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Eco matters; In & Out

In vitro culture of cells and tissues were undertaken to understand the intricacies of cellular biology *per se* until recently, when such *in vitro* grown cells and tissues have started evolving as tools of regenerative medicine. Only after such clinical applications of *in vitro* cultured cells and tissues became a possibility, various criteria about the compatibility of *in vitro* environments to the cells and tissues have gained significant attention.

Among the *in vitro* cultured cells, chondrocytes pop up as one of the most approved cell-based products by regulatory authorities of many countries including the USA, Europe and Japan[1]. In this procedure, it has been reported by several studies that human articular chondrocytes (HACs) when cultured as monolayer, they tend to de-differentiate[2] whereas 3D cultures help to establish the native hyaline phenotype[3]. Variations of such significance in the *in vitro* behaviour of other cell types have also been reported in literature[4-9] which clearly demonstrate that *in vitro* environments play a crucial role in maintaining cells with the proper phenotype and functionality for clinical transplantation.

Another major factor which needs to be studied thoroughly is cellular senescence in the *in vitro* environment. Though cells derived from older individuals may share cellular and molecular phenotypes with *in vitro* senescent cells, *in vitro* acquired cellular senescence is a proven phenomenon[10]. While the 'Hayflick limit' specifies a particular number of maximum population doubling for a specific cell type *in vitro*, the same cell type *in vivo* may undergo more than the Hayflick limit specified population doubling in a lifetime without senescence[11] creating the need for improvising current *in vitro* cell culture techniques to reflect what occurs *in vivo*.

Given the above background, the goal of *in vitro* cell and tissue engineering is to grow cells with optimal functionality while simultaneously preventing uncontrolled or premature differentiation and the onset of senescence[12]. Stressing the importance of *in vitro* environments, even regulatory agencies like the US-FDA use *in vitro* manipulation as a gauge to classify cell therapies[13].

In this issue, a diverse assortment of articles ranging from the use of scaffolds for *in vitro* culture by Gomathysankar *et al*[14] to employing tools for *in vivo* transplantation of cells by Maiti *et al*[15]and Fauzi *et al*[16] have been published. During regenerative medicine applications, cells undergo several transitions across environments, starting with an *in vivo* to *in vitro* transition when harvested from the body and subjected to culture-expansion or tissue engineering kind of processing and then a reversal back to an *in vivo* environment. While the factors and materials employed in the *in vitro* eco-system are known, their effects are known though to an extent, some of their implications still remain unknown and the mechanisms of those implications are largely obscure[17-19]. These bunch of changes in the whole eco-system inside-out and *vice versa* need a meticulous and flawless assessment which is indispensable in improvising the clinical outcome of regenerative medicine applications.

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