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Viewpoint

VSELs, stem cells or progenitors - A debate

The present viewpoint authored by Dr Deepa Bhartiya touches upon an ongoing debate on human embryonic stem cells, circling around the nature of mesenchymal stem cells (MSCs), whether these are true stem cells or progenitors. It underlines the nature of the very small embryonic-like stem cells (VSELs), their proliferative potential and heterogeneity based on the presence of the transcription factor, Oct-4. The author suggests that these VSELs are pluripotent stem cells of the adult organs, serving as a backup pool of adult stem cells (progenitors) and may also be responsible for initiating cancers with advanced age. Further, the author considers the term 'adult stem cell' as a misnomer. These are not stem cells in the true sense, but are rather 'progenitors', owing to their committed fate. This has been discussed in the context of haematopoietic stem cells (HSCs) and spermatogonial stem cells (SSCs) which only undergo symmetric cell divisions, while 'stem cells' undergo asymmetric cell division and possess the ability to self-renew and also give rise to progenitors. In this context, the author has highlighted the characteristics of VSELs, which undergo asymmetric cell division. She further argues that HSCs and SSCs have a common origin from VSELs, an argument which is presently debatable. The author points out that stem cells have been demonstrated to have the potential to differentiate into different cell types *in vitro*, however, their sustenance upon long-term regeneration *in situ* remains to be demonstrated. She firmly supports the existence of the VSELs citing their regenerative capabilities in adult mouse testes.

Despite the well presented address by the author, there are some points which cannot be overlooked. Though it is long known that stem cells give rise to tissue specific or cell specific progenitors, but to assert that this is primarily done by the VSELs is highly debatable at present time. Also, the transient nature and functional redundancy of the VSELs cannot be ignored considering the high success rate of peripheral blood autologous stem cell transplants. So, to accept the author's claim that these VSELs are unknowingly discarded during processing in various previous trials, still requires convincing proof of concept for others to accept.

This viewpoint deserves due consideration but as of now this obviously has a dogmatic bias towards considering the VSELs as the most productive stem cells giving rise to the progenitors and all other stem cells including the MSCs or ESCs producing only transient effects. Any new concept or hypothesis has to be put to rigorous testing and reproducibility is to be demonstrated which is to be done in this case as well. At this point, it would be in scientific interest to critically accept the disparity in the exact role of VSELs specially for accepting these as a distinct functional and morphological subset, and welcoming more research in the area to understand the stem cell biology in a more definitive way.

V.M. Katoch
Chairman, Editorial Board, IJMR
Director-General, Indian Council of
Medical Research & Secretary, Department of
Health Research, Government of India
New Delhi 110 029, India
vishwamohan_katoch@yahoo.co.in