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# The International Conference on Tissue Science and Engineering 2012: News on Emerging Cell - Based Therapies?

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In October 2012 the OMICS Group held an International Conference on Tissue Science and Engineering, and stem cells and biomaterials were or course among the hot topics. Here we review briefly current developments on emerging cellular therapies and point to some of the presentations of the OMICS conference related to stem cells.

The prototype of all stem cells is the pluripotent stem cell generated from the inner cell mass of a blastocyst. Such pluripotent cells are therefore called embryonic stem cells (ESC). Their artificial counterpart of ESC are the recombinantly induced pluripotent stem cells (iPSC) generated by overexpression of key factors required to maintain the transcriptome and epigenetics of a truly pluripotent cell: NANOG, OCT4 and SOX2 [1,2]. In addition, to increase the cloning efficacy, in some cases a growth-promoting factor such as MYC is employed, and to ensure sufficient telomer lengths for extended expansion of the cells the enzyme telomerase (TERT) is expressed as well. The pluripotent stem cells allow generation of all cell types and lineages of cells found in an adult individual. They therefore inspired the field of regenerative medicine. Hope was high that iPSC will open new avenues to all cells needed for therapy. However a simple application of recombinant iPSC for therapy in an adult patient may yield a very high risk to develop cancer, as iPSC tend to generate teratomas [3-5]. Therefore many approaches were developed for transient expression of the factors needed for maintenance of pluripotence in somatic cells.

An interesting approach to generate pluripotent cells is the transfection of target cells with stabilized mRNA encoding the above-mentioned factors NANOG, OCT4, SOX2 and TERT [6]. The resuting pluripotent cells are called RNA-induced pluripotent cells (RiPSC). In these cells, the half-live time of RNA is rather short. Therefore the induction of pluripotence by RNA remains transient and the genome of the cells treated is not mutated in RiPSC. In addition, by introducing RNA instability motives (AUUUA) or their mutation, or by suitable stabilizing elements (e.g. SV40 poly-A-tail) the half-life time of the therapeutic RNA can be customized. When sufficient numbers of RiPSC are produced, transfection of the cells with NANOG, OCT4, SOX2 and TERT is halted for a few days, the stage of pluripotence ends, and the cells can then be utilized for diagnostic purposes. Using the same approach - transfection of the cells with stabilized mRNA - differentiation of RiPSC to effector cells or more mature types of cells can be induced [6]. It was shown that muscular differentiation was induced by transfection of the RiPSC with MyoD, a key transcription factor involved in differentiation of striated muscle cells Warren, 2010 #49.

An important concern for tissue engineering and regenerative is the quality of cells to be applied and human adult mesenchymal stromal cells (MSC), previously called mesenchymal stem cells, hold great promise for regenerative medicine. Human MSC are under investigation for more than a decade now [7-11]. However not all clinical or therapeutic issues with MSCs are addressed in a satisfactory way. The age of the donor and therefore the cell is one of the concerns.

In his presentation at the convention Dr. David T. Harris (Univ. of Arizona, USA) pointed out that in general, younger stem cells perform better than older stem cells. Many studies have provided evidence that stem cells from younger donors yield better results compared to stem cells from older donors [12-14]. The above-mentioned RiPSC approach could therefore represent the "Jungbrunnen" (fountain of youth) as painted by the famous Lucas Cranach in 1546. Treating autologous cells from the (elderly) patient with the RiPSC method may represent a rescue from the "trap of age". This however must be proven with outmost care in suitable *in vitro* studies and *in vivo* models before being applied to humans.

Another hot topic at the OMICS convention was of course biomaterials, and especially the modification of stiffness, elasticity, hydrophobicity, and structure of the scaffold. It has been shown that differentiation of stem cells not only depends on soluble signals such as growth factors, cytokines, hormones or low molecular weight components (e.g. nutrients, oxygen, radicals) [15], but also on the signals provided by the extracellular matrix or immediate pericellular environment [16, 17], and of course on the elasticity of the substratum [18] [19].

However, chronic inflammation confronts stem cells with an overdosis of cytokines, growth factors, and even nitric oxide radicals. This may contribute to malfunction of the stem cells and cause malignancies, as Dr. Mahin Khatamin (NIH, Bethesda, USA) explained at the OMICS conference. Unresolved chronic inflammation may tip the balance between tumoricidal or tumorigenic pathways, cell death (apoptosis) on one side, and wound healing or differentiation on the other side. Here controlling chronic inflammation seems the solution for the problem.

Biomaterials are important to maintain the phenotype of a cell, and keep the cells alive and in place for regeneration. Elastic, micro-porous and nano-surfaced hydrogels were instrumental for supporting microglia cells in neuronal repair in a spinal cord injury model, as Dr. Eugen P. Goldberg (Univ. of Florida, USA) pointed out. These nano-structured surfaces allowed cell-matrix binding, and the porous scaffold acted as reservoir for growth factors. Therefore, all players are in place: the cell and the fuel it needs to do the job.

Overall the OMICS meeting covered very interesting topics. It

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offered great opportunities to contact experts from all over the globe. It was a success!

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