TITLE: USE OF SMALL MOLECULES TO TREAT DEMYELINATION AND NERVE INJURY	
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Summary: Demyelinating diseases, such as Multiple Sclerosis (MS), are a major global health concern, impacting millions of people worldwide. These diseases entail a significant economic burden, as they frequently result in progressive neurodegeneration and disability. Impaired remyelination and substantial neurodegeneration are major features of MS pathophysiology. Despite substantial research, effective treatments for preventing or curing demyelination remain elusive. Targeting and counteracting demyelination in mammals with small molecules obtained from aquatic species with regenerative abilities opens up new possibilities in the field of neuroregeneration. Hydra, a cnidarian polyp, has remarkable regenerating abilities, including the possibility for biological immortality. Hydra can regrow its entire body, even after being divided into microscopic cell aggregates. Our preliminary research has revealed small morphogenic peptides produced from Hydra that promote nervous system regeneration after injury in mice. Interestingly, these peptides stimulate neuronal and glial process outgrowth, axo-glial connections, and subcellular organelle reorganisation, all of which are necessary for remyelination. Based on this, we aim at studying the regenerative potential of Hydra-derived peptides in two rodent demyelination models: (i) mice with cuprizone-induced demyelination, and (ii) mice with neural dysfunction caused by a loss-of-function (LOF) mutation in the transcription factor Zbtb20 which is expressed by oligodendrocyte progenitors, mature oligodendrocytes, and Schwann cells. While Zbtb20 LOF mice have less glial cells, the role of Zbtb20 in demyelination, remyelination, and peripheral nerve healing is largely unknown. We will use cutting-edge techniques to examine the ability of Hydra peptides to promote remyelination and neurorepair in both cuprizone-induced and Zbtb20 LOF transgenic mice. This study is the first to look at Hydra-derived peptides for reactivating Zbtb20 expression, and it proposes a new therapeutic method for treating demyelinating diseases by combining molecular insights from Cnidarian biology with novel methodologies in mammalian neurorepair.

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