2024 Joint Usage and Research Report

<table>
<tr><td colspan="2">Title of Research Project</td><td colspan="3">STAT3 isoforms in inflammation and immunity</td></tr>
<tr><td colspan="2">Status</td><td colspan="3">New / Continued</td></tr>
<tr><td rowspan="2">Applicant</td><td>Institution</td><td>Karl Landsteiner University of Health Sciences</td><td>Circle if under 40</td><td>Circle if under 35</td></tr>
<tr><td>Job title and Name</td><td>Prof. Dagmar Stoiber-Sakaguchi

Sophie Rosa Edtmayer (PhD student)</td><td></td><td>○</td></tr>
<tr><td rowspan="4">Research collaborators
(Please add lines as appropriate)</td><td>Institution</td><td></td><td></td><td></td></tr>
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<tr><td colspan="2">Host researcher at IGM</td><td colspan="3">Prof. Akinori Takaoka</td></tr>
<tr><td colspan="2">Purpose of the Research Project (within 200 words)</td><td colspan="3">Aberrant JAK/STAT signaling is associated with several diseases including cancer development. Among the STAT family, STAT3 holds a significant role as the main mediator of interleukin 6 (IL-6) signaling, making it a crucial regulator of inflammation, immunity, and disease. While STAT3 is typically associated with promoting cancer, recent studies revealed its dual role, acting both as an oncogene and a tumor suppressor depending on the malignancy. This duality may be due to its existence in two alternatively spliced isoforms: the full-length isoform STAT3alpha and the truncated isoform STAT3beta.
Recently, we demonstrated that STAT3beta acts as a tumor suppressor in acute myeloid leukemia (AML). Our observations indicate that the balance between the two STAT3 isoforms serves as a valuable prognostic marker for predicting outcomes of AML patients. While a high STAT3beta to STAT3alpha ratio correlates with favorable prognosis, a low STAT3beta to STAT3alpha ratio is linked to poor outcome. In our subsequent study, we observed that absence of STAT3beta resulted in enhanced type I and II IFN signaling, which was linked to poor outcome in AML patients as well as in an AML mouse model.
As STAT3-mediated IFN signaling is also involved in inflammation and immunity, we would be interested in the two isoforms also in this context. Thus, we would test the expression levels of the distinct isoforms in the context of host-</td></tr>
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	parasite interaction and which roles the two isoforms play therein.
Results (including the number of web meetings; within 1,000 words)	The researchers visited the host researcher laboratory in October / November 2024, respectively. During their stay they • visited Prof. Akinori Takaoka's laboratory • held a seminar each followed by a discussion • discussed ongoing projects and possible future collaboration with Prof. Takaoka, Dr. Sato and Dr. Suzuki and students Possible collaborative work on the STAT3 isoforms in inflammation and immunity as well as cancer was discussed. Special focus was put on the connection of the STAT3 isoforms and IFN signaling and the molecular mechanism behind it. Several in vitro and in vivo experiments across both the host institution and the applicants´ institution were planned and shall be carried out in the future. Due to Prof. Takaoka´s and his group´s profound expertise on IFN signaling and the valuable input we have obtained from them we are confident that these planned experiments will provide further insight into the regulation of STAT3 isoforms in the context of cancer as well as inflammation and immunity. Outlook: In case the data derived from this project will result in a publication in a scientific journal in the field we will appropriately acknowledge this grant from the General Joint Research Program of the Institute for Genetic Medicine.
Publication *Provide the details of the conferences or journals where the above work was presented or published.	【Conference, symposium, workshop etc.】 Presenter(s), presentation title, meeting name, venue, date -
	【Journals】 Author(s), paper title, journal name, volume, pages, year, impact factor -
	【Press release】 -