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## Current status and future of stem cell therapies - novel view on stem cells isolated from adult tissues

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A dult tissues harbor a population of rare stem cells endowed with broad differentiation potential described as very small embryonic-like stem cells (VSELs) which display several epiblast/germline markers. Moreover, VSELs do express: several sex hormone (SexHs) receptors, respond to SexHs stimulation and share several markers characteristic of migrating primordial germ cells. Since VSELs can be specified e.g., into long-term hematopoietic hematopoietic stem cells and mesenchymal stem cells, this observation sheds new light on the adult stem cell hierarchy. Nevertheless, in spite of the expression of pluripotent stem cell markers, changes in the epigenetic signature of imprinted genes (e.g., by erasure of imprinting at the Igf-2–H19 locus) keep VSELs quiescent. In several emergency situations (e.g., heart infarct, stroke, skin burns), VSELs can be activated and mobilized into peripheral blood and contribute to tissue organ/regeneration. VSELs number correlates with life span in mice and we noticed a positive effect of regular physical exercise and calorie restriction on delaying age-dependent depletion of VSELs from adult tissues. Recently, we developed an efficient *ex vivo* expansion strategy in chemically defined medium to activate DNMT3L in these cells that re-methylates erased imprinted loci, what allows them for effective ex vivo expansion for potential clinical purposes.

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