

1997 Hans Sigrist Prize



Jack W. Szostak

In 1997, I was honored to receive the Hans Sigrist Award, along with my colleague Gerald Joyce, in recognition of our development of technology for the directed evolution of RNA molecules. By applying the principles of natural Darwinian evolution to the laboratory manipulation of large populations of synthetic RNA molecules, we were able to evolve RNA molecules that stick tightly to a specific target molecule, while ignoring other molecules around it. These RNAs, known as aptamers, have many potential applications, including the treatment of certain diseases.

Later, we used the same methods to evolve, in the laboratory, RNA molecules that could catalyze a wide variety of chemical reactions. This was very exciting to us because it provided support for the theory that RNA could have played a crucial role in the early evolution of life, before the evolution of proteins. In order to explore this idea further, we decided to evolve

new catalytic RNAs, known as ribozymes, that would catalyze reactions relevant to early life. The Hans Sigrist Prize helped my laboratory to continue these RNA evolution experiments. In the years immediately after the Prize award, we were able to evolve new ribozymes that catalyzed acyl-transfer reactions, which are central to protein synthesis. These experiments showed that, in very early, primitive cells, RNA molecules could have facilitated all of the chemical steps required for protein synthesis, including the attachment of amino acids to their transfer-RNAs, and their subsequent assembly into long protein chains. The first step turns out to have considerable technological significance, as many laboratories around the world are trying to develop ways of incorporating non-standard amino acids into proteins. This work continues today in the laboratory of one of my former students has continued to develop improved ribozymes

that can charge tRNAs with amino acids, simultaneously lending support to the role of RNA in the origin and early evolution of life, and developing new tools for applied biotechnology.

The Hans Sigrist Prize provided extremely welcome recognition of the significance of my research in the area of directed evolution, and therefore helped to inspire me to continue and even expand our work in this field. The Prize money itself was very helpful to me in improving the quality of my laboratory. The Prize al-

lowed me to invite promising young scientists from other countries to interview for postdoctoral positions, and helped provide more opportunities for the students and postdocs in the lab to travel to present their findings at scientific meetings. In addition this unrestricted funding contributed to the support of undergraduate research training in the lab, and better access to scientific literature through improved computational infrastructure. I am very grateful for the recognition and support provided by the Hans Sigrist Prize.

Contact address:

Prof. Jack W. Szostak, Massachusetts General Hospital, Department of Molecular Biology, WEL 931, Boston MA 02 114, USA, E-mail: szostak@mdbio.mgh.harvard.edu