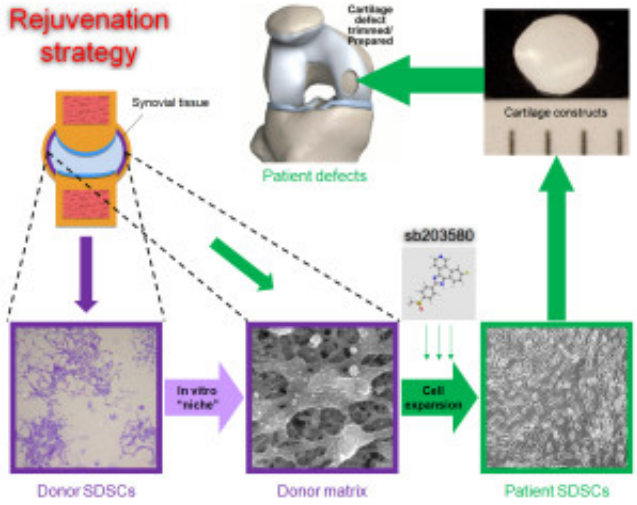
Recharged autologous stem cells to combat cartilage defects in osteoarthritic patients

Inflammation is one of the greatest challenges for physicians and researchers working to find new strategies to regenerate patients' damaged and deteriorated cartilage. Although humans have stem cells which can aid in many tissue repair processes throughout the body, on its own, cartilage has a very limited ability to repair itself. Additionally, inflammatory signals and responses from the immune system can cause damaged cartilage cells to exhibit characteristics synonymous with older, worn-out cells, which do not typically contribute to the healing process or quality cartilage regeneration.



A variety of stem cell populations are found throughout the human body and contribute to repair and regeneration of their surrounding tissues through a process known as differentiation. During differentiation, stem cells become more mature and committed to developing into a specific type of cell and ultimately part of a functional tissue. After harvesting a patient's cartilage stem cells, called synovium derived stem cells (SDSCs), it is possible to grow them in the laboratory under certain conditions to improve their regenerative capacity. After preconditioning the SDSCs, it is possible to put them back in the joint and improve cartilage regeneration for clinical therapies.

In our study, we tested two cell preconditioning strategies and the ability of such strategies to increase SDSCs' ability to proliferate in greater numbers, differentiate into healthy cartilage cells, and to resist a simulated inflammatory environment. For the first strategy, we grew human SDSCs on cell culture flasks coated with extracellular matrix deposits from a different group of SDSCs. Extracellular matrix (ECM) refers to the outer cell environment and abundance of secreted molecules which structurally and biochemically support cells. In this study, we found that decellularized ECM can be used as a growth substrate to effectively rejuvenate human SDSCs. Additionally, as a second strategy, we exposed SDSCs to a drug known as sb203580, as previous research studies suggest that this drug inhibits a key cell stress and inflammation pathway in

human cells. We found that, by combining the two preconditioning strategies of ECM and sb203580 supplementation, human SDSCs are primed for later success when exposed to a specific inflammatory signal, called interleukin-1 beta which is known to be problematic in cartilage repair. These results mean that preconditioning with ECM and sb203580 could help the patients' SDSCs resist detrimental inflammation caused by the immune system when the SDSCs are reintroduced to the joint.

Furthermore, we performed preliminary tests to determine whether or not human SDSCs grown on one of the following SDSC substrates would be safe and compatible for clinical use: (1) patients' own cell ECM, (2) another humans' cell ECM, or (3) pig (porcine) cell ECM. In the first two types of ECM, we found no significant increase in HLA-DR, an important immune system marker which has been shown to contribute to severe immune system responses. Interestingly, patient SDSCs grown on ECM substrates deposited by pigs (porcine ECM) caused the patients' own SDSCs to significantly increase this immune marker, suggesting that it is safer to use human deposited ECM substrates even if they are from another individual. Our findings indicate the feasibility of commercial preparation of these ECMs from healthy, young donors for patients who need autologous transplantation.

Publication

sb203580 preconditioning recharges matrix-expanded human adult stem cells for chondrogenesis in an inflammatory environment - A feasible approach for autologous stem cell based osteoarthritic cartilage repair.
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