Nanoparticles Enabling More Effective Chemotherapy

Interview with One of the World's Nanomedicine Leaders – Prof. FENG Si-Shen at NUS, Singapore

Abstract: Traditional chemotherapy presently has been associated with severe side effects such as hypersensitivity reaction and toxicities thus degrading the patient's quality of life. As a visionary leader in nanomedicine, Professor FENG Si-Shen has developed new concept of chemotherapy that involves nanoparticles of novel biodegradable co-polymers resulting in more effective and efficient drug delivery, significantly improving the treatment of cancers and improving quality of life of cancer patients. There are three products related to improved chemotherapy developed by Prof. Feng's group: NanoTaxanes, TargetingTaxanes and OralTaxanes. His group has also developed the 3rd generation of cardiovascular stents, as well as novel nanoparticle formulations of iron oxides and quantum dots for safer cellular and molecular imaging application. These activities have been taking place in his Chemotherapeutic Engineering Laboratory in National University of Singapore (NUS).

Following up our site visit at University of California in Santa Cruz where we learnt about Prof. ZHANG Jin (http://chemistry.ucsc.edu/faculty/zhang.html)'s hollow core shell Au nanoparticles application for targeting cancer treatment via photo-thermal ablation therapy, NanoGlobe team is back to Singapore to interview Professor FENG Si-Shen, one of the world leaders in nanomedicine. Prof. Feng is currently teaching and conducting research at the Department of Chemical and Biomolecular Engineering (75%) and Division of Bioengineering (25%), National University of Singapore (NUS) and has been actively developing nanomedicine products in his laboratory for targeted and controlled drug delivery system.

Prof Feng's expertise in drug formulation is proved in the product called NanoTaxanes® using nanoparticles of novel biodegradable copolymers, capable of performing sustained and controlled therapy for treating a wide spectrum of cancers (including ovarian cancer, breast cancer, colon cancer, small and non-small cell lung cancer, etc.). For example, one shot of his nanoparticle formulation of Paclitaxel can realize effective chemotherapy for more than 336 hours in comparison with 22 hours for Taxol® at the same dose of 10mg/kg for rats. Taxane (Paclitaxel and Docetaxel) in general is a typical chemotherapy drug that can be derived naturally or synthesized artificially. Due to its low solubility, adjuvant (Cremophor EL and Polysobate 80) has to be used in its current clinical dosage form (Taxol® and Taxotere®), which has been found to be responsible for serious side effects such as hypersensitivity reactions, nephrotoxicity, cardiotoxicity and neurotoxicity. Prof Feng's NanoTaxanes® (a novel nanoparticle formulation of taxane), devoid of any toxic adjuvant, realizes a sustained and controlled delivery as well as improves the solubility of taxanes, which therefore produces no peak plasma concentration level located above the maximum tolerance level resulting in much less side

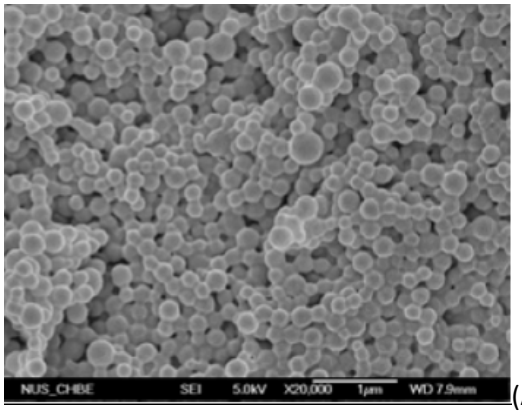
effects, and provides much higher maximum tolerance dose (MTD), resulting in much more effective therapeutic effects.

His group has also developed TargetingTaxanes® and OralTaxanes® for targeted drug delivery and oral drug administration, respectively. Oral chemotherapy is possible to maintain an appropriate drug concentration in the circulation to achieve a prolonged exposure of cancerous cells to the drug, as well as improve quality of life due to "home chemotherapy". The bioavailability of his OralTaxanes® can be as high as 91%, almost equivalent to the intravenous infusion.

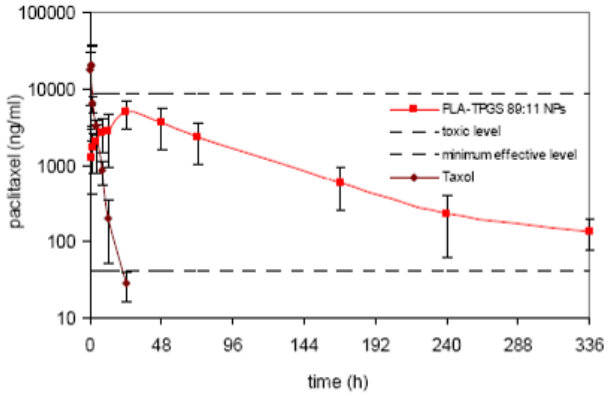
In addition to chemotherapy drug, Prof Feng's group has developed the third generation of cardiovascular stents – NanoStents®, i.e. cardiovascular stents coated by nanoparticles of biodegradable polymers in which effective drugs such as paclitaxel and sirolimus are encapsulated. In comparison wuth the 2nd generation of stents i.e. the drug-elution stents such as the Cypher stent, which releases sirolimus, and the TAXUS stent, which releases paclitaxel, the 3rd generation stents release drug-loaded nanoparticles, which can be much more effectively internalized by the smooth muscle cells.

Prof Feng's lab also developed NanoIOs® and NanoQDs®, novel formulation of imaging agents of iron oxides (IOs) and quantum dots (QDs) for cellular and molecular imaging, enabling early detection of cancer. Encapsulation of the superparamagnetic IOs and semiconductor QDs in his novel nanoparticles of biodegradable polymers, which are conjugated to molecular probes, substantially solves the problems in practical clinical applications of IOs and QDs, such as biocompability, colloidal instability, biodistribution confinement, and fast elimination/excretion.

Prof Feng, originally from China, completed his doctoral and postdoctoral training in Columbia University. He first worked as a research scientist in Department of Biochemistry, Cell and Molecular, Northwestern University and only in 1996 he joined NUS till presently. He founded Chemotherapeutic Engineering Laboratory in NUS and raised an important issue in modern medicine, New-Concept Chemotherapy with nanoparticle technology. In addition to basic research of nanoparticles interaction with the human cells, Prof Feng's research interests include nanoparticle applications in drug formulation, polymeric drug conjugation, chemo, thermal, and radiotherapy, diagnostic/molecular imaging, cardiovascular tissue reparation, gene therapy. Presently, he is also an Associated Editor of Biomaterials and Nanomedicine (UK) journals as well as a editorial board member of the other two journals in nanomedicine, i.e. Nanomedicine – Nanotechnology, Biology and Medicine, and International Journal of Nanomedicine.

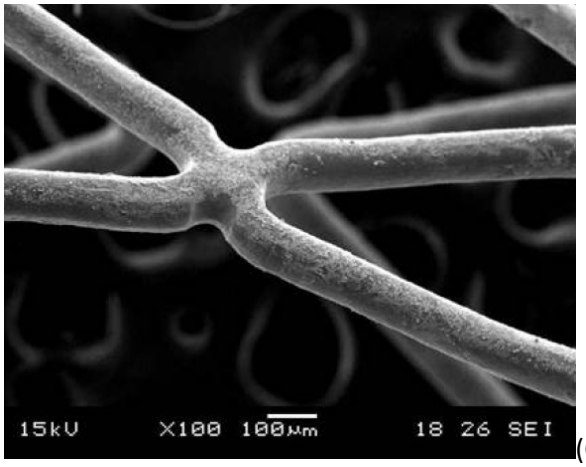


(A)

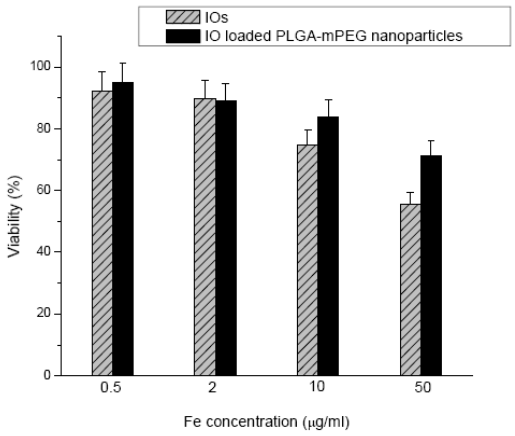


(B)

(A). Field emission scanning electron spectroscopy (FESEM) of Docetaxel-loaded, PLA-TPGS nanoparticles with 10% drug loading. The drug encapsulation efficiency is ~96%. (B). In vivo pharmacokinetics (PK) after in vivo administration of paclitaxel formulated in PLA-TPGS nanoparticles vs Taxol®. One shot of the former realized in 336-hour chemotherapy compared to 22-hour for the latter. (Source: Prof Feng SS, NUS)



(C)



(D)

(C). FESEM image of a stent coated with paclitaxel-loaded, TPGS-emulsified PLGA nanoparticles. (D). Caco-2 cell viability at various Fe concentrations after 48-hour incubation at 37°C showing that conventional IOs is cytotoxic compared to Prof Feng's nanoparticle formulation. (Source: Prof Feng SS, NUS)