

P001 Developing chemokine mutants with improved proteoglycan affinity and knocked-out GPCR activity as anti-inflammatory recombinant drugs

Andreas J. Kungl, Heide Wutschek, Barbara Brandner,
Veronica Wabitsch and Anna-Maria Piccinini
*Institute of Pharmaceutical Sciences, University of Graz,
Austria & ProtAffin Biotechnologie AG, Graz, Austria*

The interaction of chemokines and glycosaminoglycans (GAGs) on endothelial surfaces is a crucial step for establishing a chemotactic gradient which leads to the functional presentation of chemokines to their GPCRs and thus to activation of approaching leukocytes. Based on molecular modelling, biophysical investigations, cell-based and *in vivo* experiments we have developed a novel concept for therapeutically interfering with chemokine-GAG interactions, namely dominant-negative chemokine mutants with improved GAG binding affinity and knocked-out GPCR activity. These recombinant proteins displace their wild type chemokine counterparts from the natural proteoglycan co-receptors without being able to activate leukocytes via GPCRs. We will present *in vitro* and *in vivo* data which clearly demonstrate the validity of this approach which has been termed CellJamming because of the inhibitory interference during cell trafficking by our compounds.