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

## Principal Investigators

Dr. rer. nat. Faranaz Atschekzei, Prof. Dr. med. Ulrich Baumann, Prof. Dr. med. Stephan Ehli, Prof. Dr. med. Bodo Grimbacher (Coordinator), PD Dr. med. Dr. sci. nat. Fabian Hauck, Prof. Dr. med. Bimba Hoyer, Prof. Dr. rer. nat. Thomas Illig, Dr. med. Dipl. Inf. Gerhard Kindle, PD Dr. rer. nat. Alexandra Nieters, Prof. Dr. rer. nat. Andreas Radbruch, Prof. Dr. med. Philip Rosenstiel, Prof. Dr. med. Reinhold Ernst Schmidt, Prof. Dr. med. Hendrik Schulze-Koops, Prof. Dr. Alla Skapenko, Prof. Dr. med. Klaus Warnatz

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. DFRI, 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, NFκB1, 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.
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 Grimbacher (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 Grimbacher (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 Ehli (Freiburg)
7. Initial description of human DKGκ ‐ 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 Grimbacher (Freiburg)