

The Interface between Nanobiotechnology and Medicine: A Life Science Perspective

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INTRODUCTION: Modern medical research and practice is becoming increasingly influenced by advances in technology, nanobiotechnology being a good example, especially in the fields of tissue engineering (TE) and regenerative medicine. The widespread acceptance of a biomimetic approach has resulted in attempts to simulate natural interfaces, one of the exciting developments being that of a biodegradable matrix or scaffold to simulate the extracellular matrix (ECM) and equipped with essential bioactive signal molecules to elicit a physiological regenerative response. Nanofabrication techniques can be part of this interface construction. The use of “intelligent” materials, able to respond to changes in the microenvironment, can also take the form of a nanoparticulate drug or gene delivery system.

PERSPECTIVE: It is evident from the introductory remarks that a rational approach to a successful medical application of such technologies will require a high level of sophistication on the part of any life science models adopted to test such systems. Examples will be given exclusively from the use of *in vitro* models and the discussion will centre on new developments recently initiated or being planned for the future.

The complexity of the *in vivo* system at the tissue-biomaterial interface, in which heterogeneous cell types interact with each other and with the biomaterials demands co-culture models using human cells preferably as primary isolated cells. Thus, for bone TE osteoblasts and endothelial cells (EC), the latter responsible for vascularisation of the scaffold, need to be studied in a 3D-model. This can be well achieved using immunocytochemical markers of cell functionality in combination with confocal laser scanning microscopy (CLSM)¹. However, morphological studies even with sophisticated microscopical techniques and relevant phenotypic parameters (gene product) require to be complemented by parallel studies at gene transcript level. This can be readily achieved by various PCR techniques². The use of a reproducible and quantifiable 3D-model of angiogenesis with human microvascular EC and pro-angiogenic growth factors offers the possibility

to study how regenerative responses are regulated by various relevant factors³.

Co-culture models of barrier systems in the body, for example the blood-brain barrier or the alveolo-capillary barrier are important in studying strategies for drug and gene delivery, using bioresorbable polymers in nanoparticulate form. An *in vitro* model of the human air-blood barrier has already been established by our group⁴. With such complex model systems it is hoped to study how nanoparticles can be transported transcellularly as opposed to being stored intracellularly. In addition, such models could also be employed to delineate possible negative effects of clinical use of nanoparticles (“nanosafety”).

One of the very promising fields of endeavour for the future is that of adult progenitor cells, as this offers an autologous cell source, where the problems of disturbed immunological response should be minimal. Unraveling the lineage differentiation pathways for adult human stem cells will be vital in providing reproducible *in vitro* conditions in which to investigate possible cell adhesion ligands with which recruitment to a biomaterial scaffold could be achieved. At the moment we are studying these aspects in endothelial progenitor cells from the human peripheral blood.

CONCLUSIONS: Further development of more sophisticated *in vitro* systems will be essential for advances in regenerative medicine, especially to test the biofunctionality of new biomaterials.

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