Opening Lecture

Stem cells — current knowledge, ethics and hope

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The search for pluripotent stem cells (PSC) that could be applied in regenerative medicine continues. Accumulating evidence demonstrates that adult tissues contain cells that express early developmental markers such as stage specific embryonic antigen (SSEA) and transcription factors Oct-4 and Nanog. These are the marker characteristics for embryonic stem cells (ESC), epiblast stem cells (EPSC) and primordial germ cells (PGC). The presence of these stem cells in adult tissues supports the concept that adult tissues contain some population of PSC that is deposited in embryogenesis during early gastrulation and that these cells potentially could be employed in regenerative medicine. Recently my group identified in BM and other adult tissues (e.g., brain, kidney, pancreas, liver and lung) a population of very small embryonic like stem cells (VSELs) which express several PSC markers characteristic for EPSC and PGC. We hypothesize that VSELs are a population of epiblast-derived cells that are deposited during early gastrulation in developing tissues/organs and play an important role in turnover of unipotent tissue specific/committed stem cells. VSELs could be also mobilized into peripheral blood (PB) and their number of these cells circulating in PB increases after administration of mobilizing agents (e.g., G-CSF), during stress and tissue/organ injuries. Our data indicate that VSELs could potentially provide a real therapeutic alternative to the controversial use of human ESC obtained by therapeutic cloning, isolation of single blastomeres or from parthenogenetic embryos. Hence, while the ethical debate on the application of ESC in therapy continues, the potential of VSELs is ripe for exploration. Because VSELs may differentiate in vitro into cells from all three germ layers make these cells potential therapeutic candidates in regenerative medicine. From a hematological point of view, the fact that VSELs may differentiate into hematopoietic stem cells makes from these cells a candidate for long term repopulating HSC. Finally, we envision that in pathological situations VSELs are involved in the development of some malignancies (e.g., teratomas/teratocarcinomas, germinal tumors and pediatric sarcomas). Thus, by elucidating the mechanism by which VSELs could contribute to the development of some malignancies shed more light on origin of tumors. In conclusion, it is of vital importance to evaluate if VSELs could be efficiently employed in the clinic. The coming years will bring important answers to all these questions.