

PHARMACOGENOMICS AND TRANSPLANTATION: THE ROAD TOWARD PERSONALIZED THERAPY

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Despite the significant advances of surgical techniques, tissue typing and patient care, most of the progress in organ transplantation is largely attributed to the recognized importance of immunosuppressive therapy. The immunosuppressive drugs improves graft outcomes by reduction of rejections and induction of tolerance. Although therapeutic drug monitoring is performed it is still difficult to predict the individual patient's response to pharmacological immunosuppression. Therefore, additional biomarkers continue to be explored in order to personalize the immunosuppressive therapy. Genetic factors are considered responsible for a part of the pharmacokinetic variability. Immunosuppressive drugs have a narrow therapeutic range and a large inter- and intra-individual response variability, which has prompted pharmacogenetic investigations, mostly regarding their dose-concentration relationships, but also about proteins involved in their pharmacodynamics.

An overview of the literature data on immunosuppressant pharmacogenetics in organ transplantation will be made. We will also present our results on polymorphism in genes associated with the drug metabolism of calcineurin inhibitors - cyclosporine and tacrolimus, in kidney transplant patients. The feasibility of testing for pharmacogenetic variants with functional effects as an important component in post-transplant monitoring to achieve optimal and personalized immunosuppression will be also discussed.

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