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Surfing oceans of data in Neurobiology with networks and mathematical modelling. The case of oligodendrocytes.

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Abstract: Oligodendrocytes are important cells in the central nervous in charge of producing the myelin layer that protects neuron axons. During their development, the two closely related transcription factors Sox9 and Sox10 play essential roles. Interestingly, during this process Sox10 protein levels rise substantially. As this coincides with a reciprocal decrease in Sox9, we postulated that Sox10 influences Sox9 amounts in differentiating oligodendrocytes via miRNAs. To test this hypothesis in vitro and in vivo experimental data, RNAseq and Chip-seq data analysis, and network biology were combined. We found evidences that the two microRNAs miR335 and miR338 are direct transcriptional targets of Sox10, which recognize the 3'-UTR of Sox9 mRNA and reduce Sox9 protein levels post transcriptionally. Mathematical modeling furthermore showed that the identified regulatory circuit has the potential to convert a transient stimulus into an irreversible switch of cellular properties, thereby contributing to terminal differentiation of oligodendrocytes.

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