SRs and Cd81 Receptors-mediated endocytosis of PMPC-PDPA polymersomes via dynamin II-independent manner

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Abstract

Polymersomes have been revealed to be an ideal tool for the efficient intracellular delivery of a large diversity molecules. However, the molecular pathways regulating polymersomes uptake by cells remain still poorly investigated, especially regarding the role played by surface membrane receptors such as scavenger receptors and tetraspanin family proteins. This subject has crucial implications in biomedical research applied to payload delivery by polymersomes. Here, we investigated the mechanisms involved in polymersomes interaction with specific cell receptors. PMPCx-PDPAy-based self-assembly of polymersomes was carried out using the pH-switch method. After this, polymersomes were purified through a hollow fiber (tangential flow filtration system) followed by step-gradient centrifugation to isolate several subpopulations of particles having homogenous sizes. Polymersomes concentration was quantified by HPLC, while the size characterised by DLS and TEM analysis. The screening of specific receptors guiding the uptake of polymersomes was evaluated by western blot and immunofluorescence. The cytofluorometric method was used to study the kinetics of polymersomes uptake. siRNA and/or shRNA was used to knockdown the expression of endocytosis proteins and manipulate the uptake of polymersomes by carcinoma cells. The results showed that changes in the polymer lengths of PMPC affected the rate of vesicles uptake. Moreover, we deciphered an essential correlation between the degree of polymerisation(i.e., the polymer lengths) and the kinetics of polymersomes uptake. We confirmed a key role played in PMPC25-PDPA70 polymersomes uptake by scavenger receptors (SRBI and CD36) and CD81 receptor in cancer cells. Silencing of SR-BI gene using siRNA in FaDu cells decreased PMPC-PDPA polymersomes uptake by 50% in a dynamin-independent manner. Here, we highlighted the dynamics of interaction between polymersomes and plasma membrane receptors, SRs and CD81. We have shown that polymersomes uptake guidance is dynamin-II-independent.

References

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Figures

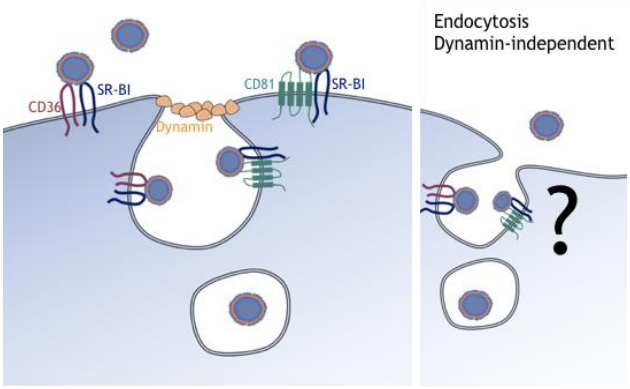

Figure 1. The SR-BI/CD36 and the tetraspanin CD81 are natural receptors for cellular uptake of $PMPC_{25}$-$PDPA_{70}$ polymersomes via dynamin-II independent manner.