

CX3CR1 Agonists

Nonconfidential

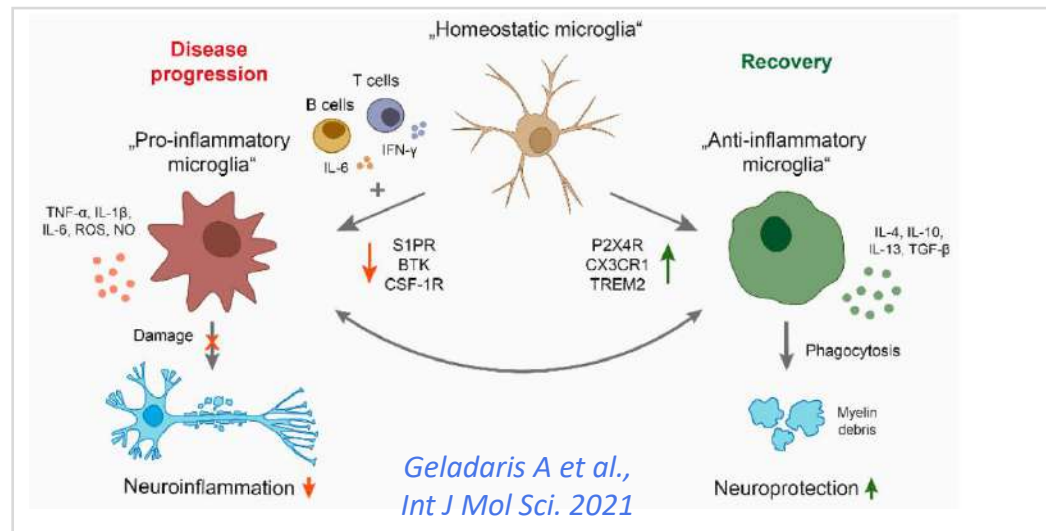
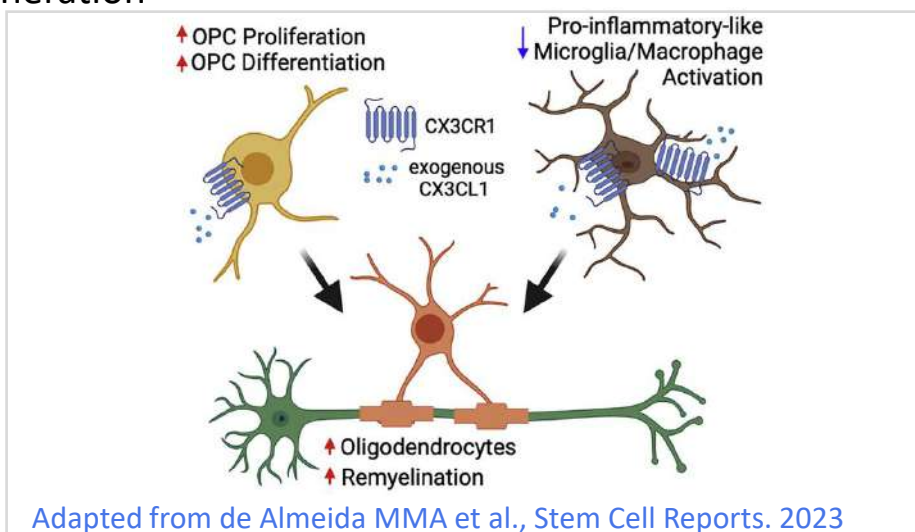
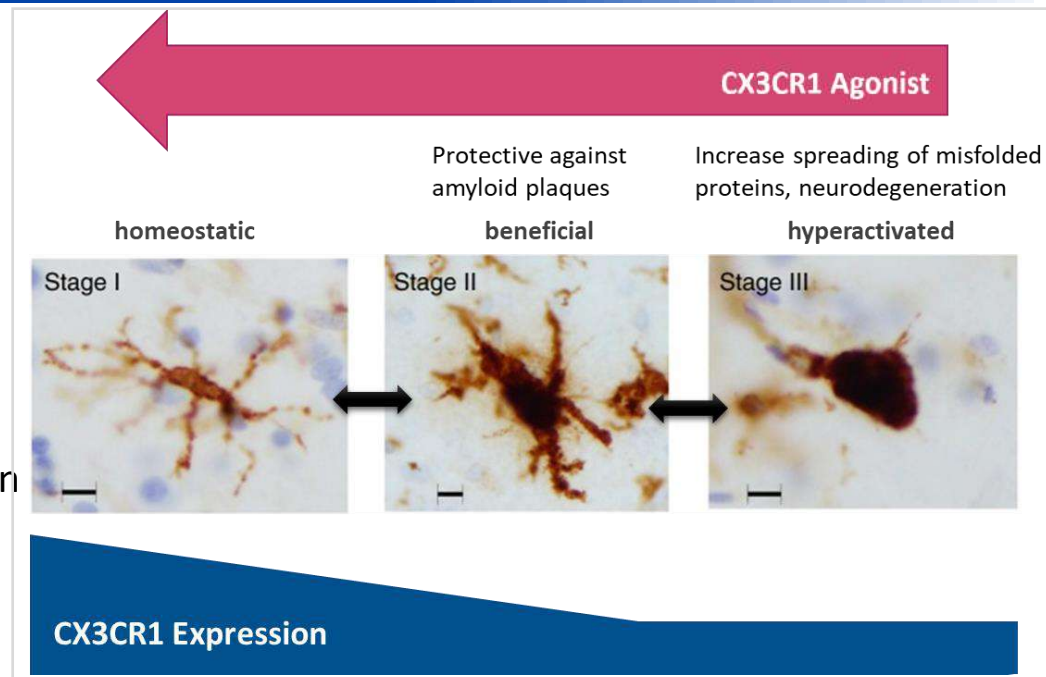
MDAnderson
~~Cancer~~ Center



Belfer
Neurodegeneration
Consortium

CX3CR1 Agonists Program

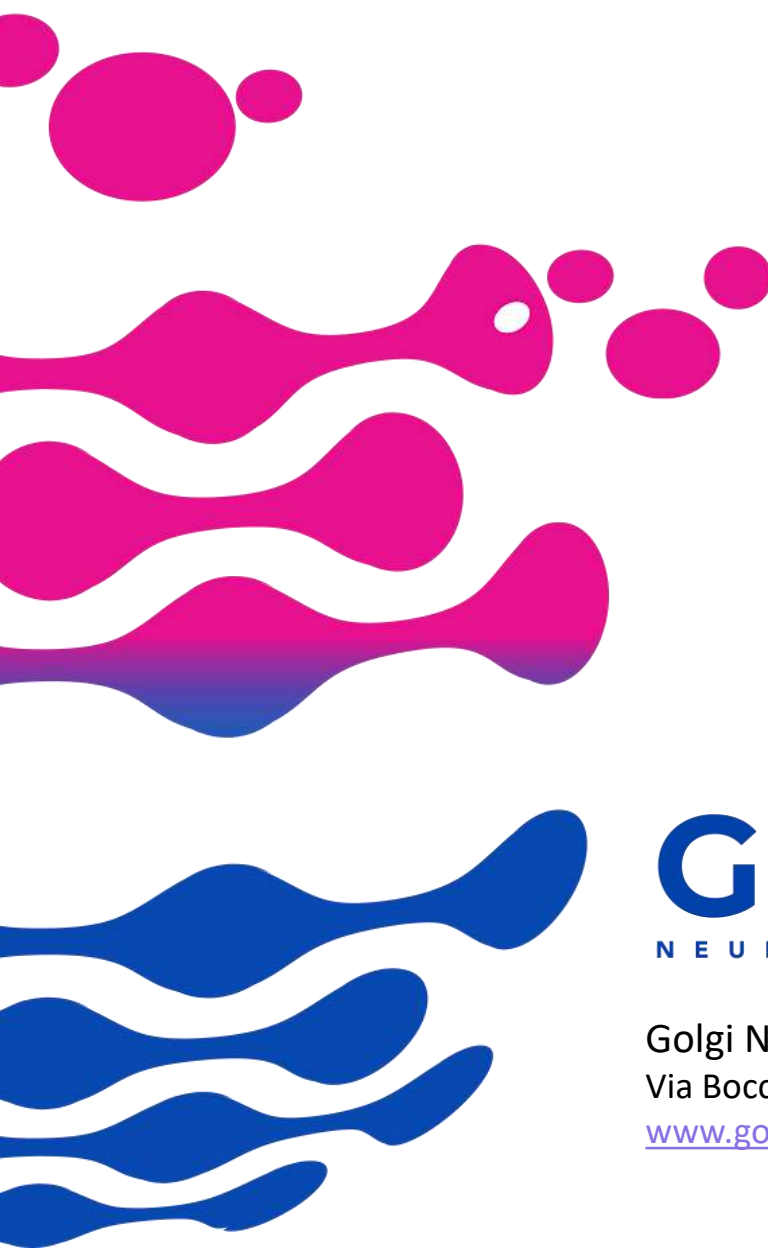
- CX3CR1 is a **Gαi-coupled GPCR** expressed in the brain almost exclusively in microglia and oligodendrocyte precursor cells (OPC)
- CX3CR1 activation by its ligand CX3CL1/Fractalkine (a large neuronal surface protein) **modulates microglia state and OPC function**
- **Loss of function/hypomorphic variants** in CX3CR1 aggravate multiple sclerosis progression and are linked to several neurodegenerative diseases (Alzheimer's disease, amyotrophic lateral sclerosis, age-related macular degeneration)
- Absence of the CX3CL1/CX3CR1 axis correlates with increased neurotoxicity in several neuroinflammation and neurodegeneration mouse models while restoring CX3CL1 is beneficial
- **Indications:** Multiple Sclerosis and other neurodegenerative disease, age-related macular degeneration



CX3CR1 Agonists Program – Executive Summary

Status	<ul style="list-style-type: none">➤ We have discovered the first small molecule agonists of CX3CR1➤ 1 class in Lead Generation (good potency, selectivity, oral bioavailability and CNS permeability)
Strengths	<ul style="list-style-type: none">➤ Very difficult to develop a good HTS-grade assay, but we have a solid one
Assets	<ul style="list-style-type: none">➤ 1 Patent granted in US, under evaluation in EU and other countries (WO2021016449)➤ Computer-Aided Drug Discovery feasible (Cryo-EM solved and mode of activation by CX3CL1 determined)➤ Recombinant assays and <i>in vitro</i> PoC assays available for the screening funnel➤ <i>in vivo</i> expertise and strong consultant network

➤ **Program available for partnership**



Golgi Neurosciences S.r.l.
Via Boccaccio, 20 - 20123 Milan (Italy)
www.golgineurosciences.com

Contacts:

Program and Innovation Manager

Lorena Za

lorena.za.lz@golgineurosciences.com

Managing Director

Chiara Liberati

chiara.liberati.cl@golgineurosciences.com