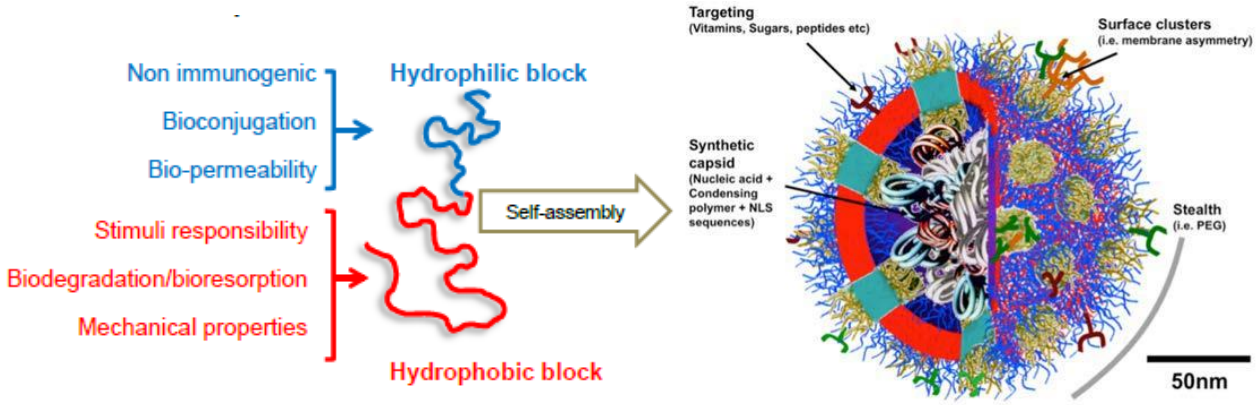
P.41 Synthetic DNA viruses for targeting breast cancer cells

L Guan and G Battaglia

Department of Chemistry and MRC Center for Medical Molecular Virology, University College London, UK

Breast cancer is the third most common cancer to cause deaths in all population and the second in women in UK, but with much lower 5 years survivals rates than other developed countries. Although enhanced permeability and retention (EPR) effect was previously demonstrated in anti-cancer macromolecules delivery in a tumor selective manner [1, 2], vectors that are highly selective and well permeable into tumors are strongly desired for early detection, diagnosis and clinical treatments. Since the statement of genetic central dogma [3] has made the gene function studies possible [4], such vectors are hoped to be potentially applicable in genetically affected diseases with efficient nucleic acids (NAs) delivery into targeted cells. As the most powerful tools in DNA transfection [5], viruses are excellent models to mimic for synthetic non-viral vectors design. Since late 90s, polymersomes have been proposed as platform for drug delivery systems [6, 7]. Polymersomes are closed vesicles (40-400nm in diameter) produced from the self-assembly of amphiphilic block copolymers in aqueous solution, which could be designed to be biocompatible and potentially biodegradable [8]. Considering their relatively robust membrane, kinetic stability, and stealth property, polymersomes were suggested to be more promising in the intercellular or intracellular delivery of macromolecules in live cells, and the determination of micro-studies compared to natural lipids [9].

Herein, we are aiming to discover the most optimal synthetic vectors to target breast cancer cells both *in vitro* and *in vivo,* and efficiently deliver DNA and/or DNA complex into nucleus as a new method to treat breast cancer by mimicking the natural viral infections. Breast cancer cell targeting will be achieved by conjugating specific ligands onto the polymersome surface at suitable intensity, while encapsulated DNA is decorated with condense components and nuclear localization sequence for nucleus entry.



[1] Azzopardi, E.A., E.L. Ferguson, and D.W. Thomas, The enhanced permeability retention effect: a new paradigm for drug targeting in infection. Journal of Antimicrobial Chemotherapy, 2012. 68(2): p. 257-274

[2] Maeda, H., H. Nakamura, and J. Fang, The EPR effect for macromolecular drug delivery to solid tumors: Improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo. Advanced Drug Delivery Reviews, 2013. 65(1): p. 71-79

[3] Crick, F., Central dogma of molecular biology. Nature, 1970. 227(5258): p. 561-3

[4] Podolska, K., et al., Gene therapy prospects--intranasal delivery of therapeutic genes. Advances in clinical and experimental medicine : official organ Wroclaw Medical University, 2012. 21(4): p. 525-34

[5] Pichon, C., L. Billiet, and P. Midoux, Chemical vectors for gene delivery: uptake and intracellular trafficking. Current opinion in biotechnology, 2010. 21(5): p. 640-5

[6] Discher, B.M., Polymersomes: Tough Vesicles Made from Diblock Copolymers. Science, 1999. 284(5417): p. 1143-1146

[7] Discher, D.E., Polymer Vesicles. Science, 2002. 297(5583): p. 967-973
[8] Lomas, H., et al., Efficient Encapsulation of Plasmid DNA in pH-Sensitive PMPC-PDPA Polymersomes: Study of the Effect of PDPA Block Length on Copolymer-DNA Binding Affinity. Macromolecular Bioscience, 2010. 10(5): p. 513-530
[9] Du, J. and S.P. Armes, pH-responsive vesicles based on a hydrolytically self-cross-linkable copolymer. Journal of the American Chemical Society, 2005. 127(37): p. 12800-1