DBT/ National Centre for Cell Science (NCCS), Pune

Improving success of bone marrow transplantation.

Stem cell transplantation (SCT) involves the transfer of hematopoietic stem cells (HSCs), a type of cells that give rise to other blood cells, from a healthy donor to a patient. SCT is the only curative therapy for various malignant and non-malignant disorders like leukemia, lymphoma, aplastic anaemia, etc. It is essential to ensure that the donor's HSCs have good engraftment ability, since the efficacy of clinical transplantation critically depends on how well these cells function. Medical science recognizes donor age to be a major concern. The use of aged HSCs in bone marrow transplantation is restricted due to their compromised ability to be engrafted successfully and function well in the recipient's body. This introduces severe limitations in bone marrow stem cell transplantation, especially when only a single tissue-matched aged donor is available. Therefore, there is a strong need to find strategies to "rejuvenate" aged HSCs.

The research carried out at the National Centre for Cell Science (NCCS) in Pune, which led to a fascinating new approach to return lost functionality to aged HSCs in mice, is strongly relevant in this context. Stromal cells, such as mesenchymal stromal cells (MSCs), are support cells present in the micro-environment of stem cells. Studies at NCCS revealed that brief interactions of aged HSCs with young MSCs can reverse the signs of aging in HSCs and restore their functionality. This effect was found to be achieved via the transfer of extracellular sac-like structures released by the MSCs, called microvesicles (MVs), to the HSCs. These MVs contain autophagy-inducing mRNAs that can rejuvenate aged stem cells. Further, these studies revealed that the MSCs display activation of a process called AKT signalling as they age, which leads to a loss of these autophagy-inducing mRNAs in their micro-vesicles. However, if this signalling is blocked in aged stromal cells by using chemical inhibitors, they behave like 'young' MSCs and secrete 'good quality' micro-vesicles containing autophagy-inducing mRNA. Interestingly, transplantation experiments showed that the rejuvenating power of MVs from such "young-like" MSCs was even better than MVs from young MSCs.

Collectively these findings demonstrated that extracellular vesicles from MSCs play a critical role in modulating HSC functionality, thus helping identify a novel approach to rejuvenate aged HSCs. This could potentially prove useful to expand the cohort of donors available for stem cell transplantations in the future, by facilitating older healthy individuals also to serve as donors. This groundbreaking work was published from NCCS in the journal, Stem Cells. The importance of these findings received special recognition through the 2019 STEM CELLS Young Investigator Award (YIA), recently awarded to the lead author of this paper and NCCS alumnus, Dr. Rohan Kulkarni. This prestigious award honours emerging young researchers who are making significant impacts in the field of stem cell biology, to encourage future clinical applications of discoveries made in this field.

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News reports *(this may not be an exhaustive list)* **-**

* https://www.thehindu.com/sci-tech/science/nccs-novel-approach-improves-success-rate-of-bone-marrow-transplantation/article21822477.ece
* https://biotechtimes.org/2018/01/02/indian-scientists-develop-mechanism-to-rejuvenate-aged-stem-cells/
* https://vigyanprasar.gov.in/isw/rejuvenate_aged_stem_cells_story.html

Social media (*(this may not be an exhaustive list)* **-**

YouTube: https://www.youtube.com/watch?v=cMIClcmXZDI

Research article on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29230885

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