Tania Simon
Dr. sc. hum.

**Quantification of Gene Expression in Renal Allograft Recipients Using Real-Time PCR**

Geboren am 03.09.1975 in Sault Ste. Marie, Kanada
Hochschulabschluss der Fachrichtung Mikrobiologie & Immunologie am 10.06.1999 an der Universität Western Ontario (Kanada)

Promotionsfach: Immunologie
Doktorvater: Priv.-Doz. Dr. med. C. Süsal

Real-Time PCR offers advantages over traditional techniques used for gene expression measurement by increasing accuracy and allowing the testing of more genes and samples. This state-of-the-art technique combined with study adaptations, such as pre-processing stabilization of samples and a DNase treatment and PCR inhibitor removal wash during RNA isolation, has resulted in the creation of an assay system that provides high-quality RNA and reproducible data. The application of this assay to post-transplantation monitoring has allowed us to present a comprehensive picture of the molecular events associated with immunosuppressive induction therapy, the early post-transplantation period in rejecting and non-rejecting clinical groups, and the effect of anti-rejection therapy on gene expression.

In patients treated with the immunosuppressant ATG, we made observations such as decreases in IFN-γ and the CTL genes perforin and granzyme B as well as increases in IL-10. Considering the traditional immunosuppressive role of IL-10 and the importance of CTL in acute rejection this may be considered beneficial to patients. Increases in the expression of the TGF-β gene were also evident and could be interpreted as beneficial in terms of immunosuppressive activity or harmful in terms of recurrent focal segmental glomerulosclerosis disease and a possible link to chronic rejection. Furthermore, increases in expression of the cytokine genes IL-7, IL-15, and TNF-α were also observed, which may be involved in immunological events not effected by ATG that may harm the transplant in the long-term.

The use of potent ATG-induction therapy and also steroid pulse therapy for the treatment of rejection was accompanied by decreases in the expression of the CTL genes perforin and granzyme B, providing a correspondence between clinical treatment and measurements of CTL gene expression. More importantly, the finding that increased expression of the CTL genes perforin and granzyme B acts as a predictor of acute rejection in its earliest stages allowed potential rejection episodes to be detected in this study up to 30 days prior to rejection diagnosis using traditional means. Gene expression measurements during the first month post-transplantation may allow for earlier intervention by the physician in terms of indication for biopsy or prophylactic increase in immunosuppression dosage.