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Margherita Maioli PhD

Associate Professor
Scientific Director CEDEBIOR
Department of Biomedical Sciences
University of Sassari

"Unfolding the stem cell world: a path among the use of molecules and physical energies"

Abstract:

Stem cells are widely defined as cells with no specific distinct features which are able to self renew and differentiate under specific environmental stimuli. Stem cells behaviour is further complicated by the presence of a stem cell niche, which mediate the interaction between stem cells and the surrounding milieu. Defining specific chemical or physical stimuli, acting as modulators of stem cells behaviour could offer novel tools for regenerative medicine and clinical application. Conditioned media have been widely used to commit stem cells toward specific phenotypes defining the appearance of tissue specific elements exhibiting defined cellular functions. In particular during the last years we used a mixed of hyaluronic, together with butyric and retinoic acid to commit mouse embryonic and human mesenchymal stem cells from different sources, as bone marrow, placenta, dental pulp and amniotic fluid toward the cardiovascular phenotype (1). Recently the same cocktail, together with the circadian related hormone melatonin, was successfully used by our group to obtain an osteogenic phenotype from dental pulp derived stem cells (2). Concerning melatonin we recently demonstrated a role of this hormone and of vitamin D in counteracting the appearance of an adipogenic fate in adipose derived stem cells, offering novel strategies in counteracting fat depot and thus obesity. Besides drugs also physical energies are able to affect stem cells behaviour (3). In 2005 we used extremely low frequency magnetic fields to induce a molecular pattern of cardiogenesis and a high yield of cardiac beating clusters in mouse embryonic stem cells (4). Recently we demonstrated that radiofrequency waves emitted by the Radio electric asymmetric conveyer (REAC) were able to induce the appearance of cardiogenic, myogenic and neurogenic phenotypes both in murine embryonic and in human adipose derived stem cells (5). REAC was also able to induce a direct reprogramming of human adult fibroblasts toward cardiac, skeletal muscle and neuronal phenotype (6). This effect was related to the activity of NADPH oxidase, an enzyme which controls the production of ROS inside the cells. So REAC could act as an hormetic effector , as for example hypoxia or other types of stressors, which at low doses stimulate cells to react by self repairing strategies. The physical energy emitted by REAC were also able to induce the neurogenic differentiation of the pheocromocitoma cells PC12, by inducing an NGF-mediated paracrine circuitry (7). Considering our results and also some clinical studies demonstrating the capability of REAC to act as a regenerative inducer, we could consider the chance to use a physical energy able to stimulate the patient's own self reparative potential. Nevertheless there are many events especially at the molecular level which still remain to be clarified,

and need further experimental dissection. Taken together our results define novel molecules and novel application of old ones, but also physical energies able to commit stem cells toward specific phenotypes, and unfold novel tool for in vitro differentiation of stem cells and future clinical applications.

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