Protein Corona Composition and Cellular Uptake of PEO-b-PCL and PEO-b-PBCL Micelles by HCT 116 and SW 620 Following Incubation with Plasma from a Colorectal Cancer Patient

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Polymeric micelles are promising nano-carriers for poorly water-soluble chemotherapeutics. There is, however, little known about their fate following administration in cancer patients. This research aims to compare the composition of protein corona from colorectal cancer patient plasma on polymeric micelles self-assembled from poly(ethylene oxide)-b-poly(Ɛ-caprolactone) (PEO-b-PCL) and PEO-b-poly(α-benzyl carboxylate-ε-caprolactone) (PEO-b-PBCL) with varying degrees of polymerization (DP). In addition, we aim to probe the effect of the biological identity of these micelles on their uptake by colorectal cancer cells. Seven di-block copolymers of different DPs were synthesized by ring-opening polymerization of either Ɛ-caprolactone or α-benzyl carboxylate-ε-caprolactone by methoxy-PEO (MW 5000g/mol) to form PEO-b-PCL (DP 19, 43, 64, 79) and PEO-b-PBCL (DP 19, 35, 60), respectively. Near-infrared fluorophore Cy5.5 was conjugated to the hydrophobic block to make the polymeric micelles traceable. The uptake of polymeric micelles was studied following 6 and 24 h incubation with HCT116 and SW620 cells using flow cytometry. For the analysis of the biological identity of micelles, they were incubated with i) cell culture media supplemented with FBS and ii) plasma extracted from a patient with colorectal cancer. The corona-coated micelles were then collected and their proteins were analyzed by liquid chromatography-mass spectrometry. Our results showed that PEO-b-PCL micelles have significantly higher uptake compared to the PEO-b-PBCL ones in both cell lines. Changing the DP of the hydrophobic block did not affect the cellular uptake of PEO-PBCL micelles, but PEO-PCLs of different DP showed differences in their cellular uptake. The protein corona profiles of the PEO-PBCL and PEO-PCL micelles were significantly different. The results reflect the critical role of block copolymer structure on their protein corona profiles. It also highlights the potential influence of protein corona profiles on improving the steric stabilization of polymeric micelles and reducing cell-micelles interactions. Support: Funded by NSERC Discovery and NSERC CREATE PoND.