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Polymalic acid: Biology and drug delivery

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Polymalic acid is a highly water soluble polyanion synthesized by the slime mold *Physarum polycephalum* for managing the synchrony of nuclear divisions in the growing polynucleated plasmodium. Alternating binding of replicative DNA polymerases and newly synthesized histones together with trafficking between nuclei are considered fundamental in the maintenance of the synchronous division cycle. Massively in excess produced polymer is highly purified from the culture medium and used as nanoscale platform for drug delivery. Being biodegradable, non-toxic, non-immunogenic, the polymer optimally qualifies as a nanoparticle platform. The polymer offers a large number of reactive carboxylates (900 per polymer of Mw 100,000) and a highly flexible architecture. A variety of interesting molecules such a chemotherapeutics, antisense oligonucleotides, proteins, peptides and polyethylene glycol (PEG) are covalently attached for targeted drug delivery, but also fluorescent molecules and DOTA-gadolinium(III) have been conjugated for imaging. Methods of physical, chemical and functional group analysis of the pharmaceutically pure all-in-one covalent nanodrug have been established, and biocompatibility including cytotoxicity and immunogenicity has been demonstrated *in vitro* and *in vivo*. All-in-one covalent contrast agents show favorable biodistribution by fluorescence and magnetic resonance imaging (MRI) and have been used for diagnosis of brain tumors in animal models. Delivery of drugs as inactive prodrugs and their activation at the site of treatment render the all-in-one covalent nanodrug a highly efficient and secure treatment modality.

Biography

Eggehard Holler has completed his Ph.D. at the age of 27 years from Johann-Wolfgang Goethe University at Frankfurt/Main, Germany and his postdoctoral studies at Cornell University and UC Berkeley. He is Professor at University of Regensburg and at Cedars-Sinai Medical Center. His scientific merits are in the fields of replication and protein synthesis, platinum anticancer mechanisms, biochemistry of myxomycetes, polymer chemistry and drug delivery. He is frontier in the design of targeted nanodrugsand treatment of tumors in brain and breast. He has contributed over 150 scientific articles and book chapters. Presently he holds position at Nanomedicine Research Center at Neurosurgical Department of CSMC.

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