

AVVISO DI SEMINARIO

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***“Bringing the Science of Proteins into the
Realm of Organic Chemistry”***

5 Ottobre, ore 15

Aula Seminari del Dipartimento di Scienze e Tecnologie Chimiche

Proponenti: Prof. Lorenzo Stella, Prof. Mariano Venanzi

Bringing the Science of Proteins into the Realm of Organic Chemistry

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Total chemical synthesis of proteins was one of the 'Grand Challenges' of 20th century synthetic organic chemistry, from the time of Emil Fischer. A general solution to this challenge was provided by the chemical ligation principle: *chemoselective covalent condensation of unprotected peptides enabled by formation of a non-native moiety at the ligation site* [1]. The most effective chemistry – 'native chemical ligation' [2] – is based on this principle and has enabled the robust total synthesis of a wide variety of protein molecules [3]. Application of synthetic organic chemistry to protein molecules enables novel protein science that can only be done by chemistry [4]. Examples include: total synthesis of mirror image proteins composed entirely of unnatural D-amino acids (and achiral glycine) [5,6]; design and synthesis of protein molecules with novel chemical features not found in Nature [7,8]; and, racemic & quasi-racemic crystallography enabled by total chemical synthesis for the determination of novel protein structures by X-ray diffraction [5,7; 9,10].

[1] Constructing proteins by dovetailing unprotected synthetic peptides: backbone engineered HIVprotease. Schnölzer, M.; Kent, S.B.H. *Science* **1992**, *256*, 221.

[2] Synthesis of proteins by native chemical ligation. Dawson, P.; Muir, T.; Clark-Lewis, I.; Kent, S. *Science* **1994**, *266*, 776.

[3] Total chemical synthesis of proteins. Kent, S.B.H. *Chemical Society Reviews* **2009**, *38*, 338.

[4] Novel protein science enabled by total chemical synthesis. KentSBH. *ProteinScience* **2019**, *28*, 313.

[5] Chemical synthesis and X-ray structure of a heterochiral {D-protein antagonist plus VEGF-A} protein complex by racemic crystallography. Mandal, K.; Uppalapati, M.; Ault-Riché, D.; Kenney, J.; Lowitz, J.; Sidhu*, S.; Kent*, S.B.H. *Proc Natl Acad Sci USA* **2012**, *109*, 14779.

[6] A non-immunogenic bivalent D-protein potently inhibits retinal vascularization and tumor growth. Marinec, P.S.; Landgraf, K.E.; Uppalapati, M.; et al.; Kent, S.B.H.; Ault-Riche, D.; Sidhu, S.S. *ACS Chemical Biology*, **2021**, *16*, 548.

[7] Convergent chemical synthesis of ester insulin: determination of the high-resolution X-ray structure by racemic protein crystallography. Avital-Shmilovici, M.; Mandal, K.; Gates, Z.P.; Phillips, N.; Weiss, M.A.; Kent, S.B.H. *J. Am. Chem. Soc.* **2013**, *135*, 3173.

[8] Chemical synthesis of an enzyme containing an artificial catalytic apparatus. Torbeev, V. ; Kent, S.B.H. *Aust. J. Chem.* **2020**, *73*, 321. doi.org/10.1071/CH19460

[9] Racemic protein crystallography. Yeates, T.O.; Kent, S.B.H. *Ann. Review Biophysics* **2012**, *41*, 41.

[10] A functional role for Rv1738 in *Mycobacterium tuberculosis* persistence suggested by racemic protein crystallography. Bunker, R.D.; Mandal, K.; Bashiri, G.; Chaston, J.J.; Pentelute, B.L.; Lott, J.S.; Kent*, S.B.H.; Baker*, E.N. *Proc Natl Acad Sci USA* **2015**, *112*, 4310.



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