P - 634: Glucuronic acid-HSA conjugates for targeted therapy of inflammation

Keywords
- Site directed targeting of drugs as albumin conjugates
- Glucuronic acid linkage as predetermined breaking point for site directed drug release
- Longer circulation time; higher bioavailability; lower systemic toxicity of albumin conjugated drugs
- Technology applicable for targeting inflammatory diseases as rheumatic diseases, uveitis, asthma, Morbus Crohn, lupus erythematoses, psoriasis.
- Convincing data from in vitro and preliminary in vivo experiments
- Technology applicable for further indications as graft-versus-host disease and mammary carcinoma

Abstract
We describe compounds and the use of compounds to provide a technology which overcomes the disadvantages of drugs of prior art for treatment of several diseases (preferably inflammation diseases). The new compounds have a circulation time like albumin and accumulate within the respective diseased tissue.

The Technology
E.g. rheumatic diseases are generally treated by administration of different kinds of steroids. Since the steroids exhibit their biological effects not only in the target tissue, undesired side effects are observed. It is apparent that therapy by use of an agent which accumulates within the target tissue would lead to a reduction of these side effects.

The inventors used albumin as transporting and targeting agent. It is known that albumin conjugates are introduced via endocytosis into fibroblasts in case of inflammation (and into tumor cells as well) and are digested by lysosomal proteases. In the same cell compartment, i.e. the lysosome, glucuronidases are localized. The inventors conjugated the albumin to the pharmacologically active drug (e.g. a steroid) by means of glucuronic acid. The glucuronic acid linker acts twice: as linkage between the drug and albumin it facilitates the albumin targeted transport into the diseased tissue, and after digestion by glucuronidases the release of the drug at the site of action is accomplished.

Applications and Commercial Opportunity
DKFZ is currently seeking a commercial partner to develop this technology under an exclusive licence and/or collaboration agreement. Exclusive licensing for specific applications/indications is possible.
Lysosomal uptake of fluorescence-labelled albumin in synovial fibroblasts of a patient with rheumatoid arthritis.²

Inventors
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Intellectual Property
An EP patent application is filed and will be granted soon (see EP 04 018 855.9).

Further Information
No other public information is currently available, but further information (speaking with the inventors) is available under a signed Confidential Disclosure Agreement (CDA).

References
2. (Funk, EULAR, Poster presentation, Paris, 2008)

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