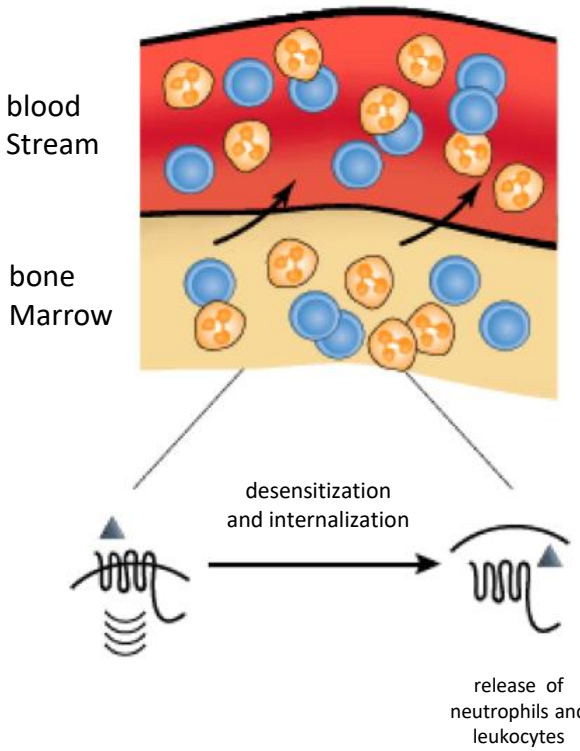
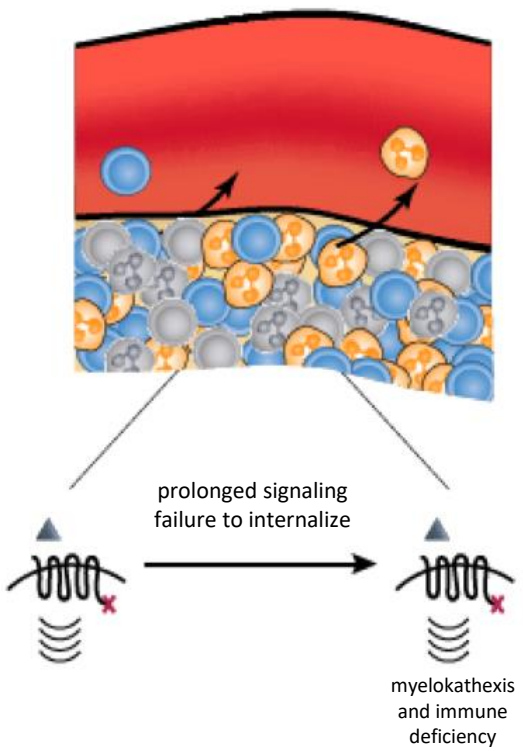
Normal CXCR4 function



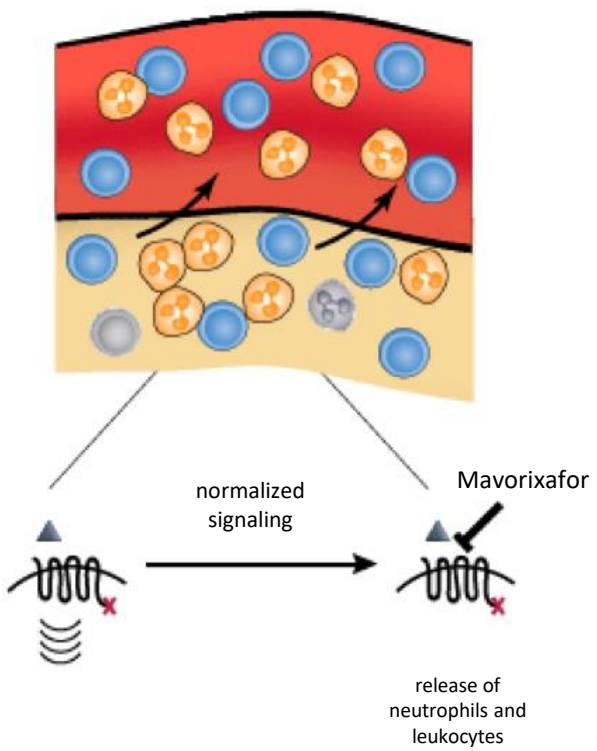
Normally the CXCR4 receptor can be internalized into the cell after CXCL12 binds to it, enabling the receptor to be appropriately “recycled” and the signaling to be diminished.

Hyperactive CXCR4 function caused by WHIM Mutation



However, in WHIM patients, a mutation truncates the intracellular portion of the CXCR4 receptor as shown by the red “x” below, which prevents the post-binding internalization (“normal recycling”) of the receptor. As a result, the CXCR4 receptor is maintained on the surface of the cell and is exposed to the ligand, which creates a perpetual “on” signaling and immobilizes the cell.

Mavorixafor modulates hyperactive CXCR4



Mavorixafor binds to the mutated CXCR4 receptor in a manner that blocks the receptor from being stimulated by CXCL12 regardless of the presence of the ligand, and results in increased mobilization and trafficking of white blood cells from the bone marrow.