

Survival signalling mediated by Tyk2 is the Achilles' heel of Anaplastic Large Cell Lymphomas

(Vienna, 30.08.2018) Anaplastic Large Cell Lymphomas (ALCL) are rare tumors of white blood cells, which fall into at least four categories. New research by the international ERIA consortium led by scientists in Vienna have now identified that all types of ALCL rely on the same signaling pathway for survival. TYK2 prevents apoptotic cell death by increasing the expression of the BCL2 family member Mcl1. Therefore TYK2 represents an attractive drug target due to its unique enzymatic domain, and TYK2-specific inhibitors show promise as novel targeted inhibitors for ALCL.

Personalised medicine is pioneered in cancer therapy, where diagnostic tools increasingly dissect tumor entities in ever smaller sub-indication with the aim to devise individual therapeutic strategies. Therefore the molecular analysis of human tumor samples for new therapeutic targets and their validation in tumor models has become a main stay of cancer research to advance clinical management of cancer patients. However, this poses several challenges for clinicians, including the extensive diagnostic work-up of patients, but also the limited amount of information how to treat small patient groups. This is even more pressing for rare tumors, like ALCL with a very small number of patients

Therefore Olaf Merkel of the Medical University Vienna and his colleagues are happy to report now in the Journal "Leukemia" that instead of subdividing ALCL subgroups even further, they could identify a common player in all ALCL patients. TYK2 is not only expressed in all patients, it mediates the same anti-apoptotic response, which keeps the lymphoma cells alive and thus supports the growth of the tumor. "Therefore we could consider TYK2 signalling as the Achilles' heel of ALCL, as in all patients we have analysed the tumor cells relied on this activity to support the essential survival signal" explains the senior author of this publication, Olaf Merkel. Withdrawing the Tyk2 signal in cell culture resulted in extensive cell death and in mice treated with an experimental drug switching off Tyk2 the researchers observed a much longer survival.

Lukas Kenner of the Ludwig Boltzmann Institute of Cancer Research and co-founder of the European Research Initiative on Alk-mediated diseases (ERIA) underscores the potential therapeutic importance in ALCL of TYK2 inhibitors. "We are looking forward to Tyk2 inhibitors becoming available, which are currently developed to treat immunological disorders, because in the more rare lymphomas we urgently need better therapies", he points out.

Dependency on the TYK2/STAT1/MCL1 axis in anaplastic large cell lymphoma

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About the Ludwig Boltzmann Institute for Cancer Research (LBI-CR):

The LBI-CR focuses on developing new murine models for cancer and exploiting them to gain novel insights into the origins of the disease. The institute conducts cutting edge research into the underlying mechanisms of cancer using the modern power of genetics. With particular attention for signal cooperation in tumour cells the researchers analyse the molecular basis of cancer with the intention to translate recent progress in cancer research into novel therapeutic approaches. The Institute conducts its research in close cooperation with the Research Institute for Molecular Pathology, Medical University Vienna, Veterinary University, Children's Cancer Research Institute and the company Tissuegnostics. The institute was a founding member of the European Research Initiative on Alk-mediated diseases (ERIA: erialcl.net/) and participates in the EU funded Horizon 2020 Marie Skłodowska Curie Innovative Training Network ALKATRAS under grant agreement 675712.

About the Ludwig Boltzmann Gesellschaft:

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