disease in humans. Surprisingly, although both species suffer from heart disease, the underlying proximate causes in each appear to be fundamentally different.

The final topic examined here is the evolutionary biology of immune responses. The striking complexity of the vertebrate immune system has been shaped by natural selection in response to challenges by pathogens throughout its evolutionary history. The maintenance and use of an immune system does not come without energetic costs; and therefore we expect immune systems to have evolved different responses to the costs and benefits of defense under different conditions. One of the chief goals of evolutionary immunology is to understand and predict how these differences play out.

Sadd and Schmid-Hempel (2009) present a lucid, and readily accessible, guide to the main principles of evolutionary immunology. They review some of the evidence for costs of immunity in various study systems, describe how different factors can give rise to different levels of investment in components of immunity, and discuss interesting ways in which pathogens can evolve to evade or manipulate host immune responses. Fairlie-Clarke et al. (2009) then probe the cross reactivity of adaptive immune responses to different antigens. Cross-reactive immune responses might arise simply through constraints on antigen recognition, but evolutionary immunology also suggests that it has evolved as an adaptive strategy. The authors carefully contrast these possibilities and offer several promising directions for future research. Finally, given that the importance of immunity to infection is likely to vary across life stages, it is to be expected that this system be physiologically coupled with other aspects of growth and development. Kopp and Medzhitov (2009) present stimulating ideas that tie together evolutionary immunology and the rich evolutionary literature on senescence and aging. They suggest that infection with pathogens might select for the ability to alter investment in growth and reproduction versus somatic maintenance. The authors review available evidence and suggest how certain components of the immune system might mediate these effects.

In closing, we wish to mention that although the collection of articles presented here provides a compelling case for the utility of evolutionary principles in medicine, this is really only half the story. Evolutionary medicine, like all interdisciplinary subjects, is at its best when information flows in both directions, and medical studies can yield valuable returns in evolutionary biology as well. The multi-cohort data-bases available for humans reflect long-term studies in which thousands of individuals and their offspring have been followed from birth to death – no other species has been studied in as much detail. There is also an accumulating set of impressive cases in which studies undertaken for medical reasons have shed new light on basic evolutionary issues: Sebastian Bonhoeffer's work on the maintenance of recombination in HIV is one good example. The focus on only one side of the story in this special issue is primarily a reflection of the scope of the journal (i.e., the application of evolutionary biology to other disciplines). We encourage interested readers to consult other sources, including Nesse and Williams (1996), Stearns and Koella (2008), Trevathan et al. (2008), the Henry Stewart talks on evolutionary medicine (http://www.hstalks.com/main/browse_talks.php?father_id=20) and the talks given at the Yale Symposia on Health and Disease (http://www.yale.edu/evomedsymposia) for a treatment of other aspects of evolutionary medicine.

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