SURFACE MODIFICATION OF PLGA MICRO- AND NANOPARTICLES - ESPECIALLY WITH GD-COMPLEXES

Until now we approached the topic of surface modification of PLGA micro- and nanoparticles from various perspectives:

- For site specific drug delivery particles were decorated with lectins for *targeting to specific sugar moieties* in the glycocalyx of certain cell types. It became evident that not only binding to the cell surface, but also uptake into the cell can be mediated by entering mainly clathrin-mediated endocytosis.
- Another focus was *enzyme substitution therapy* meeting the challenge of retained enzyme activity in spite of covalent immobilization.
- For *magnetic resonance imaging*, skilled procedures have been developed to guarantee access of water and thus, contrast enhancement by surface immobilization of Gd-chelates.
- Another by far not easy task is elucidating the effect of *surface charge* by inverting negatively charged PLGA-particles to positive ones by immobilization of polycations omitting destruction of the matrix. Appling different cell models the interactions have been characterized.
- Finally, the impact of *stabilizers* on covalent grafting of particles has been examined.

Tools:

- Preparation of PLGA micro- & nanoparticles: spray drying, solvent evaporation techniques according to hydrophilicity of the drug, high pressure homogenization
- Characterization: size and zeta potential by dynamic light scattering, nanoparticle tracking analysis, laser diffraction for microparticles; PLGA content by HPLC-analysis, custom SEM &TEM
- Detection: incorporation of hydrophobic dyes as a label for fluorescence detection in the microscope (deconvolution) or quantification (fluorescence reader), flow cytometry
- Surface modification: different activation procedures and spacers
- Cell (tissue)-particle interaction: different cell lines for single cell and monolayer experiments (intestine, bladder, blood vessels, macrophages, breast and prostate cancer), binding and uptake studies, transport studies with monolayers cultivated on filters, impact of flow on particle - cell interaction by use of an surface acoustic wave driven chip, assessment of toxicity using cell number, metabolic activity, expression of marker enzymes or proliferation as a marker

References:

Ratzinger, G., Länger, U., Neutsch, L., Pittner, F., Wirth, M., Gabor, F. **Surface modification of PLGA-particles: The interplay between stabilizer, ligand size and hydrophobic interaction.** Langmuir 26, 1855-1859 (2010).

Ratzinger, G., Fillafer, C., Kerleta, V., Wirth, M., Gabor, F., **The role of surface functionalization in the design of PLGA micro- and nanoparticles.** Crit. Rev. Ther. Drug Carr. Syst. 1, 1-83 (2010).

Ratzinger, G., Wang, X., Wirth, M., Gabor, F., **Targeted PLGA-microparticles as a novel concept for treatment of lactose intolerance.** J. Contr. Rel. 147, 187-192 (2010).

Ratzinger, G., Agrawal, P., Körner, W., Lonkai, J., Sanders, H. MHF., Terreno, E., Wirth, M., Strijkers, G.J., Nicolay, K., Gabor, F., **Surface modification of PLGA nanospheres with Gd-DTPA and Gd-DOTA for high-relaxivity MRI contrast agents.** Biomaterials 31, 8716-8723 (2010).

Al-Dubai, H., Pittner, G., Pittner, F., Gabor, F., **Biocompatible medical implant materials with binding sites for a biodegradable drug-delivery system.** Nanotechnology, Science and Applications 4, 87-94 (2011).

Wang, X.-Y., Koller, R., Wirth, M., Gabor, F., **Lectin-Coated PLGA Microparticles: Thermoresponsive Release and In-Vitro Evidence for Enhanced Cell Interaction.** Int. J. Pharm. 436, 738-743 (2012).

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