NANYANG TECHNOLOGICAL UNIVERSITY

CBC SEMINAR ANNOUNCEMENT

Professor Moses Lee
Hope College

"Hx-amides," A New DNA Sequence Recognition Element for Targeting and Controlling Gene Expression in Cancer Cells

Polyamides are non-fluorescent imidazole (I) and pyrrole (P)-containing analogs of distamycin. They bind to specific sequences of DNA via the minor groove and have the capacity to regulate gene expression. Polyamides are potential useful for the treatment of genetic or gene derived diseases, including cancer. Continuing efforts in the polyamide field are aimed at the design and development of novel DNA binding structures that have greater sequence specificity, higher binding affinity, improved cellular uptake, and enhanced localization in the nucleus. To address these challenges, our work has focused on the design of novel DNA binding molecules that are inherently fluorescent. Thus, the fluorescent moiety must be an integral component of the molecule, and it must exhibit DNA sequence recognition properties. Accordingly, we are pleased to report the design of such a sequence recognizing, fluorogenic benzimidazole moiety, which we have coined "Hx." And combining Hx with polyamides creates a new family of DNA binders, called "Hx-amides." To demonstrate the novelty and usefulness of Hx-amides, a representative molecule Hx-IP was designed and synthesized to target the inverted CCAAT box-2 (ICB2) site found within the promoter of the topoisomerase IIa gene in mammalian cells. In this presentation, the design, synthesis, plus the DNA binding and biological properties of Hx-IP will be presented. Hx-IP exhibits excellent binding affinity and specificity for the ICB2 site, brightly fluoresces when bound to its target sequence, enters cells, and effectively concentrates in the nucleus as monitored by fluorescence microscopy.

Date:	**28th February 2012 (Tuesday)**
Time:	**11:00am – 12:30pm**
Venue:	**NTU SPMS CBC Building Level 2, Conference Room**
Host:	**Professor Loh Teck Peng**