Self-Assembly of Helical Pores from Nonpolar Dendritic Dipptides

**Murali Parce**

Roy & Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA
parce@pan.upenn.edu

Natural porous proteins function as viral helical coats, transmembrane channels responsible for ion regulation and transport, molecular recognition and response, and energy transduction. Antibiotics, antimicrobials, and toxins. Remodeled porous proteins are used for reversible encapsulation of molecules and in stochastic sensing. Integral membrane proteins, including those functioning as transmembrane channels, exist in very low natural abundance, and since they form 3-dimensional functional structures only in the membrane environment, their crystallization had limited success. Therefore, the molecular details of their structure and function are not well understood. Simple synthetic assemblies that mimic the structure and function of transmembrane channels are expected to contribute to the understanding of the structure and function of the more complex natural proteins. Strategies for the synthesis and assembly of porous or tubular supramolecular structures have been elaborated. Natural porous proteins are stable in the fluid membrane environment and in solid state. However, with few exceptions, porous protein mimics do not assemble into periodically ordered structures that are stable in solution and in solid state. This behavior limits their structural analysis by combinations of solution and solid-state complementary techniques. Recently, our laboratory elaborated a new strategy to helical porous protein mimics that is based on the self-assembly of amphiphilic dendritic dipptides. The internal structure and stability of the porous structure self-assembled from dendritic dipptides is programmed by the stereoregularity and protective groups of the dipptide, the number of methylene units from the alkyl groups of the dendron, and by the primary structure of the dendron attached to the dipptide.

These experiments provided some of the molecular principles required to program the self-assembly of helical pores from dendritic dipptides. This cooperative self-assembly process involves allosteric regulation. In all previous studies the dendritic dipptide was constructed from Boc-3-Tyr-Ala-OMe dipptide containing various combinations of Tyr and Ala stereoregularity, different protective groups, and dendron architectures. In order to assess the scope, limitations, and generality of this self-assembly strategy, the synthetic, self-assembly, structural and spectroscopic analysis of the dendritic dipptides (4-3,4,3,5)2323-CH2=CH2-L-phenylalanine, in which X is all nonpolar or amino acids Gly, L-Val, L-Leu, L-Ile, L-Phe, and L-Pro, were investigated. The scheme below outlines the synthesis of the dendritic dipptides to be discussed. The results of this study will be discussed in this lecture and compared with that of the dendritic dipptide with X-L-Ala which was studied previously and was unsubstituted.

References