

### Triggering the resolution of inflammation with agonistic anti-ChemR23 antibody dampens inflammation-driven carcinogenesis and metastasis

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# Abstract

Chronic inflammation is associated with abnormal non-phlogistic clearance (efferocytosis) of apoptotic cells by macrophages and a defect of the resolution of inflammation pathways. The **resolution of inflammation** is an **active immunological process** mediated by specialized pro-resolving mediator (SPM) which target specific resolutive G-protein coupled receptors expressed by different immune cells and participate at the return to tissue homeostasis after an injury. Defects in the clearance of (chemotherapy-induced) apoptotic tumor cell debris strengthens inflammation and has been associated with exacerbated tumor growth in several preclinical models. Proresolutive therapeutic approaches, such as using exogenous resolvin E1 (RvE1), the natural lipidic proresolutive ligand of GPCR ChemR23, have been shown to dampen tumor-associated inflammation and to reduce tumor growth. We found that **ChemR23** is inducible on myeloid cells by inflammatory stimuli and mainly expressed by tumor associated macrophages in melanoma and lung cancers. We identified an agonist anti-ChemR23 mAb that accelerates the resolution of inflammation in acute inflammatory model in mice. Finally, we report that **agonist anti-ChemR23** mAb **limits chronic inflammation** in the tumor microenvironment and inhibits metastasis development.





LC-MS/MS.



### ChemR23 expression is inducible upon inflammatory settings

Human PBMCs and neutrophils (A) or bone marrow myeloid cells were subjected to inflammatory cytokines (IL-6, IL-8, TNFα) or TLR ligands (LPS) for 18-24h or 48h and stained for flow cytometry analysis with an anti-ChemR23 mAb.



Time (hours)

Time (hours)

# **Triggering the resolution of inflammation with agonistic anti-ChemR23 antibody** dampens inflammation-driven carcinogenesis and metastasis

hlgG1  $\alpha$ ChemR23

hlgG1 αChemR23

hlgG1 αChemR23 hlaG1 αChemR23









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