CX3CR1 as a Therapeutic Target in Multiple Sclerosis

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Multiple Sclerosis (MS) is a chronic autoimmune neuroinflammatory disease of the central nervous system (CNS) that currently has no definitive cure. Current drug therapies focus on relieving symptoms of the disease and lowering the frequency of relapses, but their primary goal is to prevent progression into secondary progressive MS, where drug treatment has little to no effect. Prescription medications offered to patients carry serious side effects such as flu-like symptoms, immune suppression, and increased risk of fatal neurological diseases. To reduce the amount of side effects and lower their severity, there is a need for newer drugs to be discovered. One strategy of drug therapy is regulating immune responses in the body, typically controlled by chemokines and chemokine receptors. Chemokine (C-X3-C motif) ligand 1 (CX3CL1) is a unique chemokine in that it has two biological forms and plays a significant role in immune responses through the generation of chemotactic gradients. It is through these gradients that its receptor, CX3C chemokine receptor 1 (CX3CR1), will traffic host immune cells to designated locations with higher levels of CX3CL1. Drug treatments focused on CX3CR1 inhibition are showing promise in clinical trials, but there is still a need to develop better therapeutic options. The aim of this project is to utilize bioinformatic methods and identify novel compounds and/or structurally similar compounds to those in clinical trials. With the help of chemical databases, ligand-based virtual screening can be conducted to identify structurally similar compounds to those in clinical trials. Identified compounds can then be filtered using drug classification parameters to select the most promising candidates. Following virtual screening, compounds can then be tested *in vitro* to test their efficacy in inhibiting CX3CR1 and how they impact neuroinflammatory diseases. We hypothesize that based on the intended methods, novel or structurally similar compounds to those in clinical trials will also show efficacy in treating MS and other neuroinflammatory diseases.