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## A regenerative approach to the treatment of multiple sclerosis

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Affiliations

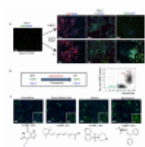
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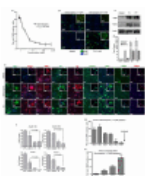
### Abstract

Progressive phases of multiple sclerosis are associated with inhibited differentiation of the progenitor cell population that generates the mature oligodendrocytes required for remyelination and disease remission. To identify selective inducers of oligodendrocyte differentiation, we performed an image-based screen for myelin basic protein (MBP) expression using primary rat optic-nerve-derived progenitor cells. Here we show that among the most effective compounds identified was benztropine, which significantly decreases clinical severity in the experimental autoimmune encephalomyelitis (EAE) model of relapsing-remitting multiple sclerosis when administered alone or in combination with approved immunosuppressive treatments for multiple sclerosis. Evidence from a cuprizone-induced model of demyelination, *in vitro* and *in vivo* T-cell assays and EAE adoptive transfer experiments indicated that the observed efficacy of this drug results directly from an enhancement of remyelination rather than immune suppression. Pharmacological studies indicate that benztropine functions by a mechanism that involves direct antagonism of M1 and/or M3 muscarinic receptors. These studies should facilitate the development of effective new therapies for the treatment of multiple sclerosis that complement established immunosuppressive approaches.

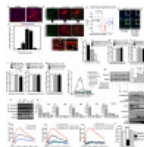
### Figures



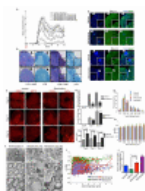
**Extended Data Figure 1.**  
High-throughput screen  
to...



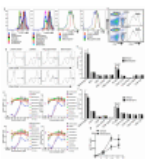
**Extended Data Figure 2.**  
Benztropine induces  
dose-dependent...



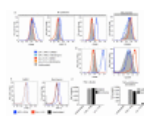
**Extended Data Figure 3.**  
Benztropine induces  
OPC...



**Extended Data Figure 4.**  
Benztropine dose-  
dependently reduces...



**Extended Data Figure 5**  
Benztropine has no...



**Extended Data Figure 6.**  
Benztropine does not...

All figures (14)

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Wekerle H, Meinel E.

Nature. 2013 Oct 17;502(7471):314-5. doi: 10.1038/nature12694. Epub 2013 Oct 9.

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### [Multiple sclerosis: Drug-enhanced remyelination in a multiple sclerosis model.](#)

Bible E.

Nat Rev Neurol. 2013 Dec;9(12):660. doi: 10.1038/nrneurol.2013.225. Epub 2013 Nov 5.

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### [Autoimmune disease: Parkinson's drug promotes myelin repair.](#)

Crunkhorn S.

Nat Rev Drug Discov. 2013 Dec;12(12):905. doi: 10.1038/nrd4181. Epub 2013 Nov 15.

PMID: 24232375 No abstract available.

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Green AJ.

Mult Scler. 2014 Dec;20(14):1814-6. doi: 10.1177/1352458514558679. Epub 2014 Nov 12.

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