

## Actin defects in primary immunodeficiencies (ACTIV)

<p><b>Project partners</b></p> <p>Université de Strasbourg (S. Jung), Universität Freiburg (L. Gámez-Díaz), Universität Basel (V. Spindler)</p>
<p><b>Project duration / Awarded funding</b></p> <p>01/03/2022 – 01/09/2023 / 46,000€</p>
<p><b>Short description of the project</b></p> <p>Primary immunodeficiencies (PIDs) represent a large group of genetic disorders characterized by immune system dysfunction. Patients with immunodeficiencies are particularly susceptible to infections. Recently, some of these immunodeficiencies have been linked to abnormalities in the actin cytoskeleton, a collection of filaments that form the cellular “skeleton” and give cells their mechanical properties. In the immune system, the actin cytoskeleton is also very important for the transmission of signals inside and between the cells. The objective of this project was to better understand two PIDs resulting from defects in the actin cytoskeleton, known as actinopathies.</p>
<p><b>Concrete implementation of the project (What was the funding used for?)</b></p> <p>We used the funding to:</p> <ul style="list-style-type: none"> <li>• Purchase various consumables for the experiments.</li> <li>• Support a research internship of the 2 PhD students associated to this project (from Strasbourg and Freiburg Universities) aimed to evaluate the static and dynamic adhesion in mutated T and B cell lines at the laboratory of V. Spindler (Basel).</li> <li>• Present preliminary results at the 2023 Joint Meeting from the French and German Society of Immunology (Strasbourg).</li> <li>• Hire 2 Master and 1 Bachelor students from Freiburg University as HiWi students. With it, they could complete their MSc theses.</li> </ul>
<p><b>Project result(s) and continuation of collaboration</b></p> <p>The general aim of the collaboration was to develop common laboratory tools for the precise characterization of actinopathies. We focused on 2 PIDs i.e., LRBA deficiency (Freiburg) and a new PID caused by a mutation in <i>ACP1</i> gene.</p> <p>We observed reduced cell migration, increased cell adhesion, and abnormal assembly of the immune synapse (IS) in LRBA knock out (KO) B cells. LRBA-KO T cells showed increased migration, reduced adhesion and normal assembly of IS with increased size. These results suggest a cell-specific role of LRBA in the cytoskeleton dynamics of lymphocytes.</p> <p>We showed a reduced migration and adhesion under shear stress, but increased spreading capacities of <i>ACP1</i> KO T cells.</p>

**Further information (links, articles, photos)**

3 oral communications and 1 poster were presented by E. Busch (PhD student, Strasbourg):

- E. Busch, N. Wadier, S. Depauw, P. Kessler, P. Hammann, A. Guffroy, AS. Korganow, S. Jung. *Primary immune deficiencies associated with actin cytoskeleton defects: dissection of pathophysiological mechanisms*. Bed and Bench Immunology (BBI) meeting, Strasbourg 2023 (oral presentation).
- E. Busch, N. Wadier, S. Depauw, P. Kessler, P. Hammann, A. Guffroy, AS. Korganow, S. Jung. *Primary immunodeficiency caused by a defect in ACP1: a potential new actinopathy*. Congress from the Strasbourg Federation of Translational Medicine, June 2023 (oral communication).
- E. Busch, N. Wadier, S. Depauw, P. Kessler, P. Hammann, A. Guffroy, AS. Korganow, S. Jung. *Primary immunodeficiency caused by a defect in ACP1: a potential new actinopathy*. Joint Meeting from the French and German Society of Immunology, Strasbourg, September 2023 (oral communication and poster).

3 oral communications and 3 posters were presented by E. Sindram (PhD student, Freiburg). One e-poster was presented by L. Gámez Díaz:

- V. Zeidler, E. Sindram, E. Mace, B. Grimbacher and L. Gámez-Díaz. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. 20<sup>th</sup> European Society for Immunodeficiencies (ESID), Gothenburg, October 2022 (oral poster presentation).
- E. Sindram, V. Zeidler, K. Malfertheimer, J. Rush-Kittle, E. Mace, V. Spindler, B. Grimbacher, L. Gámez-Díaz. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. International Symposium – From Paradigms to Paradoxes in Immunity and Immunopathology (PPII), Freiburg, October 2022 (oral science slam and poster presentation).
- E. Sindram, V. Zeidler, K. Malfertheimer, J. Rush-Kittle, E. Mace, V. Spindler, B. Grimbacher, L. Gámez-Díaz. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. Bed and Bench Immunology (BBI) meeting, Strasbourg 2023 (oral presentation)
- E. Sindram, V. Zeidler, K. Malfertheimer, J. Rush-Kittle, C. Castro, M. Reth, E. Mace, V. Dumit, J. Dengjel, V. Spindler, B. Grimbacher, L. Gámez-Díaz. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. EMBO meeting, Sant Feliu de Gu´xols, May 2023 (poster presentation)
- E. Sindram, V. Zeidler, K. Malfertheimer, J. Rush-Kittle, E. Mace, V. Spindler, B. Grimbacher, L. Gámez-Díaz. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. *LRBA drives actin cytoskeleton dynamics through interaction with Myosin-9*. Joint meeting AKKI (oral presentation) and DFGI (poster presentation), Strasbourg, September 2023.