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Myoblast-derived neuronal cells form glutamatergic neurons in the mouse cerebellum

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Productions of neuros from non-neural cells have far-reaching clinical significance. We previously found that muscle progenitor cells (myoblasts) can be converted to a physiologically active neuronal phenotype by transferring a single recombinant transcription factor, REST- VP16, which directly activates target genes of the transcriptional repressor, REST. However, the neuronal subtype of M-RV cells and whether they can establish synaptic communication in the brain have remained unknown. M-RV cells engineered to express green fluorescent protein (M- RV-GFP) had functional ion channels but did not establish synaptic communication *in vitro*. However, when transplanted into newborn mice cerebella, a site of extensive postnatal neurogenesis, these cells expressed endogenous cerebellar granule precursors and neuron proteins, such as transient axonal glycoprotein-1, neurofilament, type-III β-tubulin, superior cervical ganglia-clone 10, glutamate receptor-2, and glutamate decarboxylase. Importantly, they exhibited action potentials and were capable of receiving glutamatergic synaptic input, similar to the native cerebellar granule neurons. These results suggest that M-RV-GFP cells differentiate into glutamatergic neurons, an important neuronal subtype, in the postnatal cerebellar milieu. Our findings suggest that although activation of REST-target genes can reprogram myoblasts to assume a general neuronal phenotype, the subtype specificity may then be directed by the brain microenvironment.

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