Press Release

A New Postal Code for Cancer

Freiburg researchers find purely chemical way to target therapeutic nano-containers to cells

Scientists have discovered that a polymer can provide a key to get into tumors: Prof. **Prasad Shastri**, Director of the Institute of Macromolecular Chemistry and core member of the cluster of excellence BIOSS Centre for Biological Signalling Studies at the University of Freiburg, and graduate students **Julia Voigt** and **Jon Christensen** have developed a new paradigm to home nanoparticles, containers that measure a few 100 nanometers in size, to endothelial cells. Using just charged polymers with the right affinity for cell lipids the team has developed nanoparticles that can recognize specific cell types simply by their chemical properties. “This is a remarkable discovery, as it allows for the first time to target a specific cell type purely through biophysical principles, and without using the traditional ligand-receptor approach” says Prof. Shastri who led the study. Until now researchers placed molecules on nanoparticles that can latch onto proteins on cell surface - called receptors.

These receptors act as an address or a biological postal code. However in tumors these addresses can change rapidly with time. To solve this lack of precision Shastri and team developed particles that are delivered to endothelial cells using a biophysical approach. “This delivery approach does not require a biological postal code for targeting of nanoparticles and is an important step forward in developing nanoparticle based systems for treating cancers” says Julia Voigt the lead author of the paper.

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Cancers are very hungry tissues and they need constant nourishment. This is provided through their own supply of blood vessels. “By going after endothelial cells that make up these blood vessels, we can starve the tumor or kill it with one payload” says Jon Christensen who is a co-author on this study and works on tumor metastasis.

Nanoparticles are used to deliver therapeutics in treating cancers. These very small pills, cornerstones of nanomedicine, get injected into the body and reach the tumor cells via the bloodstream. When they find the targeted cells, they need to be eaten so that the drug can act within the cell. This mechanism is called receptor-mediated endocytosis. Shastri and his team looked to develop a new approach that targets a transport process that is dominant in endothelial cells. It turns out that a structure called caveolae is found in large amounts on endothelial cells. Caveolae are “lipid rafts” on the cell membrane and are one of the doors into the endothelial cells. Prof. Shastri and his team discovered that by decorating nano-pills made of lipids with negatively charged polymers, nanoparticles can preferentially enter through this door. “How exactly these charged polymers enable the nanoparticles to unlock this door we are not sure yet, but we feel confident that with further studies this method could usher in a new approach to delivery of drugs in general” says Shastri. This project was funded by Nano@matrix supported by INTERREG and the cluster of excellence BIOSS Centre for Biological Signalling Studies.

Original Publication:

Julia Voigt, Jon Christensen, V. Prasad Shastri: Differential uptake of nanoparticles by endothelial cells through polyelectrolytes with affinity for caveolae .PNAS Online Early Edition 2014.

Caption:

Immunofluorescence image shows nanoparticles targeted to endothelial cells. The red particles turn orange when overlapping with the green caveolin in the lipid rafts of the cells. Source: Julia Voigt / Prasad Shastri

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