1997 Hans Sigrist Prize

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In 1997, together with Prof. Jack W. Szostak, I was awarded the Hans Sigrist Prize for our work concerning the evolution of RNA in the laboratory. These studies are relevant to understanding the origin of life on Earth. It is believed that an RNA-based genetic system, usually referred to as the «RNA world», preceded the DNA and protein-based genetic system that has existed on Earth for the past 3.5 billion years. Our research aims to recapitulate the biochemistry of the RNA world in the laboratory. Prof. Szostak and I have devised test-tube evolution methods that allow us to explore the catalytic potential of RNA, especially to search for RNA enzymes that have the ability to catalyze their own replication.

Since receiving the Hans Sigrist Prize on a crisp December afternoon seven years ago, my work on RNA evolution has continued. The funds from the Prize helped my laboratory to initiate a new line of investigation concerning the minimum compositional requirements for RNA-based evolution. RNA normally consists of four different nucleotide subunits: A, U, G, and C. But is this necessarily the case? In work published in 1999, we demonstrated how a four-letter RNA enzyme could be converted, through test-tube evolution, to a corresponding three-letter enzyme that completely lacks C. In 2001 we showed how a three-letter RNA enzyme could be evolved starting from a population of random-sequence molecules that contained only three letters, and showed how this three-letter enzyme subsequently could be evolved to a corresponding four-letter enzyme. Finally, in 2002, we began with the three-letter enzyme and evolved it to obtain an RNA enzyme that contains only two letters, lacking both C and G. Two different subunits are the minimum needed to carry genetic information and thus to provide the basis for Darwinian evolution.

The family of two-, three-, and four-letter RNA enzymes all catalyze the joining of RNA molecules through a reaction equivalent to that used to copy RNA molecules in biology. Employing the four-letter version of the enzyme, we directed it to join two RNA molecules to form an exact copy of itself. The copies in turn were able to do the same, resulting in the RNA-catalyzed replication of RNA. This system behaves autocatalytically, but it does not undergo Darwinian evolution because the copies are identical to the parents. Evolution, both in nature and in the test tube, requires heritable yet mutable genetic information.

The Hans Sigrist Prize, in addition to being a special honor, provided unrestricted research funds that enabled me to initiate studies that were more risky than would normally be supported by a government research grant. Once those studies began to bear fruit, it was possible to obtain additional funding from more traditional sources. Thus the Prize served as the seed that ultimately led to further advances in our research program. It also seeded what has become an ongoing scientific collaboration between Prof. Szostak and myself. Too often science is depicted as fierce competition between scientists as they race to make some important discovery. More often, however, it is the community of scientists working together that bring about new understanding, and discoveries are made nearly simultaneously by two or more individuals because the field is ripe for such a discovery. The Hans Sigrist Foundation recognized this in awarding the 1997 Hans Sigrist Prize to both Prof. Szostak and myself. I am pleased to report that the two of us have had many scientific discussions since that December day in Bern, and recently, together with Prof. Steven A. Benner, we were awarded a collaborative grant from the U.S. National Science Foundation to establish a Center for Chemical Bonding for the study of Darwinian chemical systems.

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