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"Can Physiochemical Properties of Nanoconstructs Improve Anticancer Activity?"

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Abstract: The main limitation of conventional cancer chemotherapy is the systemic toxicity to normal tissue. The discovery of the enhanced permeability and retention (EPR) effect by Matsumura and Maeda in the early 80's has defined the principle of anticancer nanomedicine tumor targeting. The EPR effect is based on the structural malformations of tumor blood vessels which promotes the accumulation of the nanomedicine at the tumor site by "passive targeting" while preventing its extravasation from normal vessels. Following this landmark description of the EPR principle for tumor targeting, several nanomedicines were developed for anticancer chemotherapy. Central to the development of these new delivery platforms, the size of nanoparticles were found to be critical.

Extensive studies have shown that this criterion will determine their longevity in the blood circulation and their biodistribution when administrated to a patient. Unfortunately, other criteria such as the effect of drug loading, the release rate of active components, as well as connecting those physical properties to cell specific endocytic mechanisms, have not been fully studied.

Self-assembled amphiphilic SMA copolymers form micellar structures in aqueous solution which can accommodate a wide range of hydrophobic drugs. In the current studies, we have generated various SMA- micelles with a loading of 5-40 % as determined by UV spectrophotometry. In this presentation we demonstrate how active drug loading and release rate, influence the biological activity of EPR based nanoconstructs, in a cell type- specific manner.

Brief Bio: Dr Greish had basic training as an oncologist and practiced clinical oncology from 1995-2006. He received his research training in the laboratory of Professor Hiroshi Maeda, who first described the EPR effect. As a JSPS postdoctoral fellow, he developed and carried out *in vivo* pharmacokinetic studies of various tumour targeted micelles. From 2008-2011, he coordinated *in vivo* experiments on polymeric drug delivery platforms for solid tumour therapy in the Department of Pharmaceutics and Pharmaceutical Chemistry of the University of Utah. He

moved to the University of Otago in 2011 and his current research focuses is on novel nano-systems for selective drug delivery.