Nanoparticle generator improves chemotherapeutic delivery to metastatic TNBC

With partial support by the National Natural Science Foundation of China, Prof. Xu Rong (**徐戎**) at the Department of Pharmacology, School of Basic Medicine, Tongji Medical College, Huazhong University of Science and Technology, participated in a collaborative study led by Profs. Shen Haifa (**沈海法**) and Mauro Ferrari at Houston Methodist Research Institute in the United States to develop effective treatment for metastatic triple negative breast cancer (TNBC). Their work was published in the April issue of *Nature Biotechnology* (2016, 34: 414—418), with Prof. Xu Rong as the first author.

TNBC lacks the expression of hormone receptors and HER2/*neu*. It accounts for about 15% of all breast cancer cases, but is responsible for over 30% of total mortality in breast cancer patients. In the late stage TNBC, as the cancer cells have metastasized to distant organs such as the liver and lung, systemic treatment with chemotherapy does not work well due to the existence of multiple biological barriers that block drug penetration into tumor tissues. Prof. Xu and Shen's research team developed a novel technology platform, injectable nanoparticle-generator (iNPG), to overcome sequential biological barriers and deliver drug molecules to tumor cells. The iNPG is a porous silicon disk measuring 2.5 μm in diameter and 700 nm in height. The size, shape, and surface chemical property of the iNPG are optimized for its accumulation at tumor vasculature in metastatic organs due to tumor tropism. The researchers loaded polymeric doxorubicin (pDox) molecules into the nanopores in the iNPG to prepare the composite drug iNPG-pDox. Once the drug is administrated through intravenous infusion, it travels in circulation and settles at tumor vasculature, where the pDox molecules self-assemble into pDox nanoparticles (pDox NP). Upon internalization by tumor cells, pDox NP is transported in the endosomes where a pH-sensitive linker connecting doxorubicin and the polymer is cleaved in the acidic environment, thereby releasing doxorubicin to the vicinity of the nucleus for immediate drug entry into the nucleus. Systemic treatment of mouse models of metastatic TNBC with iNPG-pDox provided significant survival benefit in all treated mice, including long-term survival in 50% of the mice, a result that was not attainable by treatment with the current clinical anthracycline antitumor drug doxorubicin or liposomal doxorubicin (Doxil®).

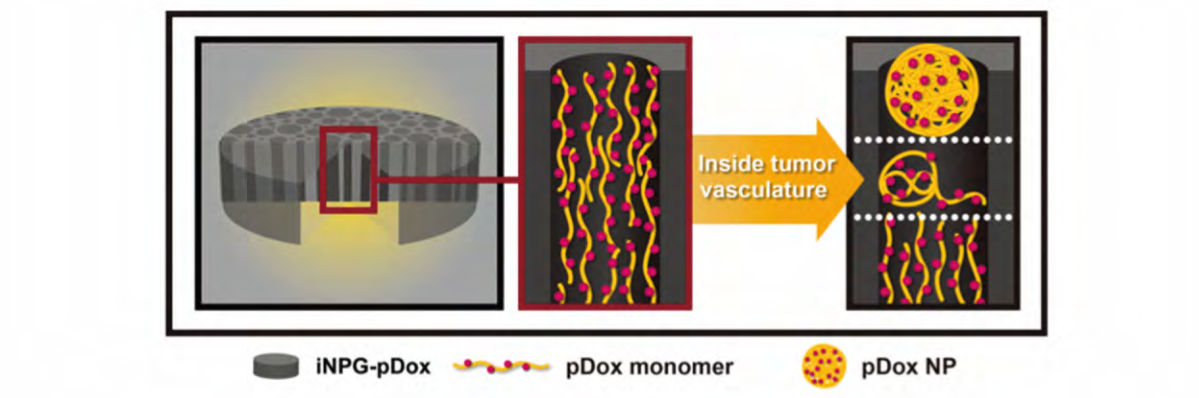

Figure Schematic view of iNPG-pDox on its composition and nanoparticle reconstitution at tumor vasculature.

The iNPG technology platform has a huge potential for development of other novel therapeutics, and its applicable disease indications are not limited to TNBC. Prof. Xu and colleagues are currently expanding their research scope, with more exciting discoveries expected in the coming years.