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Agathe Figarol et al., J Pharm Drug Deliv Res 2017, 6:4 (Suppl)
DOI: 10.4172/2325-9604-C1-020

International Conference and Exhibition on

Nanomedicine and Drug Delivery

May 29-31, 2017 Osaka, Japan

Development of an *in vitro* model to predict the passage of polymersomes nanovectors through the endothelial barrier for an optimized drug delivery to tumor cells

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Statement of the Problem: The use of polymeric nano-objects for an enhanced drug delivery has been presented as an answer to override the extremely strong secondary effects of anticancer therapy. Compared to polymeric micelles, polymersomes have the valuable ability to stably encapsulate and deliver both amphiphilic and hydrophilic components. Poly(ethyleneoxide-b-ε-caprolactone) (PEO-PCL) polymersomes are a rational model to predict the fate of a nano-vector after injecting into the blood. Both PEO and PCL polymers present indeed a relative biocompatibility. Besides, PEO-PCL polymersomes are expected to escape from the immune system defenses thanks to the PEG chains preventing opsonisation. However, there is still a lack of understanding of what occurs at the cellular scale when the polymersomes cross the endothelial barrier of the blood vessel and reach the targeted tumor.

Methodology & Theoretical Orientation: This study questions the interactions between human endothelial and cancerous cells and PEO- PCL polymersomes charged with different fluorophores (3,3'- dioctadecyloxacarbocyanine perchlorate, anthracene, or pheophorbide A). A thorough physico-chemical characterization is first conducted using dynamic light scattering, zeta potential, UV-vis measurements, and electron microscopy. The polymersomes are then incubated with primary human umbilical vein endothelial cells, chosen to mimic the blood vessel walls. The goal is to better understand the drug delivery process and the requirement of the enhanced permeability and retention effect to reach the tumor. For the latter, 3D spheroids of human colon carcinoma HCT- 116 cell line lead to result a step closer to the real-life situation compared to 2D cultures.

Conclusion & Significance: This study will be completed by numerical modeling of the polymersomes circulation in the blood, through a collaboration granted by the French National Research Agency. We will thus obtain a complete predictive model of the phenomena occurring to a polymeric nano-vector from the injection to the drug delivery.

Biography

Agathe Figarol has developed her expertise in nano-bio interactions since her MSc. She has done her thesis on Health and the Environment (Cranfield University, UK). Looking at the cellular impact of silica nanomaterials on keratinocytes, she already started to combine the different approaches of physical chemistry and biology relying on her technical background in Biology Engineering (Université de Technologie de Compiègne, France). She further enhanced her pluridisciplinary along her PhD exploring the impacts on physico-chemical characteristics of carbon nanotubes on macrophages (Ecole Nationale Supérieure des Mines de St-Etienne, France). Her confirmed enthusiasm for the dynamic and state-of-the-art field of nanobiology led her, after a year of discovery of the industrial strategy on toxicology, to join a collaborative project on polymeric nanovectors (IPBS and IMRCP laboratories from the Université Paul Sabatier de Toulouse, France).

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