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Syndecan-2: more than just a stromal cell marker

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The large-scale clinical expansion of MSCs to therapeutically relevant doses is a challenge to those in the cell therapy space phase. In addition, identifying donors that produce cells capable of withstanding the effect of extended passaging can be difficult. In order to assess whether cells are maintaining their activity and potency, we have focused developing assays around a novel cell-surface stromal cell marker, CD362/Syndecan-2 (SDC2). The heparan sulfate proteoglycan syndecans are transmembrane proteins involved in multiple physiological processes, including cell-matrix adhesion and inflammation. We found that the protein expression of SDC2 in umbilical cord-derived MSCs (ucMSCs) is lost with serial passaging and consecutive bioreactor expansions and this effect correlates with loss of IDO-1 activity/expression and reduced suppression of CD4+ T-cell proliferation. Furthermore, inflammation-induced loss of SDC2 by TNF-α or IL-1β promotes apoptosis, and increased CD54/ICAM-1 and MHC II expression in these cells and this phenotype is mirrored with adenoviral knock-down or siRNA directed against SDC2. This indicates that loss of stromal cell SDC2 has a negative impact on the potency of ucMSCs. Furthermore, certain donors with higher IFN -stimulated indoleamine 2, 3-dioxygenase IDO-1 and SDC2 expression, continue to express high levels through passaging and perform better in-vitro than those with lower starting expression, allowing the potential pre-selection of donors from as early a passage as P1-P2.

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