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Investigating the Role of Notch 1 and Notch 3 in Human Adipose-Derived Stem Cell Adipogenesis

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Human adipose-derived stem cells (hASCs) are multipotent stem cells that have the ability to self-renew and differentiate into a limited number of cell types of the mesodermal lineage making these cells an attractive tool for regenerative medicine and cell-based therapies. The Notch signaling pathway is a contact dependent cascade that modulates many important cellular processes, including cell-to-cell communication, cell-fate determination during development, and cell proliferation. Irregularities of the Notch pathway are linked to a variety of devastating developmental disorders and cancers.

Following exposure to adipogenic media hASCs displayed increased levels of Notch1, Notch3, and downstream target genes, *hes1* and *hey1*. In order to better understand the role of Notch3 we performed an siRNA-mediated knockdown of Notch3 during adipogenesis. Oil Red O staining revealed that the loss of Notch3 promoted the accumulation of lipid vesicles while qRT-PCR and western blot assays revealed that the expression level of known adipocyte markers increased following the loss of Notch3 as did the level of activated Notch1. Finally, immunofluorescence was performed to investigate the localization of both Notch3 and Notch1 and revealed that Notch1 was only enriched in adipocyte differentiated hASCs, while Notch3 was activated in hASCs undergoing adipogenesis.

These results suggest that Notch1 is expressed in adipocytes to promote lipid accumulation while expression of Notch3 in adjacent hASCs is activated by differentiated adipocytes to maintain multipotency. As our investigation continues, we will have a more thorough understanding of the role of Notch1 and Notch3 in stem cell self-renewal and adipogenesis.