



Thomas Wekerle, MD

Department of Surgery
Division of Transplantation
Währinger Gürtel 18-20
A-1090 Vienna, Austria
phone: + 431 40400 5621
fax: + 431 40400 6872
Email: thomas.wekerle@meduniwien.ac.at
Web: www.meduniwien.ac.at/transplant-lab

Research interests

Our group focuses on translational research in the area of two common immunological conditions: organ transplantation and allergy. We are interested in the development of experimental tolerance regimens with relevance for these two indications and the in-depth mechanistic analysis of such models. In particular, we pursue the concept of chimerism induction through the transplantation of hematopoietic stem cells which leads to robust, lasting tolerance towards antigens expressed on the transplanted cells. Protocols of allogeneic *mixed (cellular) chimerism* generated through the transplantation of donor bone marrow for the induction of donor-specific tolerance in transplantation, and protocols of *molecular chimerism* generated through the transplantation of syngeneic hematopoietic stem cells that have been retrovirally transduced *ex vivo* with a disease-causing antigen are being investigated.

Thesis projects

The two thesis projects will build on our current understanding of established murine models for tolerance induction in transplantation and type I allergy.

Pertinent questions to be addressed include:

1. What are the requirements for murine protocols inducing mixed chimerism and transplantation tolerance under stringent immunological conditions?
2. How can allergen-specific tolerance be induced through transplantation of hematopoietic cells retrovirally transduced with an allergen, and which mechanisms contribute to tolerance induction in such models?

Ph.D. students performing the proposed thesis projects will employ relevant *in vivo* models combined with state-of-the-art *in vitro* methodology of cellular and molecular immunology to develop and investigate new tolerance protocols. Students will be part of an established group with extensive experience in the relevant models and methods, and will benefit from active national and international collaborations with recognized leaders of their respective fields.

Selected publications

Wekerle, T., Kurtz, J., Ito, H., Ronquillo, J. V., Dong, V., Zhao, G., Shaffer, J., Sayegh, M. H., and Sykes, M. Allogeneic bone marrow transplantation with co-stimulatory blockade induces macrochimerism and tolerance without cytoreductive host treatment. *Nature Med* 6:464-9 (2000).

Blaha, P., Bigenzahn, S., Koporc, Z., Schmid, M., Langer, F., Selzer, E., Bergmeister, H., Wrba, F., Kurtz, J., Kiss, C., Roth, E., Muehlbacher, F., Sykes, M., and **Wekerle, T.** The

influence of immunosuppressive drugs on tolerance induction through bone marrow transplantation with costimulation blockade. *Blood* 101:2886-93 (2003).

Bigenzahn, S., Blaha, P., Koporc, Z., Pree, I., Selzer, E., Bergmeister, H., Wrba, F., Heusser, C., Wagner, K., Muehlbacher, F., and **Wekerle, T.** The role of non-deletional tolerance mechanisms in a murine model of mixed chimerism with costimulation blockade. *Am J Transplant* 5:1237-47 (2005).

Linhart, B., Bigenzahn, S., Hartl, A., Lupinek, C., Thalhamer, J., Valenta, R., and **Wekerle, T.** Costimulation blockade inhibits allergic sensitization but does not affect established allergy in a murine model of grass pollen allergy. *J Immunol*: 178: 3924–3931. (2007).