

Department of Surgery

Division of Transfusion Medicine and Hemostaseology

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Research focus

- Development of new minimally invasive photopheresis methods
- Functional modulation of dendritic cells
- Collection of monocytes for the generation of dendritic cells (DC)
- Clinical research related to hemostaseology
- Clinical research related to hemotherapy
- Mesenchymal stromal cells (MSC)
- Optimization of collection procedures to get regulatory T cells (Tregs)
- Legislation of transfusion

Structure of the Division

Professorships: 1

Personnel: 76

- Doctors (of Medicine): 6
- Scientists: 6 (thereof funded externally: 0)
- Graduate students: 10

Clinical focus areas

- Clinical transfusion medicine
- Blood component supply
- Immunohematological and hemostaseological diagnostics
- Outpatient and inpatient coagulation counseling
- Production and storage of stem cell preparations
- Minimally invasive photopheresis methods

Research

Research in the Division of Transfusion Medicine and Hemostaseology focuses on the characterization of specific blood components, stem cell concentrates, and new experimental cellular preparations. Clinical problems with respect to hemotherapy and coagulation management are also investigated. In the GMP laboratory of the Division, interdisciplinary experimental preparations for innovative clinical trials are produced and tested (Advanced Therapy Medicinal Products, ATMP).

COVID-19 Immunotherapy

PI: Prof. Dr. H. Hackstein
In the course of the SARS-COV-2 pandemic, the department received in April 2020 as one of the first institutions in Germany the permission to

produce Covid-19 immune plasma. COVID-19 immune plasma is produced from convalescents in accordance with the German Drug Law and contains virus-specific antibodies. To test the clinical efficacy, the department has initiated a randomized phase II study together with Med. Klinik IV (Prof. Dr. Mario Schiffer): Assessment of Efficacy and Safety of Therapy With COVID-19 Convalescent Plasma in Subjects With Severe COVID-19 (IPCO).

Development of new minimally invasive photopheresis methods

PI: Prof. Dr. H. Hackstein

Current standard photopheresis methods are only able to treat small children to a limited extent. The project group has modified the clinical photopheresis methods and is developing new minimally invasive treatment methods so that critically ill infants can also be successfully treated with a graft versus host disease after bone marrow transplantation. This new mini-photopheresis procedure is characterized by the fact that only very small amounts of blood (100-200 ml whole blood) are required and thus even very small children or vital unstable, critically ill adult patients with contraindications to classical apheresis can be treated.

Functional modulation of dendritic cells

PI: Prof. Dr. H. Hackstein

The project group is investigating pharmacological substances that control or block key functions of dendritic cells with the aim of activating or blocking antigen-specific immune responses. The immunosuppressant rapamycin, for example, is the first clinically used drug that inhibits both, antigen uptake and mobilization of dendritic cells *in vitro* and *in vivo*. Current research projects investigate the role of RNA-editing enzymes in the hematopoietic differentiation of dendritic cells and translational protocols for the accelerated differentiation of monocytes in dendritic cells.

Collection of monocytes for the generation of dendritic cells (DC)

PI: Prof. Dr. E. Strasser

Circulating monocytes are precursors of DC, which play a key role in the immune system's function by presenting antigens to specific lymphocytes. The collection and cultivation of these cells enables the development of new strategies in the treatment of malignant diseases. Members of the Division of Transfusion Medicine and Hemostaseology cooperate with colleagues from the Department of Dermatology to adjust the collection procedures optimally to the specific clinical and experimental demands of procedures aimed at the cultivation, expansion, and priming of DC.

Clinical research related to hemostaseology

PI: Prof. Dr. R. Zimmermann, Prof. Dr. E. Strasser
Other research interests include thrombophilia, traveller's thrombosis, and hemostasis dysfunctions resulting in bleeding disorders. Other current study objectives are preanalytical determi-

nants of fibrinolysis tests, hemostasis tests in systemic lupus erythematoses, and other currently relevant topics.

Clinical research related to hemotherapy

PI: Prof. Dr. V. Weisbach, Prof. Dr. R. Zimmermann, Prof. Dr. E. Strasser

We examine antibodies against red cell antigens, characterize factors influencing the quality of stored red cell concentrates, and study the complex dysfunctions of the coagulation system.

Mesenchymal stromal cells (MSC)

PI: Prof. Dr. V. Weisbach

Mesenchymal stromal cells (MSC) are the predecessors of osteoblasts, chondrocytes, and adipocytes. The term "MSC" especially covers cells cultivated and expanded *ex vivo*. These cells are a mixture of stem and progenitor cells up to mature stroma cells and are named MSC according to a definition of the International Society of Cellular Therapy. It is expected that MSC will play a major role in future applications of regenerative medicine. The main focus of the working group is the preparation, characterization, and expansion of MSC especially from placental tissues.

Optimization of collection procedures to get regulatory T cells (Tregs)

PI: Prof. Dr. E. Strasser, PD Dr. J. Strobel

T cells play an important role in adoptive immune response in many diseases (infectious and inflammatory diseases, tumors). DC act as antigen presenting cells for specific T cells activation. The collection of circulating T cells as well as the culture and expansion of T cells, especially regulatory T cells (Tregs), enables the development of new strategies for the anti-inflammatory and immunosuppressive therapies. Members of the Division of Transfusion Medicine and Hemostaseology cooperate with colleagues from the departments of Medicine 1, Dermatology, and Medicine 5 to optimally adjust the collection procedures to the specific clinical and experimental demands of procedures aimed at the cultivation and expansion of Tregs. In the context of cell preparation, analysis of factors responsible for cell damage (cell apoptosis and necrosis) is relevant to optimize the quality of leukocyte products.

Legislation of transfusion

PI: Prof. Dr. R. Zimmermann

Under the auspices of the Legal Counsel and Managing Director of the UK Erlangen, Dr. A.W. Bender, the Division of Transfusion Medicine and Hemostaseology is involved in publications on the legislation and law of blood transfusion in Germany. In the center of attention is the book "Transfusion Law", published by the Wissenschaftliche Verlagsgesellschaft Stuttgart, that has become the benchmark in this field of law and has found its way into the jurisdiction of the German Federal High Court of Justice. Alongside, book contributions and articles on different aspects of the legislation and law of blood transfusion are published.

Teaching

The Division of Transfusion Medicine and Hemostaseology is involved in compulsory and optional courses in the curricular teaching of Medicine and Dentistry. Particularly noteworthy is the interdisciplinary teaching of laboratory diagnostics and clinical pathology together with the Department of Medicine 5 and the Clinical Chemistry Laboratory and the participation in the block training in surgery. We supervise MD and PhD theses.

Selected publications

Buchele V, Hackstein H. A simplified extracorporeal photopheresis procedure based on single high-dose ultraviolet A light irradiation shows similar in vitro efficacy. *Transfusion*. 2021 Mar;61(3):883-893.

Strasser EF, Steininger PA, Korn K, Achenbach S, Tenbusch M, Cunningham S, Zimmermann R, Überla K, Hackstein H. Validation of a SARS-CoV-2 RNA RT-PCR assay for high-throughput testing in blood of COVID-19 convalescent plasma donors and patients. *Transfusion*. 2021 Feb;61(2):368-374.

Hackstein H, Kalina A, Dorn B, Keil IS, Baal N, Michel G, Brendel C, Neubauer A, Jakob T, Bein G. CD11c+ dendritic cells mediate antigen-specific suppression in extracorporeal photopheresis. *Clin Exp Immunol*. 2021 Feb;203(2):329-339.

Kausche LE, Adler W, Zimmermann R, Hackstein H, Strasser EF. Thrombin Generation in Fresh and Frozen-Thawed Platelet Poor Plasma - Is there a Difference? *Clin Lab*. 2020 Jun 1;66(6).

Cunningham S, Buchele V, Brox R, Strasser E, Hackstein H. Thrombocyte apheresis cassettes as a novel source of viable peripheral blood mononuclear cells. *Transfusion*. 2020 Jul;60(7):1500-1507.

Schwab L, Michel G, Bein G, Hackstein H. CD71 surface analysis of T cells: a simple alternative for extracorporeal photopheresis quality control. *Vox Sang*. 2020 Jan;115(1):81-93.