

A Statement of Research Achievements in Chemistry

The innovation of Chi-Ming Che's research is based on Inorganic Chemistry and Photochemistry, and he has made important contributions to integrating Inorganic Chemistry with Materials Science, Catalysis, and Biomedical Science. He has developed a number of interdisciplinary research areas: notably in **[A] Phosphorescent Transition Metal Compounds**, **[B] Reactive Metal-Ligand Multiple Bonded Complexes for Biomimetic Atom and Group Transfer Reactions**, and **[C] Inorganic Medicines**.

[A] Phosphorescent Transition Metal Compounds

Shining light onto molecules is a unique approach to the synthesis of new excited state molecules that are highly energetic with unprecedented structures and reactivities. Such structures and reactivity are difficult to be obtained through examining the chemistry and reactivities of ground state molecules. The realization of the importance of electronic excited state molecules in bimolecular chemical reactions and molecular recognitions heavily relies on their lifetimes and concentrations in solutions upon irradiation with light. Directly probing the chemistry and photophysical processes of electronic excited state molecules depends on the availability of a spectroscopic handle for monitoring the excited state molecules. All these requirements can be readily met through investigating phosphorescent transition metal compounds that have long-lived and emissive excited states in solutions.

Due to the heavy atom effect, phosphorescent transition metal compounds have emissive triplet excited states with sufficiently long lifetimes in solutions for bimolecular reactions to take place. The decay of the lifetime and/or intensity of the emission can serve as a probe for monitoring the excited state molecules. It should be noted that the emission quantum yield and excited state lifetime are strongly affected by non-radiative decay processes, which may be regulated through molecular design, that is, judicious choice of metal ions and auxiliary ligands.

Che has made seminal contributions to the development of "*Phosphorescent Transition Metal Compounds*". His achievements in this area could be summarized as follows:

[A.1] *Light-Induced Outer-Sphere Electron and Energy Transfer Reactions*. Che has made use of the triplet excited states of transition metal compounds as powerful one-electron oxidants and one-electron reductants for investigating both intramolecular and intermolecular highly exothermic electron transfer reactions in biological systems. He and co-workers first reported the use of the triplet excited states of d^6 -metal polypyridyl compounds and metalloporphyrins for examining highly exothermic bimolecular biological electron transfer reactions [*Journal of the American Chemical Society*, **1984**, *106*, 5143–5145; **1986**, *108*, 2814–2818].

[A.2] *Electronic Excited States for Light-Induced Multi-Electron and Atom Transfer Reactions*. Che made use of a synthetic chemistry approach and employed resonance Raman spectroscopy to expand the scope of photochemistry research in this field. His team pioneered the development of photophysical and photochemical properties of diverse classes of highly

phosphorescent transition metal and organometallic complexes particularly those of Pt(II), the $^3[\text{nd}\sigma^* (\text{n}+1)\text{p}\sigma]$ excited states of binuclear Au(I), Ag(I), and Cu(I) systems, as well as the photochemistry of d^2 -Os(VI)-oxo and -nitrido compounds. His work has generated diverse interests, from synthetic inorganic and organometallic chemists to chemists working on light emitting organometallic compounds. Based on the excited state chemistry of d^2 -metal ligand multiple bonded compounds previously reported in literature and subsequently expanded by Che, the following problems have been addressed:

- [1] Light-induced oxygen atom transfer reactions for hydrocarbon and water oxidation have been accomplished using *trans*-dioxoosmium(VI) compounds [*Coordination Chemistry Reviews*, **1990**, 97, 93–104; *Inorganic Chemistry*, **1994**, 33, 3199–3200].
- [2] Direct observation of a nitrido coupling reaction between two metal-nitrido units to give dinitrogen bridged compounds using the excited state chemistry of Os(VI)-nitrido compounds published in *Journal of the Chemical Society, Chemical Communications*, **1989**, 1883–1885. This reaction may be viewed as the microscopic reverse of the cleavage of dinitrogen compounds to metal-nitrido units subsequently reported in literature [*Science*, **1995**, 268, 861–863].

[A.3] *Photo-Catalysis and Excited State Inner-Sphere Atom Abstraction Reactions.* To realize light-induced multi-electron transfer catalysis, it is essential to develop excited state molecules with high energy and long lifetimes, which are capable of undergoing inner-sphere atom transfer reactions. Che, Gray and Roundhill are the pioneers in the development of a molecular photocatalyst, $[\text{Pt}_2(\text{P}_2\text{O}_5\text{H}_2)_4]^{4-}$, which can catalyze light-induced cleavage of C-H bonds of hydrocarbons without the need for a sacrificial reductant. *This $[\text{Pt}_2(\text{P}_2\text{O}_5\text{H}_2)_4]^{4-}$ catalyzed photochemical reaction [*Accounts of Chemical Research*, **1989**, 22, 55–61] remains to this date the only example in literature that illustrates the conversion of light to chemical energy using only light photons and a molecular photocatalyst.*

[A.4] *Luminescent d8 and d10 metal complexes.* Substrate binding reaction at the inner coordination sphere of excited state molecules is a prerequisite for the development of luminescent sensory devices, excited state molecular recognitions, and inner-sphere multi-electron transfer and atom transfer photocatalysis. Che is leading the development of the excited state chemistry of coordinatively unsaturated metal complexes particularly those have a d10 or d8 electronic configuration. He is a pioneer in the photochemistry of phosphorescent platinum(II) complexes. He first reported the intriguing luminescent properties of platinum(II)-acetylide complexes [*Coordination Chemistry Review*, 1994, **132**, 87-97] and observation of long-lived metal-metal to ligand charge transfer excited states of weakly interacting diplatinum(II,II) complexes in solutions [*Journal of the Chemical Society Chemical Communications*, 1992, 1369-1371], both papers have significantly impacted the development of and responsible for the subsequent huge amount of literatures on phosphorescent platinum(II) complexes, which has become an area of topical interest nowadays. He has independently pointed out the importance of metal-ligand coordination and excited state complex formation in governing the rich and yet complex photoluminescent properties of closed shell d^{10} metal ions. Che's team unequivocally established the $\text{nd}\sigma^* \rightarrow (\text{n}+1)\text{p}\sigma$ excited states of weakly interacting d^{10} - d^{10} binuclear complexes of Au(I) [*Journal of the American Chemical Society*, 1999, **121**, 4799-4803.], Ag(I) [*Journal of the American*

Chemical Society, 2000, **122**, 2464-2468], and Cu(I) [*Coordination Chemistry Reviews*, **2005**, *249*, 1296–1309; *Angewandte Chemie, International Edition*, 2000, **39**] and first explained and verified visible emission from solvent molecules and counter-anion exciplexes in the $[\text{Au}_2(\text{diphosphine})_2]^{2+}$ system, which is the first reported example of this type of exciplex formation involving metal-ligand coordination in excited states in literature [*Angewandte Chemie, International Edition*, **1999**, *38*, 2783–2785]. His work has paved the way for the development of multi-electron photocatalysis, wherein binding of substrate molecules to the inner-sphere coordination sphere of excited state molecules is required.

[A.5] *Luminescent Signaling*. There have been extensive studies on the binding interactions between d^6 metal polypyridyl complexes and Nuclei acids / proteins in literatures. Che's team was the first to make use of luminescent Pt(II) complexes as probes for the binding reactions with biomolecules and as light switch on probes for the detection of DNAs [*Chemical Communications*, **1996**, 1039–1040; *Topics in Current Chemistry*, **2004**, *241*, 27–63; *Chemical Communications*, **2005**, 1025–1027] including that of secondary G- Quadruplex DNA [*Journal of the American Chemical Society* 2009, **131**, 1835-1846], and for the detection of proteins at ng level [*Chemistry-A European Journal* 2009, **15**, 3652-3656]. The luminescent Pt(II) complexes developed by Che's team have a vacant coordination site, which allows for inner-sphere interactions with incoming analytes. This interaction significantly affects the non-radiative decay of the triplet metal-to-ligand charge transfer excited state of Pt(II). Che has extended the applications of luminescent platinum(II) complexes to study the bindings with secondary DNA structures such as G-Quadruplex [*Journal of the American Chemical Society* 2009, **131**, 1835-1846] and with enzymes such as Topoisomerase [*Current Opinions in Chemical Biology* (in press)]. The triplet metal-metal to ligand charge transfer emission of weakly interacting dinuclear Pt(II) compounds, first established by Che and co-workers to exist in solutions [*Journal of Chemical Society, Chemical Communications*, **1992**, 1369–1371], is sensitive to subtle environmental changes, and has been shown to be a useful operation principle in luminescent signaling studies.

[A.6] *Materials Science Applications*. Phosphorescent transition metal compounds have tremendous practical applications in organic optoelectronics. Prior to the work by Thompson and Forrest, Che and coworkers independently reported the applications of phosphorescent transition metal compounds as emitting materials for organic light emitting diodes (OLEDs) [*Synthetic Metals*, **1998**, *94*, 245], and was the first to report the use of the triplet emission from inexpensive Cu(I) materials for use in OLED applications [*New Journal of Chemistry*, **1999**, *23*, 263–265].

Robust phosphorescent Pt(II) compounds have a tremendous impact in the development of high performance OLEDs. Che is a pioneer in this field. In 2003, he first introduced luminescent Pt(II) complexes other than platinum(II) porphyrin that can be used as dopant emitters for high performance OLEDs [*Chemical Communications*, 2002, 206-207; *Chemistry – A European Journal*, **2003**, *9*, 1263–1272 ; patent: US 6,653,654 B1; *Journal of the American Chemical Society*, 2004, **126**, 4958–4971]. Che subsequently developed different robust Pt(II) systems and used these systems to fabricate high-performance yellow [*Chemical Communications*, **2005**, 1408–1410; US Patent Application No. 10/835,481] and orange [*Inorganic Chemistry*, **2005**, *44*, 4442–4444] devices. Besides single color devices, high-efficiency white OLEDs have also been fabricated by Che's team using Pt(II) complexes as one of the emitters [*Chemical Communications*, **2004**, 1484–1485; US Patent Application No.

10/825,231; *Chemistry - A European Journal*, **2007**, *13*, 417–435; *Advanced Materials*, **2007**, *19*, 3599–3603].

The phosphorescent excited states of carbon-rich organic compounds are an important area of research in functional molecular materials. Che's team employs optically transparent $[\text{Au}(\text{PCy}_3)]^+$ to switch-on the triplet emissions of C_n^{2-} [*Journal of the American Chemical Society*, **2001**, *123*, 4985–4991] and arylacetylides [*Journal of the American Chemical Society*, **2002**, *124*, 14696–14706] in solutions at room temperature. This research forms a platform with which to explore the triplet excited states of π -conjugated hydrocarbons in solutions at room temperature.

Molecular nanostructures formed by self-assembly reactions of organometallic complexes are complementary to the well-developed inorganic and polymer-based nanomaterials. Che's recent pioneering works [*Angewandte Chemie, International Edition*, **2006**, *45*, 5610–5613 and *Chemical Communications*, **2006**, 3972–3974] on one-dimensional nanowires and nanorods self-assembled from discrete neutral/cationic organoplatinum(II) complexes demonstrated that metal···metal interactions can be employed as a driving force for the anisotropic growth of molecular nanostructures. Subsequent works by Che's team have established that Pt(II)-based nanomaterials can be used as sensory materials for the detection of volatile organic compounds, semiconducting materials for Light-Emitting Organic Thin-Film Field Effect Transistors [*Angewandte Chemie-International Edition* 2008, **47**, 9895-9899], Photo-responsive two dimensional Nano-Sheets, and Supramolecular polyelectrolytes [*Angewandte Chemie-International Edition* 2009, **48**, 7621-7625].

[B] Reactive Metal-Ligand Multiple Bonded Complexes for Biomimetic Atom and Group Transfer Reactions

Reactive metal-ligand multiple bonded complexes, namely highly oxidizing metal-oxo complexes and electrophilic metal-imido and -nitrido complexes, are key intermediates in biological multi-electron transfer reactions including biological oxidations, dinitrogen fixation and nitrite reduction to ammonia. In organic catalysis, electrophilic metal-oxo, -imido, and -carbene complexes are the key species directly involved in carbon-oxygen, carbon-nitrogen, and carbon-carbon bond formation reactions. As a consequence of the oxidizing nature of the metal ions involved, the oxidizing metal-ligand multiple bonded complexes are usually electrophilic and short-lived in solutions and in some circumstances their existence is controversial. The mechanism with which these species react with carbon-hydrogen bonds leading to the formation of carbon-oxygen, carbon-nitrogen, and carbon-carbon bonds remains poorly understood. The reaction medium and auxiliary ligands greatly affect the catalytic metal center. Group transfer reactions cannot be properly elucidated at the molecular level without directly following and probing the primary reactions of reactive metal-ligand multiple bonded complexes that have well-defined structures and redox properties. The tremendous impact of “*Reactive Metal-Ligand Multiple Bonded Complexes for Biomimetic Atom and Group Transfer Reactions*” can be viewed by the followings:

[1] Fe(V)=O or $(\text{Por}^+)\text{Fe(IV)=O}$ species in Cytochrome P-450 Oxidations.

[2] H. Taube's proposal on dinitrogen activation via disproportionation of $\text{M-N}\equiv\text{N-M}$ into $\text{M}\equiv\text{N}$ species [*Inorganic Chemistry*, **1979**, *18*, 2208–2212].

[3] Carbon-nitrogen bond formation and biological reduction of nitrite to ammonia.

- [4] Enantioselective epoxidation of simple alkenes.
- [5] Oxidation of water to dioxygen.
- [6] Metal-catalyzed carbenoid transfer reactions.

[B.1] *Biomimetic Organic Oxidations*. Che is a leading figure in the oxidation chemistry of ruthenium porphyrins with practical interest in organic synthesis [*Chemical Communications* 2009, 3996-4015]. He has extensively developed the chemistry of dioxoruthenium(VI) porphyrins [*Journal of the American Chemical Society*, 1989, **111**, 8812–8818; *Chemistry - A European Journal*, **2002**, 8, 2495–2507; **2005**, 11, 7040–7053]; these high-valent ruthenium complexes can catalyze the aerobic epoxidation of alkenes without the use of a co-reductant. *He demonstrated the first aerobic enantioselective alkene epoxidation through the use of a chiral dioxoruthenium(VI) porphyrin catalyst* [*Chemical Communications*, **1998**, 1583–1584]. This was the first time and still remains as the only example that the feasibility of using a molecular catalyst for the enantioselective transfer of an oxygen atom from a dioxygen molecule to an organic molecule without the use of a co-reductant can be accomplished. Che also developed a practical and mild method for highly selective formation of aldehydes from Wacker-type oxidation of terminal alkenes by using ruthenium porphyrins as catalysts and air as terminal oxidant [*Angewandte Chemie, International Edition*, **2004**, 43, 4950–4954; *Angewandte Chemie International Edition*, 2008, **47**, 6638-6642.

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[B.2] *Reactive Metal-Oxo Oxidants*. Che pioneered the synthesis and study of various highly oxidizing metal-oxo complexes, including their isolation, structural characterization via X-ray crystallography, and systematic tuning of their redox properties and structures [*Journal of Chemical Society, Chemical Communication*, 1985, 988–990; *Inorganic Chemistry*, 1987, **26**, 2289–99]. This has included families of ruthenium-oxo complexes including monooxoruthenium(IV), monooxoruthenium(V), *cis*- and *trans*-dioxoruthenium(VI), and employing diverse ligands including porphyrins, N-atom donor macrocyclic and polypyridine ligands. His early work on Ru=O complexes containing macrocyclic tertiary amine ligands published in *Chemical Communications* 1985, 988-990 has subsequently been adopted in the discovery of non-heme iron-oxo complexes such as [FeIV(TMC)O(CH₃CN)]₂⁺ by Que and coworkers. He has developed both water soluble ruthenium-oxo compounds for examining proton coupled electron transfer reactions [*Journal of the American Chemical Society*, 1990, **112**, 5176–518.] and neutral dioxoruthenium(VI) complexes which are soluble in non-polar organic solvents. The redox potentials of ruthenium-oxo oxidants containing both porphyrin and non-porphyrin ligands span a range of over 1 V, making it feasible to study the driving force dependence of the rate constants of hydrocarbon oxidations. With his *cis*-dioxoruthenium(VI) chemistry, Che has provided mechanistic evidence showing that the *cis*-dihydroxylation of alkenes proceeds via concerted [3+2] cycloaddition reaction [*Journal of the American Chemical Society*, 2005, **127**, 14239–14249]. His *cis*-dioxoruthenium(VI) complexes remain the only structurally characterized non-OsO₄ metal-oxo complexes capable of reacting with alkenes to give *cis*-diol products. He has been able to develop practical protocols using ruthenium nanoparticles or molecular ruthenium complexes for *cis*-dihydroxylation of alkenes by NaIO₄ and H₂O₂, respectively [*Angewandte Chemie, International Edition*, **2004**, 43, 3303–3307; *Chemistry - An Asian Journal*, **2006**, 1, 453–458; **2008**, 3, 70–77]. He has isolated the first and only example of a highly oxidizing low-spin d³ metal-oxo species, for use in modeling the oxidation chemistry of the putative mono-iron(V) in biological systems [*Journal of the American Chemical Society*,

1990, 112, 2284–2291]. The monooxoruthenium(IV) complex of tetramethylcyclam synthesized by Che and co-workers in 1985 [*Chemical Communications*, **1985**, 546] is isostructural to the first non-heme iron oxo complex structurally characterized by X-ray crystallography [*Science*, **2003**, 299, 1037–1039].

Chiral metal-oxo intermediates are postulated in Jacobsen's Mn(III)-catalyzed enantioselective alkene epoxidation and alkane hydroxylation reactions. Che and co-workers pioneered the synthesis and isolation of highly reactive chiral metal-oxo complexes [*Journal of the Chemical Society, Chemical Communications*, **1995**, 2007–2008] and have investigated the primary steps involved in enantioselective oxygen atom transfer reactions to organic substrates [*Chemistry - A European Journal*, **2002**, 8, 2495–2507].

[B.3] *Electronically Excited Metal-Oxo Oxidants*. Che pioneered the development of highly oxidizing metal-oxo oxidants using photochemical methods. He investigated the triplet excited states of luminescent dioxoosmium(VI) complexes, which have microsecond lifetimes and an E° over 2.2 V, and are capable of oxidizing saturated hydrocarbons and water [*Coordination Chemistry Reviews*, **1990**, 97, 93–104; *Chemical Communications*, **1997**, 1443–1444]. *Trans*-dioxoosmium(VI) photochemistry is a good model for probing the oxide-to-metal charge-transfer excited state chemistry of metal-oxo oxidants.

[B.4] *Reactive Metal-Imido Complexes and Carbon-Nitrogen Bond Formation*. Highly oxidizing/electrophilic metal-tosylimido complexes are widely postulated to be the intermediates in metal-catalyzed carbon-nitrogen bond formations, but have never been isolated nor properly studied. Che pioneered the chemistry of reactive metal-tosylimido complexes including those containing chiral ligands for enantioselective imido group transfer reactions. He and co-workers investigated the effects of driving force and C-H bond dissociation energy on H-atom abstraction reactions by reactive metal-imido species [*Journal of the American Chemical Society*, **2005**, 127, 16629–16640]. He developed chiral ruthenium-imido porphyrins for probing the primary steps involved in enantioselective imido group transfer reactions [*Chemistry - A European Journal*, **2002**, 8, 1563–1572] and was the first to realize enantioselective intramolecular amidation of saturated C-H bonds with $\text{PhI}(\text{OAc})_2$ catalyzed by metal complexes [*Angewandte Chemie, International Edition*, **2002**, 41, 3465–3468; *Tetrahedron Letters*, **2005**, 46, 5403–5408]. In addition, Che was the first to report reversible proton-coupled metal-imido/metal-amido/metal-amine redox couples for examining the redox properties of highly oxidizing metal-imido complexes [*Journal of Chemical Society, Dalton Transactions*, **1992**, 1411–1416].

[B.5] *Nitrido Coupling Reactions for Dinitrogen Cleavage Reactions*. Che reported the first direct observation of nitrido coupling of reactive metal-nitrido complexes to give dinitrogen-bridged metal complexes using photochemical means (see Section [A.2] described above).

[B.6] *Reactive Metal-Carbon Multiple Bonded Complexes and Metalloporphyrins as Catalysts for Practical Organic Synthesis*. Che pioneered the advancement of highly selective metalloporphyrin-catalyzed atom and group transfer reactions as useful tools for practical organic synthesis. His recent work has demonstrated the feasibility of highly selective functionalization of primary C-H bonds and highly enantioselective functionalization of secondary C-H bonds with practical interest through carbenoid insertion to C-H bonds of unactivated hydrocarbons catalysed by highly robust metallo-porphyrin complexes [*Angewandte*

Chemie International Edition, 2008, **47**, 9747-9751]. Che is a leading scientist in the area of ruthenium-carbenoid transfer reactions, which become alternatives to the $[\text{Rh}_2(\text{RCO}_2)_4]$ -mediated carbon-carbon bond formation reactions widely used in organic synthesis. Che contributes significantly to our understanding of the electronic structures of reactive metal-carbene species by providing a description of ruthenium-carbon multiple bonding, which has been verified by computational studies and spectroscopic and electrochemical means [*Journal of the American Chemical Society*, **2005**, *127*, 13997–14007]. His group has isolated and structurally characterized a large family of highly reactive ruthenium-, osmium-, and iron-carbene complexes supported by porphyrin ligands [*Journal of the American Chemical Society*, **2001**, *123*, 4119–4129; **2001**, *123*, 4843–4844; **2002**, *124*, 13185–13193; *Chemistry – A European Journal*, **2004**, *10*, 3486–3502]; all of these complexes can undergo carbenoid transfer reactions with alkenes or C-H bonds. He first reported the use of metalloporphyrin/metallosalen catalysts attached to the inner surface wall of MCM-41 for organic catalysis [*Chemical Communications*, **1997**, 65–66; 1789–1790].

[C] Inorganic Medicines

The increasing levels of drug resistance toward the clinically-used drugs create an urgent need to develop new anti-cancer and anti-viral drug leads. Compared with traditional organic compounds in medicines, metal ions have unique properties, including redox transfer/electron shuttling and diverse oxidation states and coordination numbers/geometries, which render metal and metal compounds to have tremendous potential for medicinal applications. With the support of the Areas of Excellence (AoE) Program administered by the University Grant Committee of Hong Kong for setting up the Institute of Molecular Technology for Drug Discovery and Synthesis in 2001, Che's team has made original contributions to the development of “*Inorganic Medicines*” by combining coordination chemistry, proteomics, and molecular biology [see the Dalton Perspective article: *Dalton Transactions*, **2007**, 4884–4892 and *Current Opinions in Chemical Biology* (in press) by Che and co-workers].

[C.1] *Physiologically-Stable Anti-Cancer Gold(III) Complexes*. The medicinal development of Au(III) compounds has been heavily hampered by their poor stability in solutions. Che has identified a series of physiologically stable Au(III) porphyrin complexes that have shown selective cytotoxicities toward different types of human cancer cell lines but remain relatively non-toxic to normal human cells at the anti-cancer dosage concentrations. Some of these metal complexes exhibit up to 100-fold stronger anti-cancer activities *in vitro* and *in vivo* compared with the clinically-used cisplatin, and are capable of overcoming multidrug- and cisplatin-resistant cancer cells (*Chemical Communications*, **2003**, 1718–1719; *European Journal of Pharmacology*, **2007**, *554*, 113–122; *Coordination Chemistry Reviews* 2009, **253**, 11-12). Che and coworkers employed proteomic and molecular biological approaches to study the mechanism of action of these Au(III) complexes toward nasopharyngeal cancer cells SUNE1 (*Cancer Research*, **2005**, *65*, 11553–11564; *Proteomics*, **2006**, *6*, 131–142), and have undertaken extensive preclinical *in vivo* studies using nude mice xenograft models of colon cancer and nasopharyngeal carcinoma (NPC). One of the Au(III) porphyrins, namely gold-1a, was found to reduce the tumor size and prolong the animal survival time significantly [*Cancer* 2009, **115**, 4459-4469]. To facilitate further development of the gold-1a as an anti-cancer agent, Che specifically targeted terminal cancers where no treatment is available. Using a Buffalo rat liver cancer model,

this Au(III) complex was found to significantly prolong the survival time of the tumor-bearing rats while cisplatin proffered no protection (*International Journal of Cancer*, **2006**, *118*, 1527–1538; *International Journal of Cancer* 2009, **124**, 1971-1979). Gold 1a has also been found to inhibit the growth and induce apoptosis of Neuroblastoma Cells (*British Journal Of Cancer* 2009, **101**, 342-349). A recent new derivative of gold-porphyrins gold-2a developed by Che and workers has been shown to be a particularly effective Histone Deacetylase Inhibitor Targeting Wnt/beta-Catenin Pathway [*Cancer Research* in press]

Besides Au(III) porphyrins, Che has developed a series of physiologically stable Au(III) compounds $[\text{Au}(\text{C}^{\wedge}\text{N}^{\wedge}\text{C})\text{L}]^{n+}$ ($n = -\infty$; $\text{HC}^{\wedge}\text{N}^{\wedge}\text{CH} = 2,6$ -diphenylpyridine). The $[\text{Au}(\text{C}^{\wedge}\text{N}^{\wedge}\text{C})\text{L}]^{n+}$ system can act as a cytotoxic agent itself, or as a cytotoxic drug carrier through ligation of non-toxic N-donor or cytotoxic phosphine ligands, respectively. Importantly, *in vivo* studies using NPC-bearing rats showed that one of these compounds significantly reduces the tumor size and prolongs the survival time of the rats (*Chemistry - A European Journal*, **2006**, *12*, 5253–5266).

[C.2] *Anti-Viral Ruthenium and Vanadium Complexes*. While there has been extensive research on cytotoxic metal compounds, related studies on anti-viral metal-based compounds remain sparse. Che isolated a polyanionic ruthenium-oxo oxalato cluster $\text{Na}_7[\text{Ru}_4(\mu_3\text{-O})_4(\text{C}_2\text{O}_4)_6]$, which is remarkably stable in physiologically-relevant solution and exhibits potent anti-viral activity toward both R5- and R4-tropic HIV-1 replication. This metal compound is capable of reducing the percentage of apoptosis of HIV-1 infected Hut/CCR5 cells, probably by inhibiting the HIV replication in Hut/CCR5 cells and hence reducing the HIV-associated cell death (*Journal of the American Chemical Society*, **2006**, *128*, 4938–4939).

Che circumvented the degradation problems of vanadium complexes in solutions containing the biological reductant glutathione (GSH) by employing porphyrin ligands to chelate vanadium ions. His team has prepared and characterized a series of physiologically stable oxovanadium(IV) porphyrins that exhibit potent inhibitory effects on HIV-1(BaL) replication in Hut/CCR5 cells [*Chemical Communications*, **2005**, 3544-3546]. This work is highlighted in the *Editorial* and on the inside front-cover of *Chemical Communications*, **2005**, issue 28.

[C.3] *Chemistry and Biology of Silver Nanoparticles*. Metal nanoparticles have been attracting increasing attention due to their wide range of potential applications. Che 's team has extended the bio-medical horizon of metal nanoparticles by reporting that silver nanoparticles exhibit potent anti-HIV [*Chemical Communications*, **2005**, 5059–5061], anti-HBV [*Antiviral Therapy* 2008, **13**, 253-262], and anti-inflammatory properties [*ChemMedChem* 2009, **4**, 1129-1135]. His team examined the antibacterial action of silver nanoparticles through proteomic and biochemical studies [*Journal of Proteome Research*, **2006**, *5*, 916–924] and investigated the antibacterial activities of partially oxidized silver nanoparticles [*Journal of Biological Inorganic Chemistry*, **2007**, *12*, 527–534].