Conceptual Biological Research in Darwinian Medicine

Author: Apari Péter

Thesis points

The Doctoral School of Biology of the
Faculty of Natural Sciences of Eötvös Loránd University
Director: Dr. Anna Erdei, member of HAS, full professor

Doctoral Program in Theoretical and Evolutionary Biology
Director: Dr. Eörs Szathmáry, member of the HAS, full professor

Supervisor: Dr. Viktor Müller, PhD, research assistant professor
Department of Plant Taxonomy, Ecology and Theoretical Biology

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Aims and Methods

In my dissertation I examined the evolutionary background of infectious diseases with the tools of conceptual biology. In particular, I investigated the evolution of sexually transmitted infections, the adaptive phenotypic plasticity of the virulence of the human microbiome, and the evolutionary logic of sepsis.

The methodology of my dissertation was purely qualitative, placing my work in the recently developed field of conceptual biology. The essence of conceptual biology is the generation of hypotheses, which has long been practiced by the synthesis of facts and observations, as is apparent, e.g., in the monumental work of Darwin. Similarly, Weissman used it in his germ-soma theory, and C. D. Darlington in the area of cell biology, which was very hostile and conservative to this kind of speculation at that time. The main difference between the age of Darwin, Weissmann and Darlington and our time is in the amount of information, which has undergone explosive growth to produce millions of new articles in the recent decades.

In the eighties Don Swanson, an information scientist (one of the first to turn towards bioinformatics), started to develop the methodology of literature mining to synthesize facts and observations (primarily in the medical sciences), and called attention to the increasing capacity and importance of this approach. The last decades of the 20th century then witnessed the explosion of biological data, creating a lot of hidden knowledge in the published literature, which can be “discovered” by compiling and linking independently obtained observations. Then a paper by Blagoskonny and Pardee heralded the dawn of conceptual biology: the authors pointed out that the rapid expansion of biological knowledge has effectively turned this approach into a new field of biology in its own right. This is indicated also by the rapid proliferation of article types (“Hypothesis”, “Opinion”, “Perspectives” etc) dedicated to conceptual biology, and an increasing number of journals (e.g., *Bioessays*, the *Trends* and *Nature Reviews* family) specialize on these kinds of publications.

Among the benefits of this approach, it is very cheap compared to expensive experimental work, and it is therefore more readily available to the scientists of low-income countries. Moreover, it is capable not only of generating new theories, but also testing the predictions of earlier hypotheses by identifying observations that had been unknown to (or ignored by) the original creators of the hypothesis. This approach can often be much more cost-effective than
conducting new experiments. However, the authors emphasize that this method does not substitute, but rather complements the classical experimental approach.

Results

1. The development of the adaptive sterilization hypothesis of sexually transmitted pathogens

In this work we argued that the capability of sexually transmitted infections to cause infertility is an evolutionarily adaptive trait.

1.1. We compiled data from the literature to demonstrate a bidirectional relationship between sexually transmitted pathogens and infertility: STI pathogens often cause infertility, and infertility facilitates (by destabilizing partnerships) the transmission of these pathogens.

1.2. We pointed out that the mechanisms of inducing infertility do not provide a direct competitive benefit for the parasites inside the host, but they might have costs; furthermore, these mechanisms affect targets that are involved in infertility very selectively.

1.3. We used evolutionary considerations to show that the two factors described above (plus additional observations) strongly argue that the pathogens’ ability to cause infertility is not a by-product but an adaptive trait.

2. The general theory of microbiome mutiny

Based on evolutionary considerations, it has been suggested that symbionts might benefit from increasing their virulence adaptively when the mortality of the host increases due to other reasons (unrelated to the symbionts). Recent research has revealed that many members of the human microbiome are indeed able to change their virulence adaptively. We show that the new results can be explained by evolutionary logic in the light of the earlier hypothesis.
2.1. We compiled data from the scientific literature to show that facultatively pathogenic members of the microbiome can indeed switch to high virulence when the health of the host declines.

2.2. We collected evidence that the symptoms associated with the high-virulence state of the pathogens indeed facilitate intensive short-term transmission.

2.3. We developed the criteria of the microbiome mutiny (detection mechanisms, phenotypic plasticity of virulence etc.), which can also be regarded as predictions. For microbes that are implicated in the ‘mutiny’ we predicted the testable presence of the required mechanisms.

2.4. We suggested that the molecular mechanisms of the microbiome mutiny might offer new therapeutic targets: by inhibiting these mechanisms, symptoms could be alleviated without killing the microorganisms.

3. The evolutionary logic of sepsis

Sepsis results from an intense immune reaction to systemic infection, and can frequently lead to the death of the host organism. From the perspective of the causative organisms, sepsis has been thought to be a non-adaptive accident that does not contribute to the transmission of the microbe. In our latest work we showed that some cases of sepsis might follow the logic of the microbiome mutiny, and the ability to cause sepsis might be an adaptive trait for the pathogens.

3.1. We identified the conditions that are needed for the evolutionary logic of the microbiome mutiny to apply to sepsis.

3.2. We pointed out that cadaver-borne transmission can turn death due to sepsis from a dead-end to a means of efficient transmission for the pathogen.

3.3. To enable further testing of the hypothesis, we compared in detail the predictions of the alternative interpretations of sepsis (‘classical’ vs. microbiome mutiny).
Publications linked to the thesis


2. Rózsa L, Apari P & Müller V (2015). From bad to worse: can our microbiome turn against us when we are old or seriously ill? *Biology Direct* 10: 3.


Other publications


Conferences

2016

Rózsa L, Apari P, Müller V. The facultative roles of the microbiome: essential mutualists, lethal pathogens, and decomposers. In: Luis Ovidiu Popa, Costică Adam, Gabriel Chişamera, Elena Iorgu, Dumitru Murariu, Oana Paula Popa (szerk.) International Zoological Congress of
2015

Apari P, JD De Sousa, Müller V. Why Sexually Transmitted Bacteria Tend to Cause Infertility: An Evolutionary Hypothesis In: 15th Congress of the European Society for Evolutionary Biology (XVth ESEB Meeting). Place and date of conference: Lausanne, Switzerland, 10.08.2015-14.08.2015. Université de Lausanne, pp. 293-294.

2014


2012