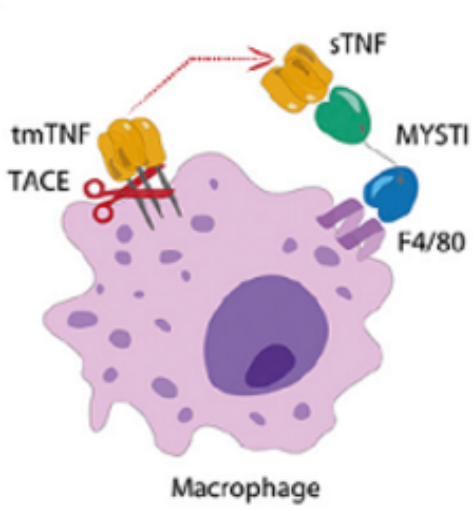
Technology Offer

Bispecific antibodies for cell-type-specific TNF inhibition

Reference Number 22-00020

Challenge
Elevated TNF levels are a hallmark of inflammation. Therefore, agents blocking TNF have offered patients tremendous improvements in the treatment of various autoimmune diseases including rheumatic arthritis, systemic lupus erythematosus or Chron's disease. Biologics like the antibody adalimumab (Humira®, sales 2015: 14 Bn USD) are still hugely successful blockbusters, but patents start to expire and the first biosimilars are entering the market. Notably, TNF does not only have pathogenic functions but is also acting in a protective way. Therefore, agents systemically blocking TNF exhibit several side effects, like an increased risk for developing serious infections. Hence, there is a significant need for novel agents specifically blocking TNF involved in pathogenic pathways.



Bispecific antibody binding to the macrophage-specific F4/80 marker and TNF simultaneously.

Technology
Studies in conditional knock-out mice examining the effects of cell-type-specific TNF ablation showed different functions of this cytokine depending on the cellular context. While TNF derived from myeloid cells was pathogenic in experimental disease models for arthritis, TNF originating from T cells had protective functions in models including tuberculosis infection (TB). Experiments with conditional TNF knockout mice have also demonstrated that myeloid cell-derived TNF is not absolutely necessary for the resistance to TB, while T cell-derived TNF again is playing a unique protective role.
In view of these results, bispecific antibodies capable of binding specifically to macrophages and neutralizing TNF in the same time were designed and characterized. The antibodies consist of two single-domain antibodies with an anti-TNF domain and a domain binding to a macrophage-specific cell marker, joined by a flexible linker. In-vitro experiments show selective and potent blocking of TNF derived from macrophages while no interaction with other cell types was detected. Evaluation of the antibodies in an in-vivo mouse model of TNF-induced hepatotoxicity demonstrated that they are more effective in protection from hepatotoxicity than control antibodies neutralizing TNF systemically. Hence, the technology provides means for selective blocking of pathogenic TNF while TNF with protective functions regarding different infection pathways is not affected. As an example, the increased risk for TB is still a major side effect in current anti-TNF therapies. The present antibodies therefore may represent a basis for safer and more effective treatments in autoimmune diseases.

Commercial Opportunity
Available for licensing or collaboration

Patent Situation
National patents and patent applications based on WO2014064287 with priority of October 26,2012:
US patent US9,688,757 (granted in 2017)
EP patent application EP2912068 pending
Russian patent application RU2015119641 pending

Further Reading
PNAS 2016, 113 (11), 3006-3011
Sci. Rep. 2013, 3, 1809

DRFZ BERLIN
Deutsches Rheuma-Forschungszentrum
Ein Institut der Leibniz-Gemeinschaft

Licensing Contact:
Dr Michael Karle
Technology Manager
T: +49 30 948930-02
karle@ascenion.de

Ascenion GmbH
Herzogstraße 64
D-80803 München
T: +49 89 318814-0
info@ascenion.de
www.ascenion.de