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Model cell membrane interaction with a bioinspired amphoteric polymer

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We present recent investigation by means of nanoscale techniques on biocompatible linear polyamidoamines with amphoteric character, namely AGMA1 [1] and ARGO7 [2]. These polymers have been shown of extremely promising and already proved medical interest, comprising their strong protection actions against virus infection, mainly papilloma and herpes [1-5] and the extremely low toxicity of their DNA complexes, with respect to other used polymers such as PEI and protamine, applied in nanovector design for gene delivery. Our studies focus on the most important of these polymers, AGMA1, a prevailingly cationic 4-aminobutylguanidine-deriving PAA, whose mechanism of action is so far not fully understood. The current understanding is that its interaction with cell surfaces by means of glycosaminoglycans (HSPG) has a major role in its protective action against viruses. Yet, AGMA1 is active also against HPV-31, whose attachment does not appear to be dependent on HSPG [4]. HPV-31, whose attachment does not appear to be dependent on HSPG [4]. Therefore, AGMA1 binds other (as yet unidentified) receptors on the cell surface. As the known recipient is the HS carbohydrate moiety, other sugars rich membrane components have been proposed as probable AGMA1 target. Therefore, to shed a light on the mechanism of interaction of the polymer with sugar containing biologically relevant molecules, not HS, we have investigated AGMA1 in interaction with glycophyngolipids, Specifically, we studied multicomponent symmetric vesicles enriched in ganglioside GM1 [6] built to mimic biological membrane domains, in the presence of AGMA1, At physiological pH, electrostatic effects should be the relevant interactions between GM1 and AGMA1. Taking advantage of the same mechanism we investigated the possibility of building lipid based core-shell particles to vehiculate AGMA1/siRNA complexes. Moreover, since it is probable that AGMA1 interacts with the barrier of mucus which cover the involved tissue we have extended our investigations also to mucin, constituting the biological barrier to the target tissues of the medical application of the polymers.

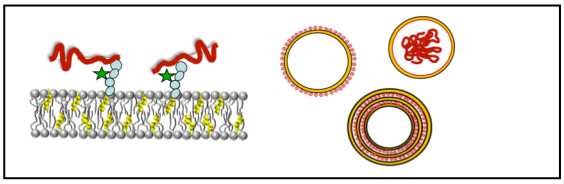

Figure 1. Artificial model membrane enriched in ganglioside in interaction with AGMA1. Coated vesicle and multilayer vesicle are formed in different conditions.

References

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