Heart Sound Melody and Stem Cell Reprogramming

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Rationale

For decades Scientists have used chemical tools to affect cell behavior. Even in modern times, governing cell function for therapeutic purposes has been mainly afforded through chemistry. However, this view, and the idea that therapy of human diseases is essentially based on a chemical armamentarium are now deeply challenged. We have previously shown that stem cells, a type of cells that have the ability to transform themselves virtually into all the cell types of an adult individual, became myocardial cells, the contracting units of the heart, when exposed to extremely low frequency magnetic fields (ELF-MF) (1,2). More recently, we provided evidence that exposure to radio electric fields conveyed with an innovative device named "Radio Electric Asymmetric Conveyer (REAC)", was able to transform stem cells into cardiac, neural and skeletal muscle cells (3,4). Moreover, radio electric conveyed fields acted as a sort of "time machine" even able to "reprogram" adult non-stem human cells, like skin fibroblasts, into cell types in which these cells would never otherwise appear, like cardiac, vascular, neural and muscular cells (5).

These findings demonstrate that stem cell fate can be remarkably modulated by physical energy. Consonant with these observations is our discovery that cells can produce acoustic vibrations. In fact, we have demonstrated and patented for the first time the ability of cells to express "vibrational" signatures of their health and differentiating potential (6). By the aid of an atomic force microscope (AFM), which is able to measure local structures and properties of living cells at atomic level, we discovered that every living cell produces a vibration pattern that changes depending upon the task the cell are performing. "Sonocytology" is the term that we have introduced to identify a novel area of inquiry based on the fact that, after an accurate process of amplification, the cellular vibrations recorded by AFM could be transformed into audible sounds, providing a thorough assessment of the functional properties of the cell (6).

Using a Heart Sound Melody to Reprogram Human Adult Stem Cells to a Cardiovascular Lineage

Based on these achievements, we are currently working on the hypothesis that application of sound energy may govern the process of cellular differentiation. In particular, we are now intrigued about the possibility that sounds emitted at organ level may entail information crucial to regulate the cellular function at a very subtle, molecular, submolecular, or even quantum level. Within this context, we are collaborating with the worldwide renowned Jazz Musician Milford Graves, who recorded with a very sophisticated system the sound of the human heart and converted it into electro-audio signals, encompassing defined sequences of frequencies coherent with the heart micro-rhythms (heart sound melody). In this project, we are exploring the effect of these signals on stem cell growth and differentiation. For this purpose, we have exposed human mesenchymal stem cells isolated from a *microfractured* adipose tissue obtained with a novel non-enzymatic method (7) to the heart sound melody obtained by Milford Graves. The sound vibration has been delivered at 0.9 g by a custom-designed mechanical transducer, producing a very linear output in the range between 20 and 20,000 Hz. To receive the vibration, the cell culture dishes were placed onto a specially designed plate adapted to the transducer.

Stem cell exposure led to a remarkable modulation in the transcription of stemness-

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related genes, including Nanog, Sox-2, and Klf-4. These genes have been shown to finely tune stem cell potency, inducing a pluripotent state, which involves the ability to be committed along a multineage repertoire. Interestingly, the heart sound melody enhanced the gene expression during the first 12-24 hours, then leading to a progressive down regulation, as compared to unexposed cells. This biphasic effect is worthy of consideration, since it is now evident that after their induction Sox-2, Nanog and Oct-4 need to be down regulated to allow stem cell progression towards a differentiated state. Consonant with the observed effect on stemness gene expression, stem cell exposure to the heart sound melody elicited a significant increase in the transcription of the cardiogenic genes GATA-4 and Nkx-2.5, also enhancing the transcription of the vasculogenic genes VEGF (Vascular Endothelial Growth Factor) and HGF (Hepatocyte Growth Factor).

We are currently investigating whether stem cell treatment with the heart sound melody may drive the expression of myocardial specific proteins (i.e. alpha-sarcomeric actinin, alpha-myosin heavy chain, TnI) and vascular (entothelial) specific markers, and whether, in the affirmative, such a terminal commitment may be associated with the transformation of human adult stem cells into contractile myocardial cells.

Preliminary Considerations

That music touches the core of our being is a discovery as old as human consciousness. Plato grappled with the powers of music in "The Laws" and other dialogues, and he was hardly the first to do so. Shakespeare in several of his most poignant scenes dramatized music's soothing effect on troubled spirits. Healers of many sorts try to harness music for therapeutic purposes. But could music ever take its place as medicine? A new perspective is approaching that will enable Artists and Scientists to work together discovering cells as actors capable of 'speaking' or 'screaming,' and how listening to cellular or heart sounds may eventually change the way Scientists think about cells, as subjects that are dynamic, environmentally situated, and experiential. We also believe that these collaborations, bringing Artists and Scientists together, will inspire individuals to think about Arts and Science as already interrelated and relevant to our Society, blurring the dividing line of the "Two Cultures" (Humanistic and Scientific) and help usher in a new Culture that is overdue – a Culture of creative thinkers from the Arts and Sciences who join together to combine their knowledge and skills to come up with innovations, collaborations and most of all the development of novel paradigms. We also think that these collaborations may offer a new "vision" for integrating Science with a "Global Territory of Culture", and may lead to the growth of a novel "Experimental Art", autonomously inspired by scientific tools and approaches.

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