

GAIN: German network for the research and treatment-optimization of patients with multi-organ autoimmunity



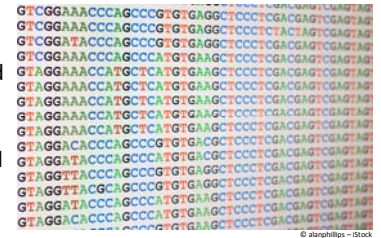
Principal Investigators

Dr. rer. nat. Faranaz Atschekzei¹, Prof. Dr. med. Ulrich Baumann², Prof. Dr. med. Stephan Ehl³, Prof. Dr. med. Bodo Gimbacher³ (Coordinator), PD Dr. med. Dr. sci. nat. Fabian Hauck⁴, Prof. Dr. med. Bimba Hoyer⁵, Prof. Dr. rer. nat. Thomas Illig⁶, Dr. med. Dipl. Inf. Gerhard Kindle³, PD Dr. rer. nat. Alexandra Nieters³, Prof. Dr. rer. nat. Andreas Radbruch⁷, Prof. Dr. med. Philip Rosenstiel⁸, Prof. Dr. med. Reinhold Ernst Schmidt¹, Prof. Dr. med. Hendrik Schulze-Koops⁹, Prof. Dr. Alla Skapenko⁹, Prof. Dr. med. Klaus Warnatz³

- ¹ Department of Immunology and Rheumatology, Hannover Medical School, Germany
- ² Department of Pediatric Pneumology, Allergy and Neonatology, Hannover Medical School, Germany
- ³ Institute for Immunodeficiency, Center for Chronic Immunodeficiency (CCI), Medical Center - University of Freiburg, Germany
- ⁴ Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University, Munich, Germany
- ⁵ CCIM, Department Rheumatology and Clinical Immunology, UKSH, Campus Kiel, Germany
- ⁶ Hannover Unified Biobank and Department of Human Genetics, Hannover Medical School, Germany
- ⁷ DRFZ, Leibniz-Institute, Berlin, Germany
- ⁸ Excellence Center for Inflammation Medicine, UKSH, Campus Kiel, Germany
- ⁹ Division of Rheumatology and Clinical Immunology, Ludwig-Maximilians-University, Munich, Germany

Topic

Multi-organ autoimmune diseases belong to the “ultra-rare” disorders and have only recently been recognized being caused by monogenetic mutations in immune-regulatory genes. Patients are typically characterized by multi-organ inflammation including, but not limited to the bone marrow, gut, lungs, kidneys, skin, and the central nervous system (CNS). Genes recently added to the list include *CTLA4*, *LRBA*, *NFKB1*, *NFKB2*, *STAT3*, and *LAT*. This cohort of patients provides a frontier in medicine, as these rare monogenetic disorders are highly instructive for understanding and treating also more prevalent polygenic autoimmune disorders.



Objectives

Principal research questions:

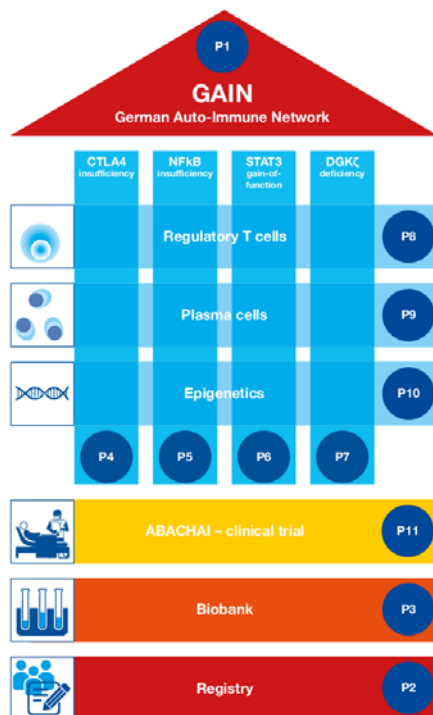
1. What are the underlying molecular and cellular pathomechanisms in these multi-organ autoimmune diseases?
2. By which molecular interventions can we influence/correct this cellular pathology?

Primary goal of the consortium:

1. Improve the understanding of the pathophysiology in patients with inborn errors of multi-organ autoimmune disease.
2. Improve the management of patients with inborn errors of multi-organ autoimmune disease.

Main results expected:

1. Create a disease registry and biobank for these rare diseases.
2. Identify/diagnose and treat these patients in Germany according to common protocols.
3. Understand the disease pathomechanisms, the reduced penetrance and variable expressivity of these disorders.
4. Develop novel treatment strategies.
5. Founding of a patient-support group and/or a foundation in support of families with inborn errors of multi-organ autoimmune disease.



Projects

1. Coordination of GAIN
Prof. Dr. med. Bodo Gimbacher (Freiburg)
2. Registry of the German multi-organ Auto-Immunity Network (GAIN-registry)
Dr. med. Dipl. Inf. Gerhard Kindle (Freiburg), PD Dr. rer. nat. Alexandra Nieters (Freiburg)
3. Consortial Biobank for patients with Inborn Errors of Multi-Organ Autoimmune Diseases
Prof. Dr. rer. nat. Thomas Illig (Hanover)
4. CTLA4 insufficiency
Prof. Dr. med. Bodo Gimbacher (Freiburg)
5. Immune dysregulation due to NFKB1D defects
Prof. Dr. med. Klaus Warnatz (Freiburg)
6. STAT3 gain-of-function (GOF) associated disease
Prof. Dr. med. Stephan Ehl (Freiburg)
7. Initial description of human DGKζ-deficiency
PD Dr. med. Dr. sci. nat. Fabian Hauck (Munich)
8. The role of GARP in monogenic traits of multi-organ autoimmunity
Prof. Dr. Alla Skapenko (Munich), Prof. Dr. med. Hendrik Schulze-Koops (Munich)
9. Monogenetic immune dysregulation syndromes and their effect on the plasma cell compartment
Prof. Dr. med. Bimba Hoyer (Kiel), Prof. Dr. rer. nat. Andreas Radbruch (Berlin)
10. Identification of epigenetic factors in multi-organ autoimmunity
Dr. rer. nat. Faranaz Atschekzei (Hanover), Prof. Dr. med. Reinhold Ernst Schmidt (Hanover)
11. Safety and Efficacy of abatacept (s.c.) in patients with CTLA4 insufficiency and LRBA deficiency (ABACHAI)
Prof. Dr. med. Bodo Gimbacher (Freiburg)