Research Directions of Group Members in
The Center of Novel Functional Molecules
The Chinese University of Hong Kong

1. Dennis K. P. Ng - Development and Screening of Novel Functional Molecules for Photodynamic Therapy and Drug Delivery

Our group has been studying the synthesis, properties, and applications of phthalocyanines and structurally related macrocyclic compounds. Recent focuses have been placed on supramolecular chemistry of phthalocyanines and development of phthalocyanine-based photosensitizers for photodynamic therapy. We plan to construct supramolecular systems of various tetrapyrrole derivatives including phthalocyanines and porphyrins, using axial coordination, host-guest interactions, and mechanically interlocking methods. The ground-state as well as excited-state interactions of the tetrapyrrole components will be studied. For the latter project, we work closely with Prof. WP Fong's group. We are now evaluating the photodynamic activities of our new compounds in vivo, and attempting to enhance the targeting properties by incorporating tumor-selective ligands to the photosensitizers. We are also in collaboration with Prof. Chi Wu's group in studying multi-functional polymeric micelles as efficient drug delivery systems.

2. W. P. Fong - Development and Screening of Novel Functional Molecules for Photodynamic Therapy and Drug Delivery

In collaboration with Prof. Dennis Ng's group, we are interested in studying the biochemical actions of the photosensitizers. The photodynamic activities of the photosensitizers will first be examined by using different cell lines. The cell death mechanism will be studied. The more potent compounds will then be used in animal study where their tissue distribution, clearance and toxicity will be investigated. Their photodynamic activities on tumor regression will be assessed using the tumor-implanted nude mice animal model.

3. C. Wu - Development of Novel Non-Viral Vectors for Molecular Medicines

Due to few recent fatal accidents involving viral vectors, using polymer to transfer plasmid DNA and other molecular medicines into cells has attracted much renewed interest. On the other hand, many effective molecules ("drugs") could be listed in the Drug Handbook because of their toxicity. With some effective and specific targeted carriers, we might solve this problem in the future so that they can be used as real drugs. To develop a new generation of low toxic and high efficient non-viral vectors, one must consider all critical steps in transferring active molecules into a cell. Taking DNA as an example, it involves 1) the formation of small polymer/DNA polyplexes, stable not only in aqueous solution, but also in serum; 2) the site specific delivery; 3) the cell uptake; 4) the endosomal release; 5) the intracellular dissociation of polyplexes; and 6) the effective transportation of plasmids to nucleus. Instead of investing in new chemistry, we propose to concentrate on the modification of the first-generation carriers. Specifically, we propose *non-randomly* graft proper amounts of *hydrophilic functionlized* poly(ethylene glycol) (PEG) and *hydrophobic/biodegradable* /biocompatible poly(lactide) (PLA) chains on poly(ethyleneimine) (PEI), one of the most effective polymer carriers, to form a novel terpolymer, which can be literally viewed as a string of connected amphiphilic "triblock copolymers". By varying the content, length and distribution of the PLA and PEG chains on PEI, we will be able to prepare small stable polyplexes with different sizes and surface charge densities for further gene transfection tests. In the first step of this proposed study, we will mainly focus on the formation kinetics and stabilization mechanism of these polyplexes.

4. Z. W. Xie - Development of Boron-Containing Functional Molecules for Boron Neutron Capture Therapy and Functional Carborane-Based Catalysts for Olefin and Lactone Polymerization

A key requirement for boron neutron capture therapy (BNCT) is to design and synthesize new boron-containing compounds which can deliver an adequate concentration of ^{10}B atoms to tumor cells. Our group is interested in syntheses of supraicosahedral carboranes since they offer high boron content, excellent kinetic stabilities, low toxicities, and relatively simple derivatization for incorporation in organic vehicles. Another focus of

our research is to develop carborane-based metal catalysts for producing polymers/copolymers of defined structure.

5. H. F. Chow - Development of Functional Dendritic Macromolecules as Carriers for Biomolecule Imaging and Drug Delivery and as Modifiers for Materials Applications

We are interested in the synthesis of functional dendritic molecules with unusual architecture and properties. We have recently prepared a series of highly hydrophobic dendrons and used them as carriers for the internalization of fluorescent tags using in real time protein imaging (in collaboration with Covalys in Switzerland). Such dendrons can also been used to modify the surface properties of many materials due to their unusual hydrophobicity.

6. Tony K. M. Shing - Chemical Synthesis and Biological Studies of Novel Functional Molecules for Glyscosidase Inhibitory, Antitumor or Antiviral Activities

Prof. Christopher H. K. Cheng and I have teamed up since 2003 and been researching on the chemical syntheses of valienamine-containing pseudo-amino-disaccharides that would be initially tested for glycosidase inhibitory activities. Chemical synthesis gives novel pseudo-amino-disaccharides (structurally related to acarbose) for biological evaluation as a means of providing improved drugs and novel structure-inhibitory activity relationship. Our group is responsible for the chemical synthesis and Prof. Cheng' group for the bio-assays.

Our group is and will be interested in syntheses of natural products and their analogs with potential antitumor and antiviral properties.

7. Christopher H.K. Cheng – Identification and Biological Evaluation of Novel Functional Molecules

Our group is interested in the identification and evaluation of synthetic and naturally occurring functional molecules as therapeutic agents, particularly inhibitors of critical enzymes in disease processes. We are also interested in the applications of synthetic

dendritic functional molecules as carrier molecules for DNA and proteins into cells, and also on the applications of such molecules as probes to monitor the concentration of metabolites in cells or as carriers of drugs into cells.

8. Henry N. C. Wong - Synthesis of Functional Molecules for Materials, Biological and Catalytic Applications

My research areas are on (1) Synthesis and studies of pentacenes, hexacenes and heptacenes. (2) Synthesis of bioactive naturally occurring molecules using furans as precursors. (3) Synthesis of bioactive five-membered organic peroxides. (4) Synthesis of novel small molecules for asymmetric catalysis.

9. Thomas C. W. Mak - Crystal Engineering and Supramolecular Assembly

We are interested in two research directions:

(1) Metal Complexes Containing Naked All-Carbon Species and Related Ligands

Our recent efforts have concentrated on the synthesis and characterization of silver double and multiple salts containing the acetylenediide dianion C_2^{2-}, the 1,4-butadienyl-1,4-diide C_4^{2-}, and related carbon-rich acetylide ligands. This type of complexes are of interest in regard to the discovery of novel coordination modes, the role of argentophilic interactions in supramolecular assembly, as well as their potential applications as non-linear optical materials and molecular wires.

(2) Crystal Engineering and Coordination Network Assembly

Recently we showed that the short-length flexible ligand 2-pyridinyl-3-pyridinylmethanone (**L**) is an excellent ligand for the generation of infinite single helical complexes with various metal salts. By precise solvent-control, we have prepared the first pair of helical metal-organic conformational polymorphs (both having the same structural formula $\{[Ag(\mathbf{L})](CF_3SO_3)\}_\infty$), in which the 2_1 helices of opposite chirality in one supramolecular isomer are stacked alternately to form a racemate, while the 4_1 helices in the other are assembled homochirally by inter-chain argentophilic interaction to generate a conglomerate. Using the ligand 2-pyridinyl-4-pyridinylmethanone (**L'**), we have synthesized a series of nine isostructural complexes $[Ag(\mathbf{L'})]_2X_2$ with various counter

anions, all comprising a disilver metallacyclophane skeleton. The following ordered sequence of the coordinating ability of the series of polyatomic monoanions has been established on the basis of structural parameters derived from their interaction with the metallacyclophane skeleton:

$NO_2^- \sim HCO_2^- > CF_3CO_2^- > ClO_3^- > NO_3^- > CF_3SO_3^- > ClO_4^- > BF_4^- > PF_6^-$

10. Jimmy C. M. Yu - Novel Advanced Functional Materials for Enviromental and Materials Applications

I am interested in the following research topics: (1) Health hazards of nanomaterials. (2) Advanced materials for anti-terrorist purpose. (3) Compounds for solar energy conversion. (4) Photocatalytic disinfection technology.