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Multivalent Nanosystems to Target Inflammation

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Polymer therapeutics in medicine are increasingly gaining acceptance and recognition as an independent area of scientific endeavor and pharmaceutical development. The combination of a high density of endgroups and a compact well defined molecule structure makes particularly dendritic architectures attractive for biomedical applications.1 Due to their low degree of molecular weight dispersity and flexible design, dendritic polyglycerols (PGs) have a broad range of potential applications in medicine.2Dendritic polyglycerol architectures have already been demonstrated to be useful in therapeutic approaches related to multivalency because of the synergy between the nano-sized dimensions combined with the high density of functional groups.3,4 Based on polyglycerols, several attempts have been made to mimic specific glycoarchitectures, (i) with neutral hydroxyl end groups representing analogues of polysaccharides, and (ii) polyanionic derivates similar to negatively charged polysaccharides, such as heparin.

Most recently, our group demonstrated that polyanionic, dendritic polyglycerol sulfates (dPGS) exert strong binding affinity to cellular targets involved in the inflammatory process by inhibiting leucocyte infiltration.4 Translation into the diagnostic application was accomplished by in vivo fluorescence imaging in a rat rheumatoid arthritis (RA) model, demonstrating fast and highly selective targeting of tissue inflammation.5 We also demonstrated that dPGS acts favorably in RA and osteoarthritis models, leading to chondroprotective properties6. Furthermore, we demonstrated chemical versatility by synthesizing shell-cleavable dPGS and mixed polyanions to modify pharmacokinetics and selectivity in bone targeting7 and include dPGS into micelles or nanogels for targeting and drug transport8

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