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ItPS Friday Seminars

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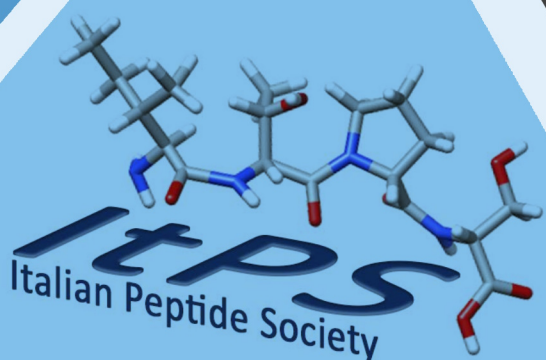


Chemical Ligation - the apotheosis of total protein synthesis

Total synthesis of proteins was one of the 'Grand Challenges' of 20th century chemistry. Despite decades of development by skilled chemists throughout the world, conventional solution organic chemistry and stepwise solid phase peptide synthesis (SPPS) were each able to reproducibly make only the smallest protein molecules in homogeneous form. In the 1990s, my laboratory introduced chemical ligation - condensation of unprotected peptide segments by chemoselective reaction enabled by formation of an unnatural bond at the ligation site; and native chemical ligation - thioester-mediated condensation of unprotected peptide segments to give a native peptide bond at the ligation site.

Using peptide segments made by highly optimized SPPS and combined with rigorous analytical control, chemical ligation enables straightforward total synthesis of protein molecules.

Synthetic proteins are characterized high resolution methods such as isoelectric focusing, direct infusion electrospray MS, multidimensional NMR, and X-ray crystallography.



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