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10th World Congress and Expo on Cell & Stem Cell Research _ZSCAN10 expression corrects the genomic instability of iPSC from aged donors by controlling redox status_ Kitai Kim_ Weill Medical College of Cornell University_ USA

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Induced pluripotent stem cells (iPSC) can be used to produce transplantable tissues. However, iPSC generated from aged donors (A-iPSC) exhibit higher genomic instability, defects in apoptosis, and a blunted DNA damage response compared to iPSC generated from younger donors (Y-iPSC). We defined the underlying mechanism as a homeostatic imbalance between reactive oxygen species (ROS) and glutathione (a ROS scavenging metabolite). Excessive glutathione activity can blunt the normal DNA damage response signalling pathway, allowing cells with genomic mutations to persist that otherwise would have been eliminated by apoptosis. We found that the pluripotent specific factor, ZSCAN10, was poorly expressed in A-iPSC, and ZSCAN10 expression allows the establishment of A-iPSC without the negative effects of aging. We found that A-iPSC have a higher level of glutathione due to excessive expression of glutathione synthetase (GSS), which causes an imbalance of ROS and glutathione. ZSCAN10 directly binds the GSS promoter to suppress GSS expression. We also found that ZSCAN10 not only controls GSS to determine the total quantity of glutathione) but also glutathione peroxidase (GPX2), which suppresses the excessive catalytic activity of glutathione by controlling its transition from an oxidized inactive form to a reduced active form. We found that GPX2 is controlled by the exosome-mediated RNA degradation pathway which ZSCAN10 expression induces RNA exosome complex expression. We found the third mechanism that ZSCAN10 controls activity of pluripotent stem cell-specific glucose transporter 3 (GLUT3) and facilitates a shift in carbon source metabolism that suppresses oxidative phosphorylation and limits ROS production, consequently providing a selective advantage for cells with elevated glutathione during reprogramming to take care of the ROS-glutathione balance. Correcting the genomic instability of A-iPSC may particularly benefit older patients who are more likely to suffer from degenerative diseases with safer transplantable tissues. Pluripotent stem cells hold promise within the field of regenerative medicine. Because they will propagate indefinitely, also as produce to each other cell type within the body (such as neurons, heart, pancreatic, and liver cells), they represent a single source of cells that would be wont to replace those lost to wreck or disease. Since iPSCs are often derived directly from adult tissues, they not only bypass the necessity for embryos, but are often made during a patient-matched manner, which suggests that every individual could have their own pluripotent somatic cell line. These unlimited supplies of autologous cells might be wont to generate transplants without the danger of immune rejection. While the iPSC technology has not yet advanced to a stage where therapeutic transplants are deemed safe, iPSCs are readily getting used in personalized drug discovery efforts and understanding the patient-specific basis of disease. An attractive feature of human iPS cells is that the ability to derive them from adult patients to review the cellular basis of human disease. Since iPS cells are self-renewing and pluripotent, they represent a theoretically unlimited source of patient-derived cells which may be became any sort of cell within the body. iPS cells are generated for a good sort of human genetic diseases, including common disorders like mongolism and polycystic renal disorder .
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