Nano-composites in human cells "disease-in-a-dish" models

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Oral presentation

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In Frankfurt, integrated in a multidisciplinary (*i.e.*, life sciences, engineering and exact sciences) international collaborative network, one of our main goals is characterizing and validating wildtype- and cancer- human cell interactions with biomaterial complex composites for tissue engineering and subsequent applications in regenerative medicine. Our focus is on cancers of the head and neck region, which cannot be completely resected or resected with a thin margin. The vision is to fill the cavity of these so-called R1-, R2- and Rx-resected tumours with composites pre-loaded with certain chemotherapeutics (*e.g.*, hedgehog signalling inhibition), in order to commence local treatment of the cancer immediately following its surgical resection. As far as we know, this is a new concept of locally treating these tumours before radiotherapy begins. Through this specific combined-modality treatment the high rate of locoregional recurrences –a major unsolved problem despite improvements in 'conventional' combined-modality treatment, for example for advanced head-and-neck cancer (Balermpas *et al.*, 2009), could be reduced and systemic chemotherapy reduced or avoided. Hedgehog targeting suppresses head and neck squamous cell carcinoma and enhances chemotherapeutic effects (Mozet *et al.*, 2013). Newly designed and approved drugs are being investigated in *in vitro* studies, and after proof-of-principle of promising scenarios further preclinical *in vivo* studies will be performed, hopefully leading to clinical Phase-I-studies.

Basically, the composite must fulfil the criteria for guided tissue regeneration (*i.e.*, prevent premature connective tissue ingrowth whilst promoting specific tissue regeneration) as well as control and induce a favourable immunological reaction, *e.g.* (M1- and M2-macrophages) against the biomaterial and the tumour. Our group has shown in *in vivo* studies that biomaterials induce either a mono- or multinuclear cellular inflammatory cell response (Ghanaati *et al.*, 2010 and 2012). A principal goal is an inverse relationship between composite degradation and tissue regeneration. Finally, in a timely fashion, the composite should be integrated, thereby preventing further surgical intervention and morbidity.

Our composites will be composed of scaffolds (*e.g.*, PLA-, collagen matrices or polymer hydrogels), and designed to include autologous (stem) cells, human growth factors, chemotherapeutics (in R1-2 situations), combination of ions and nanoparticles. The particular composition as well as the controlled degradation and subsequent release are essential for tissue regeneration and tumour therapy. The nano-object interactions with relevant human cells with and without therapeutic incorporation will be investigated. Factors such as the age of the subject, the structure of the scaffold and the type of tissue, wound or cancer involved generate the need for a more personalised regenerative medicine.

Our goals are clinically driven and we work together with industry. In the presentation we will give some examples of our above-mentioned clinical endpoints and needs that require to be integrated into the concept boundaries in order to provide tailored solutions.

References

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