Expanding the Loop Segments in β-hairpin Nonapeptides in Protein Folding and Biological Functions

Rajagopal Appavu*

Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States Minor Outlying Islands

Editorial

Analysis of β-hairpins in proteins, have revealed several examples of antiparallel β-strands connected by short linking segments, which contain more than two residues [1-6]. The design of synthetic peptide hairpins formed with central two residue turns has been facilitated by the ease with which specific types of β-turn structures can be generated in short peptides. Earlier work in this laboratory has addressed the question of expanding the central connecting loop in designed peptide β-hairpins. (Figure 1) schematically compares the two residue and three residue β-hairpins. Successful expansion of the loop region has been achieved using a centrally positioned 3-Pro-4-Pro-5-Ala segment. A detailed NMR study of the nonapeptide Boc-Leu-Phe-Val-3-Pro-4-Pro-5-Ala-Leu-Phe-Val-OMe revealed that registered antiparallel strands are formed in solution. The hairpin facilitating three residue turn requires the 3-Ala residue to adopt an αi conformation (φ~60°, ψ~30°) [2-7]. When the residue at position (6) was replaced by 1-Ala, the nonapeptide yielded a two residue hairpin structure with the 3-Pro-4-Pro segment forming a type-II β-turn. The 1-Ala(6) residue is now incorporated into the C-terminus segment, with "slipped" strand registry. The significant conformational transitions were appeared replacing the 3-Ala(6) to Gly(6), and 1-Ala(6) in the protein secondary structure conformation. This conformation, referred to as a "slipped hairpin" structure, together with the three residue hairpin is illustrated in Figure 1. Inspection of the structures shown in Figure 1 suggests the two conformations are clearly distinguishable, if the aromatic ring orientations are considered. Thus, in addition to cross-strand nuclear over hauser effects (NOEs) and delineation of NH bonded groups, aromatic proton chemical shifts may prove to be a convenient diagnostic for the conformations present in this class of designed nonapeptides. The Editorial describes a systematic analysis of peptides in which the residue at position 6 is varied in the sequence Boc-Leu-Phe-Val-3-Pro-4-Pro-5-Yyy-Leu-Phe-Val-OMe. Studies on related peptides in which 3-Pro(5) is substituted by Aib and 1-Ala are also reported in this laboratory [5-7]. NOE effect clearly reveals the replacement of Xxx and Yyy positions L, and D Amino Acids yield a mixed population of three residue β-hairpins and two residue β-hairpins stabilization of Aromatic-Aromatic interactions.

References


*Corresponding author: Rajagopal Appavu, Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Y6.0006, Houston, Texas 77030, United States Minor Outlying Islands. Tel: 409-256-9987; Fax: 713-794-5369; E-mail: dominiquerajagopal@gmail.com

Received January 28, 2016; Accepted February 18, 2016; Published February 23, 2016

Citation: Appavu R (2016) Expanding the Loop Segments in β-hairpin Nonapeptides in Protein Folding and Biological Functions. Transcriptomics 4: e116. doi:10.4172/2329-8936.1000e116

Copyright: © 2016 Appavu R. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.