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## Mari Dezawa

Tohoku University Graduate School of Medicine, Japan

### Endogenous reparative muse cells may provide novel therapeutic approaches

ultilineage-differentiating stress enduring (muse) cells are naturally existing unique endogenous stem cells that are nontumorigenic and are pluripotent-like. They express pluripotent markers, can generate cells representative of all three germ layers from a single cell and are able to self-renew. Since they express specific receptor for damage signal, they can preferentially home into damaged site after topical injection or intravenous injection with lower entrapment in the lung and spleen. After integration, they replenish lost cells by spontaneous differentiation into tissue-compatible cells, leading to robust tissue and functional regeneration. The unique reparative functions of Muse cells were demonstrated in animal models of liver cirrhosis, partial hepatectomy, stroke, skin ulcer of diabetes mellitus and chronic kidney disease. They do not have to be "induced," or genetically manipulated, to be pluripotent or be purposive cells before transplantation as required with some other cell varieties. They can be collected as cells positive for SSEA-3, a surface marker for pluripotent stem cells, from readily accessible sources such as the bone marrow (~0.03% of the total mononucleated cell population), and from cultured fibroblasts (several %), as well as from the dermis and adipose tissue. Recently, Muse cells are shown to circulate in peripheral blood in healthy donors, and the number increases in stroke patients in an acute phase, suggesting that endogenous Muse cells are mobilized into peripheral blood to repair tissues while their number is not sufficient to recover, and that supply of exogenous Muse cells is expected to deliver statistically meaningful functional recovery. Overall, Muse cells are a feasible source for cell-based approaches and may safely provide clinically relevant regenerative effects compatible with the 'body's natural repair systems' by simple cost-effective strategy-collection of Muse cells from sources, large scale expansion and intravenous injection.

#### **Biography**

Mari Dezawa has completed her graduation from Chiba University School of Medicine in 1989, and got PhD degree in 1995 at the same institution. She moved to Yokohama City University as Assistant Professor of Department of Anatomy in 2000 where she started to work with mesenchymal stem cells (MSCs). After moving to Kyoto University Graduate School of Medicine as Associate Professor in 2003, she discovered methods to induce neurons and skeletal muscle cells from human MSCs. In 2008, she became Professor and Chair of Department of Stem Cell Biology and Histology, Tohoku University Graduate School of Medicine, where she discovered muse cells (PNAS, 2010, PNAS, 2011, Nat Protocol, 2013, JASN, 2017).

mdezawa@med.tohoku.ac.jp

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