UNIVERSITÀ DEGLI STUDI FIRENZE

DICUS
DIPARTIMENTO DI CHIMICA
"UGO SCHIFF"
ECCELLENZA 2023-2027

Da un secolo, oltre.

UNIVERSITÀ DEGLI STUDI FIRENZE
PhD
Chemical Sciences

PROF. DR. TOM MUIR
PROFESSOR OF CHEMISTRY

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Thursday July 24, 2025

15:00

Aula 16

Blocco Aule - Campus Sesto Fiorentino

Via Bernardini 6, 50019 Sesto Fiorentino (Firenze)

Link for online connection
meet.google.com/cjf-durq-gjw

will present the lecture

Harnessing Inteins in Chemical Biology: From Ligases to Transposases and Logic Gates

Organised in the context of the PhD Programme in Chemical Sciences

You are kindly invited to participate

Prof. Dr. Anna Maria Papini
Coordinator of the PhD
in Chemical Sciences

Prof. Dr. Anna Maria Papini
Organizer

Biographical Sketch

Prof. Dr. Tom Muir, Professor of Chemistry
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Tom W. Muir received his B.Sc in Chemistry from the University of Edinburgh in 1989 and his Ph.D. in Chemistry from the same institute in 1993 under the direction of the late Professor Robert Ramage, FRS. Following postdoc studies with Stephen B.H. Kent at The Scripps Research Institute, Muir joined the faculty of The Rockefeller University in 1996, where he rose through the ranks eventually being appointed the Richard E. Salomon Family Professor and Director of the Pels Center of Chemistry, Biochemistry and Structural Biology. In 2011, Dr. Muir joined the faculty of Princeton University as the Van Zandt Williams Jr. Class of '65 Professor of Chemistry, serving as Chair of the Chemistry Department from 2015-2020.

A chemical biologist, Muir has made lasting contributions to the fields of peptide and protein chemistry. He has published over 270 peer reviewed articles (Scopus ID 7103048598 - 26,287 Citations by 16,217 documents, 261 Documents, 84 h-index) and has given many hundreds of lectures on his research, including some 50 named lectureships. He is well known for developing general methods for the preparation of proteins containing unnatural amino acids, posttranslational modifications (PTMs) and isotopic probes. These chemical tools, now widely employed in academia and industry, have yielded detailed functional insights in many systems including protein kinases, ion channels and chromatin. His work on chromatin, which remains a major focus of his group, has yielded fundamental insights into many epigenetic processes, including how enzymes that act of chromatin are regulated by post-translational modifications on histones and how cancer-associated histone mutations corrupt transcriptional programs and transform cells. Muir is also well known for his work in the bacterial quorum sensing where over the course of more than two decades he has dissected the signaling pathways that control virulence in *Staphylococci*. This work has yielded detailed molecular mechanisms governing the biosynthesis of the active thiolactone-containing signaling peptides and how they regulate the virulence response through a two-component signaling cascade. Notably, this work yielded the first global inhibitors of a bacterial quorum sensing pathway and demonstrated that these molecules can prevent *S. aureus* infections in animals. The quorum sensing work also provided valuable reagents to the research community including the first antibodies against phosphohistidine.

Professor Muir has given over 400 lectures on his research around the world, a tally that including over 50 named lectures. He has also won a number of honors for his research, including; the Alfred P. Sloan Research Fellow Award, Pew Scholar, the Leonidas Zervas Award in Peptide Chemistry, 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, a MERIT award from the NIH-GMS, the 2012 Jeremy Knowles Award from the Royal Society of Chemistry, the 2013 Arthur C. Cope Scholar Award from the American Chemical Society, the 2016 Breslow Award in Biomimetic Chemistry from the American Chemical Society, the 2017 E.T. Kaiser Award in Protein Chemistry from the Protein Society, the Ira Remsen Award, American Chemical Society and the 2026 BMS Award in Enzyme Chemistry from the American Chemical Society. Dr. Muir is a Fellow of the Royal Society, the American Academy of Arts and Science, the American Association for the Advancement of Science, the Royal Society of Chemistry, the Royal Society of Edinburgh. He is also an elected member of the US National Academy of Sciences.

Title: Harnessing Inteins in Chemical Biology: From Ligases to Transposases and Logic Gates

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 translational applications. Here I discuss our recent efforts to engineer inteins for protein engineering applications in the test tube and in cells. I will also describe the development of an autonomous decision-making protein device driven by proximity-gated protein trans-splicing that can perform various Boolean logic operations on cell surfaces, allowing highly selective recruitment of enzymatic and cytotoxic activities to specific cells within mixed populations.

Most relevant publications

Hua, Y., Tay, N.E.S., Ye, X., ... Thompson, R.E., Muir, T.W. Protein editing using a coordinated transposition reaction. Science, 2025, 388, 6742), 68–74.

Hananya, N., Ye, X., Koren, S., Muir, T.W. A genetically encoded photoproximity labeling approach for mapping protein territories. Proceedings of the National Academy of Sciences of the United States of America, 2023, 120, 16, e2219339120

Seath, C.P., Burton, A.J., Sun, X., ... MacMillan, D.W.C., Muir, T.W. Tracking chromatin state changes using nanoscale photo-proximity labelling. Nature, 2023, 616, 7957, 574–580.

Thompson, R.E., Muir, T.W. Chemoenzymatic Semisynthesis of Proteins. Chemical Reviews, 2020, 120, 6, 3051–3126.

Nacev, B.A., Feng, L., Bagert, J.D., ... Muir, T.W., Allis, C.D. The expanding landscape of 'oncohistone' mutations in human cancers. Nature, 2019, 567, 7749), 473–478.

Camarero, J.A., Muir, T.W. Chemoselective backbone cyclization of unprotected peptides. Chemical Communications, 1997, 15, 1369–1370.

Dawson, P.E., Muir, T.W., Clark-Lewis, I., Kent, S.B.H. Synthesis of proteins by native chemical ligation. Science, 1994, 266, 5186, 776–779.