Design of multivalent polymersomes for range-selective binding

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The success of nanomedicine is nowadays strictly associated to the ability of selectively targeting the site of interest: the more specific a therapy is, the more likely it is to be efficient.

The use of multiple ligands, i.e. multivalency, with low affinity for their receptors has proved to successfully address this 'selectivity' requirement [1]. In fact, thanks to the ligand-receptor simultaneous interactions, the collective binding (avidity) compensates for the low affinity and generates a switch-like behaviour where the binding occurs only above a certain receptors density [2].

This mechanism, widely spread in nature for the mediation of several aspects in cell biology [3,4], has recently inspired the design of several drug delivery polymeric nano-constructs functionalized with suitable ligands to guide the carriers according to the level of receptors expression and to deliver their cargos where most needed [5].

Polymersomes, self-assembled amphiphilic diblock copolymer vesicles, have been widely used as nano tools for drug delivery purposes thanks to their versatility and increased stability within biological environments. A recent research carried out on pegylated polymersomes has shown, through cellular uptake studies, that these nanovesicles can display a superselective behaviour by tuning the effective contribution, in terms of chemical potential, of different parameters including the polymer brush length, particle sizes, ligands number [6].

Taking inspiration from these results, the main purpose of the present study was to explore a new type of selectivity where multivalent polymersomes only bind targets when the receptor density is within a certain range. To this aim, a statistical mechanical modelling study was firstly carried out in order to characterise the region where to expect the range selective targetin. Then, Angiopep2-decorated polymersomes were prepared by a solvent switch approach. The formulations were characterised by DLS and TEM and binding studies between functionalized polymersomes and highly-expressing LRP1 FaDu cell line were carried out through fluorometer and laser confocal scanner microscopy.

Understanding the behaviour of the modelled system will significantly improve the design of precise nano-devices with the ability of performing *ad hoc* selective transport and site targeting within cellular environment.

References

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