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A strategy to target gliosis for enhanced myelin repair

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Regeneration of oligodendrocytes in the context of demyelinating diseases by reprogramming or direct cell conversion is a promising strategy for myelination. Recent studies demonstrate that astroglial cells can be directly converted into functional neurons or oligodendrocytes both in vitro and in vivo. Here, we report that a single transcription factor Sox10 could reprogram astrocytes into oligodendrocyte-like cells. Primary astrocytes from mouse pups were extracted, purified, and transduced with lentiviral particles that expressed Sox10 and GFP. Next, we cultured the cells in oligodendrocyte progenitor medium. The induced oligodendrocyte progenitor cells (iOPCs) expressed related markers. After directed differentiation they showed oligodendrocyte morphology and expression of myelinating cell markers, MBP and PLP. For in vivo transdifferentiation, Sox10 expressing viral particles were injected into oxalic acid bis(cyclohexylidenehydrazide) (cuprizone)-induced demyelinated mice brains after which we assessed for the presence of specific oligodendrocyte markers by immunohistofluorescence (IHF). We also transduced several astrocytes in vitro and transplanted them into demyelinated brains. After three weeks, in vivo transduced cells and transplanted astrocytes showed an oligodendrocyte fate. Our findings showed the feasibility of reprogramming astrocytes into oligodendrocyte-like cells by using a single transcription factor, Sox10 under in vitro and in vivo conditions. This finding suggested a master regulatory role for Sox10 which enabled astrocytes to change their fate to oligodendrocyte-like cells and establish an oligodendroglial gene regulatory network.

Biography

Akram Mokhtarzadeh Khanghahi is a sixth year PhD student. She has been accepted for PhD program in Developmental Biology based on her exceptional talent rights (without entrance exam) in Royan Institute for Stem Cell Biology and Technology (RI-SCBT) (2012). And now she is a Research Assistant in Royan Institute of Stem Cells and Developmental Biology in Dr. Javan Laboratory.

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