HFSP AWARDS 2019

RESEARCH GRANTS ABSTRACTS

Research Grants (Program Grants and Young Investigators) are listed separately, alphabetically. The first named for each award is the Principal Investigator.

NGHE Philippe,
Laboratoire de Biochimie, ESPCI, Paris, France
HAYDEN Eric,
Dept. of Biological Sciences, Boise State University, USA
RAMESH Arati,
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SMERLAK Matteo,
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Title: From self-reproduction to evolution in the RNA world

Abstract: Is evolution possible in the absence of template-based replication?

Evolution, in life as we know it, relies on the copying of DNA with errors, providing the basis of reproduction with heredity and variation. Likewise, in the hypothetical RNA world, copying of RNA with errors is thought to have played the same role. However, the high complexity of RNA polymerases suggests that replication must have been preceded by reproduction and evolution based on simpler catalysts. Reproduction can occur by autocatalytic synthesis of single ribozyme species from RNA fragments, or by collective autocatalysis of multiple ribozyme species, all denoted AutoCatalytic Systems (ACS). For ACS to evolve in an open-ended way, theory indicates that there must exist a large diversity of such ACS throughout the sequence space. Further conditions for evolution are that ACS must amplify within compartments (enabling reproduction with heredity), propagate to other compartments as a function of their differential amplification (selection), and that rare events trigger the appearance of novel ACS (variation).

We aim to test the hypothesis that RNA reproduction based on ACS is widespread in the sequence space, and from this diversity, demonstrate that evolution in ACS is indeed possible.

For this, we will generate a large landscape of self-reproducing molecules using the natural group I intron family as an input for statistical inference methods. Self-reproducers will be constructed by fragmentation of these ribozymes by generalizing the strategy formerly applied to a ribozyme from the Azoarcus bacterium, and developing innovative in vitro screening methods with droplet microfluidics. We will show how the autocatalytic dynamics of individual self-reproducers, and their propensity to catalyse the formation of other self-reproducers or self-reproducing networks, allow to implement the properties of reproduction with heredity and variation underlying evolution.

Evolution will be tested in bulk and in compartmentalized populations, by submitting ACS to cycles of incubation and propagation. Finally, the probability of emergence of evolution in ACS and its open-ended character will be assessed based on the density of functional reproducers and their evolutionary accessibility in the sequence space.