PROGRAMMING NANOPARTICLES FOR CELL INDENTIFICATION

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The last three decades of nanomaterial research have provided us with a plethora of materials with a tremendous number of unique properties. For biomedical applications cancer therapy has, thereby, been one of the most intensively investigated fields of application. The passive accumulation of particles in cancer tissue following intravenous administration spurred this development and is a significant advantage over other target sites. However, transporting drugs via nanomaterials is a difficult trade-off. While on the one hand it allows to deliver drugs that would fail to reach their targets on their own, nanocarriers suffer from poor tissue distribution. A prerequisite that is often discussed to reach better tissue accumulation is their direct binding to target cells. (1) While this has been postulated for cancer (1) it is even more true for tissues, that have little or no capacity to retain nanoparticles by passive mechanisms.

In this respect the retina and kidney glomeruli are two tissues for which such direct mechanisms of interaction between nanoparticles and target cells play a major role. Even though it has been known for many years that ligand-receptor interactions play a pivotal role for cell identification, it is for many applications not sufficient to outfit nanoparticles with the ability to bind to a single target structure. Such particles may lack the necessary specificity to avoid binding to cells that carry a corresponding receptor but that are located in an off-target tissue. We believe that nanoparticles would profit tremendously from an ability that viruses have. Rather than relying on the presence of a single target structure on cell surfaces, they check in a stringent sequence for the presence of several structures that need to be present. To this end viruses bind heteromultivalently to several targets on the cell membrane. Only when a cell matches all criteria, a virus particle will regard it as its host cell. Thereby, viruses do not only make use of ligand-receptor interactions but also of enzyme reactions with substrates. Either way, the interaction follows a flow diagram that is typical for an array of logical operations. In recent years we could show that nanoparticles that are able to mimic such 'Boolean' operations have a superior specificity for their target cells which is of tremendous advantage for ocular as well as renal tissue targeting. (2) The exact placement of molecules for cell recognition in the nanoparticle corona is, thereby, a prerequisite for material design. (3)

The talk will provide insight into the interaction of nanomaterials with ocular and renal tissues. It will furthermore discuss material design criteria that are of particular significance for the presentation of ligands, cell avidity, as well as for the development of particles that identify cells using logical operations.

References:

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Short Curriculum Vitae:

Achim Goepferich is Professor of Pharmaceutical Sciences in the Department of Chemistry and Pharmacy at the University of Regensburg in Germany where he is head of the Pharmaceutical Technology group. His research interests are in the field of drug delivery, biomaterials and nanomaterials for therapeutic and diagnostic applications. He earned his PhD from the University of Heidelberg for his work on transdermal drug delivery. After his graduation he was a post-doctoral fellow in the Department of Chemical Engineering at MIT working on biodegradable materials and polymer erosion. In the years to follow he held positions as a visiting scientist in the Department of Chemical Engineering at MIT, the Department of Bioengineering at Rice University in Houston, the Wyss Institute at Harvard University and as a research associate in the Department of Pharmaceutics at the University of Erlangen, Germany. Currently his research focus is on the intersection between pharmaceutical sciences, biology and material sciences. With his research he tries to understand how cells interact with materials and how we can use this information for the rational design of materials that deliver drugs more efficiently than existing technology.