Highly fluorinated amino acids have been used to stabilize helical proteins, with limited studies on sheet-containing proteins. Here we will present the effect of these highly fluorinated amino acids on two protein secondary structures: alpha-helix and beta-sheet. Furthermore, we will present a three-step chemoenzymatic stereoselective gram-scale synthesis of fluorinated leucines. We will also show the effect of introducing fluorines on the hydrophobicity of the amino acids. The helix propensity was measured using Ala-based peptides, whereas the effect on beta-sheet stability was measured using protein GB1 domain (GB1). Various amino acids were studied including 5,5,5',5',5'-hexafluoroleucine, 5,5',5'-tetrafluoroleucine, pentafluorophenylalanine, leucine, phenylalanine, and alanine. The peptides and proteins were synthesized by solid phase peptide synthesis. The hydrophobicity of the amino acids were measured by thin layer chromatography under neutral and acidic conditions. The $R_f$ values were used to derive the logarithm of the partition coefficient ($\log P$) as a gauge for hydrophobicity. The circular dichroism spectra of the Ala-based peptides were used to derive the helix propensity. Thermal denaturation of GB1 derivatives were monitored by circular dichroism spectroscopy and used to explore the effect on sheet stability. In general, complete fluorination of the methyl or phenyl groups resulted in increase in hydrophobicity; partial fluorination of these groups led to decrease in hydrophobicity. Helix propensity decreased significantly upon fluorination. In contrast, sheet stability increased upon introducing the fluorines. Therefore, highly fluorinated amino acids may be more suitable for stabilizing beta-sheets in sheet-containing proteins compared to helical proteins.

**CBC SEMINAR ANNOUNCEMENT**

**Effect of Highly Fluorinated Amino Acids on Secondary Structure Stability**

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**Date:** 26th January 2011 (Wednesday)
**Time:** 11am – 12.30pm
**Venue:** NTU SPMS CBC Building Level 2, Conference Room
**Host:** Asst. Professor Brendan Orner