Technology Offer

Overcoming disease persistence in myeloproliferative neoplasms (MPN) through combinatorial inhibitor treatment

Ref.-No.: MI 0204-5895-MG

The mRNA processing factor YBX1 is a novel target in Myeloproliferative neoplasms (MPNs), which in an combinatorial inhibitor treatment with JAK inhibitors completely overcomes disease persistance.

Background

Myeloproliferative neoplasms (MPNs) are a group of hematological diseases of the bone marrow in which excess cells are produced. They are related to, and may evolve into, myelodysplastic syndrome and acute myeloid leukemia. Activated JAK2 signalling represents a central feature of all MPNs and has led to new therapies for these diseases. While JAK inhibitors reduce inflammatory activity and hyperproliferation of myeloid progenitors, JAK2-mutated clones that maintain the disease persist. Therefore, unexpectedly, JAK inhibitors in clinical use have minor effects on overall disease burden or evolution of persistent clones.

Technology

Scientists from the Max-Planck-Institute of Biochemistry in collaboration with the Universitätsklinikum Jena have identified the mRNA processing factor YBX1 by in-depth phosphoproteome profiling as JAK2 target and important mediator for persistence of JAK2-mutated neoplasms. In combination with pharmacological JAK inhibition, YBX1 inactivation induces apoptosis in JAK2-dependent mouse and primary human patient cells, causing regression of the malignant clones *in vivo*, and inducing molecular remission. Pharmaceutical targeting of downstream pathways regulated by YBX1 (e.g. MEK-ERK-signaling) in combination with JAK-inhibitors *in vivo* resulted in eradication of JAK2-mutated clones in > 80 %. Consistent with these findings, direct pharmacologic targeting of YBX1 in combination with JAK-inhibitors abrogated ERK-phosphorylation, reduced proliferative capacity and enhanced induction of apoptosis in murine and human JAK2-mutated cells. Thus genetic and pharmacologic targeting of YBX1 or its dependent downstream effectors represents a novel therapeutic strategy to target JAK2-mutated clones and overcome disease persistence in JAK2-mutated cancers such as MPNs.

We are now looking for either a licensing partner, or a collaboration partner to further develop this project.

Publication

Jayavelu et al., 2020. *Nature*. DOI: 10.1038/s41586-020-2968-3

Patent Information

A patent application was filed on April, 23rd 2021: WO2021214303A1. National in EP and US.

Contact

Dr. Mareike Göritz
Senior Patent- & License Manager
Chemist
Phone: +49 (0)89 / 29 09 19 - 32
eMail: goeritz@max-planck-innovation.de

Max-Planck-Innovation GmbH
Arnulfstr. 58
80335 München
www.max-planck-innovation.de