

## **Regulation of the chemokine system by atypical chemokine receptors**

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Chemokines are a distinct large family of cytokines orchestrating leukocyte recruitment through activation of a dedicated panel of G protein-coupled receptors. A set of chemokine receptors indicated as “atypical”, in that structurally unable to mediate direct cell migration, are emerging as a major regulatory mechanism of chemokines biological activity. Atypical chemokine receptors are structurally and functionally heterogeneous, but they share the biological role of regulating signaling receptors’ activity by clearance, transport, or presentation of their cognate ligands. The atypical chemokine receptor D6 in particular is expressed on lymphatic vessels, binds and drives to degradation the majority of inflammatory CC chemokines, and by this chemokine scavenger function affects mobilization and trafficking of specific leukocyte subsets, including Ly6C<sup>high</sup> monocytes and  $\gamma\delta$  T cells, thus regulating inflammation and inflammation-driven tumor progression in different organs, including skin, liver, colon, lungs, and placenta.