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EDITORIAL

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Missing *in vitro* links between the origin and *in vivo* destiny of mesenchymal stem cells

Mesenchymal Stem Cells (MSCs) have been isolated from different sources, cells, tissues and organs. The markers for MSCs vary between such sources[1]. Moreover, in general, MSCs have been postulated to have no specific marker and more often, their identity is established by exclusion or analysing a group of markers[2]. The differentiation potential of MSCs are also ambiguous depending on the source and methodologies about which there are many conflicting reports too[3,4]. When it comes to their application as an allogeneic source, MSCs have been considered to be immunomodulatory which literally means immune enhancement and/or immune suppression. However, this ambiguity of their swinging nature between two poles hasn't been defined to specific pathways yet[5]. Still, products of allogeneic MSCs for Graft versus Host Disease (GVHD) has been approved and in clinical use[6] based on their immune-suppressive effect. Having given the above background, we postulate MSCs to be a heterogenous group of cells with several subsets and each subset likely to differ in their nature based on the source and likely to be behaving in different manners subject to the environment they are placed in either in vitro or in vivo.

In this issue of JSRM two publications have brought certain interesting insights into the heterogeneous nature of MSCs.

1. Terunuma *et al* state that the characteristics of MSCs vary depending on the tissue types they originated from and hence while designing stem cell-based therapeutic approaches, they suggest to choose MSCs derived from a particular tissue type over others based on the gene expression characteristics[7] to suit the specific application for optimal therapeutic outcome.
2. Sacchetti *et al* report that MSCs from different sources, though share the same surface markers, their differentiation potential and behaviour upon *in vivo application* vary which cannot be ascertained by the existing *in vitro* assays[8]. Their findings suggest that there is a void to be filled up, on arriving at specific *in vitro* methods to predict the *in vivo,* post transplantation differentiation potentials relevant to the source of the MSCs.

Based on the above two papers it is evident that the source of MSCs have a very strong correlation with the post transplantation in vivo destiny which at this moment we are unable to evaluate and confirm during in vitro culture..

Li *et al*., state that MSCs are a '*double-edged sword in regulating immune responses*'[9]. They report that though it is the immunosuppressive effect of MSCs which has been reasonably well studied that forms the rationale behind MSCs being used for treating GVHD, MSCs can also enhance immune cell proliferation especially when inducible nitric oxide synthase (iNOS) production was inhibited. Though the differences in immunosuppressive potentials of MSCs from different source of origin was not studied in their work,, Contreras *et al*.,[10] describe that there are discrepancies in the immunosuppressive properties and therapeutic potential of MSCs depending on the tissue from which they are isolated due to intrinsic molecular particularities based on the source or the impact of the microenvironment *in vivo*.

To address the dysfunction or damage of a specific tissue using MSCs, going by the present data available, if a specific source for deriving those MSCs is likely to bring an optimal outcome, going by the reports in this issue and the literatures mentioned above, the *in vitro* processing methodologies could also be tuned and evaluated whether they are going in the right direction to enhance the outcome of the specific clinical application. Evaluating the gene expression is something very vital while several other criteria might have to be added to a list of such evaluations.

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