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MEETING ABSTRACT

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Exploring the impact of STAT3-targeting on NK-cell-mediated killing in acute myeloid leukemia

Clio-Melina SPERL, Bernhard ZDÁRSKY, Theresa HARM, Agnieszka WITALISZ-SIEPRACKA[#], Dagmar STOIBER-SAKAGUCHI[#,*]

Division of Pharmacology, Department of Pharmacology, Physiology and Microbiology, Karl Landsteiner University of Health Sciences, Krems an der Donau, Austria; ([#]contributed equally)

Background: Signal transducer and activator of transcription 3 (STAT3) is an integral component of the Janus kinase (JAK)-STAT pathway, which plays a critical role in cancer development. In the context of cancer, STAT3 primarily functions as a facilitator of tumor growth, promoting cell proliferation, suppressing apoptosis, facilitating angiogenesis, promoting metastasis, and aiding tumor cells in evading immune detection by natural killer (NK) cells. NK cells are innate lymphocytes capable of killing transformed cells. Recently, NK-cell-based therapies gained attention in the treatment of hematopoietic cancers, especially in acute myeloid leukemia (AML). The interaction between AML and NK cells is tightly regulated by surface ligands capable of either triggering or inhibiting the lysis of target cells. In most cancer types, blocking STAT3 signaling results in increased immune cell activation in the tumor environment.
Methods: We aim to investigate the interaction between NK cells and AML in the absence of STAT3, using AML knockout cell lines achieved through CRISPR-Cas9 technology. Our ongoing research involves analysing the impact of pharmacological STAT3 inhibition in AML on the NK-cell surveillance using flow cytometry, qPCR and western blot.
Results: Our findings demonstrate that the lack of STAT3 in human AML cell lines leads to diminished surveillance by primary human NK cells. Our data so far revealed a decrease in ICAM-1 and CD48 expression in AML cells lacking STAT3, which both contribute to immunological synapse formation. In the STAT3 knockout AML cell lines, we observed less conjugate formation between AML and NK cells compared to the wild-type AML cell line counterparts.
Discussion: As a result, we propose that the diminished killing of STAT3 knockout AML cells is likely attributable to disrupted synapse formation and the subsequent lack of NK-cell activation. Our novel finding reveals the unforeseen influence of STAT3 on the vulnerability of AML cells to NK-cell-induced elimination, potentially improving the treatment possibilities for patients.
Keywords: STAT3 – NK cells – acute myeloic leukemia

*Corresponding author e-mail: *dagmar.stoiber@kl.ac.at*