Houdini Proteins: Discovery and Applications of Ultrafast Inteins

Inteins are auto-processing domains found in organisms from all domains of life. These proteins are consummate molecular escape artists that spontaneously excise themselves, in a traceless manner, from proteins in which they are embedded. Chemical biologists have long exploited various facets of intein reactivity to modify proteins in myriad ways for both basic biological research as well as therapeutic applications. While many thousands of inteins have been identified at the sequence level, only a handful of these proteins have been characterized in any biochemical detail. Here I discuss our recent efforts to mine this genomic database, leading to the discovery of ultrafast split inteins that ligate proteins together several orders of magnitude faster than any inteins previously known. I will also discuss the remarkable folding properties of these split proteins, and how this has led to the development of new methods for the manipulation of protein structure in the test tube and in cells.

Professor Tom Muir is chair of the Department of Chemistry at Princeton University. He received his Bachelor of Science degree in chemistry from the University of Edinburgh in 1989, and his doctorate in chemistry from the same university in 1993, under the direction of Professor Robert Ramage. After post-doctoral studies with Stephen B.H. Kent at the Scripps Research Institute, he joined the faculty at the Rockefeller University in New York City in 1996, where he was the Richard E. Salomon Family Professor and director of the Pels Center of Chemistry, Biochemistry and Structural Biology. In 2011, Muir joined the Princeton Faculty as the Van Zandt Williams Jr. Class of ’65 Professor of Chemistry. He became chair of the department in 2015. He has published more than 150 scientific articles and has won a number of honors for his research, including the Burrough Wellcome Fund New Investigator Award, the Pew Award in the Biomedical Sciences, the Alfred P. Sloan Research Fellow Award, the Leonidas Zervas Award from the European Peptide Society, the Irving Sigal Award from the Protein Society, the 2008 Vincent du Vigneaud Award in Peptide Chemistry, the 2008 Blavatnik Award from the New York Academy of Sciences, the 2008 Distinguished Teaching Award from The Rockefeller University, the 2012 Jeremy Knowles Award from the Royal Society of Chemistry and a 2013 Arthur C. Cope Scholar Award from the American Chemical Society. Professor Muir is the recipient of a MERIT Award from the U.S. National Institutes of Health and is a Fellow of American Association for the Advancement of Science and the Royal Society of Edinburgh.