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Biodegradable nanobrushes for drug delivery

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Biodegradable polymers such as polylactic or polyglycolic acid when conjugated with polyethylene glycol find wide applications as material for nanoparticles due to their self association in aqueous milieu. Self assembly restricts these polymers to spending their surface for intermolecular contacts and allows only one or a few covalent attachments on the interface to bulk solvent. In contrast, biopolymers composed of units with pendant functional groups can use multiple attachments to obtain highly reactive nanobrushes. Such a particularly useful biopolymer is poly(β -L-malic acid), which can be obtained in high purity from biological sources. Among these covalently attached functional groups are antibodies, antisense oligonucleotides and/or chemotherapeutic prodrugs, membrane destabilizing peptides, protecting polyethylene glycol, gadolinium MRI contrast agent and fluorophores for imaging. While being biodegradable and nontoxic, these nano conjugates have demonstrated high efficacy in the treatment of brain and breast cancer and proven as powerful MRI contrast agents for the diagnosis of primary and metastatic brain tumors in preclinical animal models. Because antibodies obscure the nanobrush character, we replace them by affinity peptides. These polymalic acid-based nanobrushes are expected to have, among other advantages, reduced manufacturing costs, increased loading capacity increased shelf stability, superior penetration efficacy into deep tumor tissue, reduced immunogenicity. We have succeeded in the design of such nanobrushes using public referenced receptor-specific affinity peptides. The breakthrough was finding appropriate linkers for optimal geometric arrangements. Emerging results obtained by *in vivo* imaging demonstrated excellent tumor specificity identifying human HER2-positive breast cancer or solid brain tumor.

Biography

Eggehard Holler has received his PhD in Germany 1967 in Chemistry and his *Venia Legendi* 1974 in Biochemistry. After ground breaking research in enzymology and pharmacology, he joined 2008 the emerging Nanodrug Research Center at Cedars-Sinai Medical Center, Los Angeles, California, and introduced polymalic acid as a biodegradable and versatile platform for drug delivery.

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