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EDITORIAL

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# Biomimicry in mending the broken heart; Will hypoxia and pulsatile flow play Cupids?

Oxygen, the most important cellular nutrition, is delivered through a pulsatile blood flow in vertebrates to the tissues and cells *in vivo*, wherein the oxygen concentration, its availability gradient between systolic and diastolic phase of cardiac activity differ between organs. In the *in vitro* conditions, manipulation of oxygen availability to the cells under culture have yielded varying behaviours depending on the type of cells, their stemness etc.[1-5]. Adding a pulsatile component to such *in vitro* conditions has shown the cells behaving in different manners in such environments[6,7]. While our earlier editorial titled *"Hypoxia is no hype: Perspectives across Phylogeny, Stem Cell differentiation & Geochemistry"*[8] had described the importance of hypoxia in stem cell-based research wherein stemness is preserved more efficiently under hypoxia[4,5], an article in this issue titled "*Comparing the **in vivo** and **in vitro** effects of hypoxia (3% O2) on directly derived cells from murine cardiac explants versus murine cardiosphere derived cells"*[9] has further intrigued us to analyse this phenomenon.

The pumping chamber of the heart, the left ventricle is supplied mostly during the diastole when it relaxes, whilst the other tissues get the supply during systole. The gradient of oxygen concentration that occurs between the peak *vs* the low availability, is the highest in cardiac tissue, while lowest in the periphery[10]. Hence, the effects of fluid dynamics and oxygen concentration may have a significantly higher influence on culture of cardiac tissue-derived cells and the application of this phenomena on cells, which are tailored to address myocardial regeneration. Several attempts are being made to employ hypoxic pre-conditioning to improve the therapeutic potential of cardiac tissue-derived stem and progenitor cells with studies reporting significant enhancement in the anti-apoptotic and migratory potential of these cells *in vitro*, and better survival and cardiac function after *in vivo* transplantation. Amirrasouli *et al* [9] report their findings on comparing the effect of hypoxic preconditioning on pro-angiogenic potential of cardiac tissue explant-derived cell (EDCs) and cardiosphere-derived cells (CDCs). Since they rationalize that culture of CDC and Csph formation is 'time consuming, expensive and not always successful', their findings support their rationale, wherein hypoxic preconditioning of the EDCs has shown to enhance cell growth, viability and expression of stem cell and pro-angiogenic markers more than the CDCs thus giving rise to a therapeutically valuable cell population in EDCs.

We intend to point out the importance of hypoxic pre-conditioning during the *in vitro* processing of cells aimed at treating cardiac diseases as the myocardial cells are greatly influenced by hypoxic conditions. Adding a pulsatile component to hypoxia[11] or delivering the oxygen in a manner resembling the *in vivo* variabilities produced by a pulsatile blood flow are worth considering an in-depth exploration. If such systems could also mimick the heart rate of the particular individual whose cells are subjected to *in vitro* processing, it could bring the *in vitro* systems much closer to the individual's physiology as the oxygen delivery to cardiac tissues vary according to heart rate[12]. Biomimicry is an indispensable component to several inventions in Biology; it is the biomechanical force produced by the first heartbeat that triggers the development of hematopoietic stem cells (HSC) themselves[13,14].

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