

A close-up photograph of a petri dish containing a bacterial culture on a light-colored agar surface. The culture shows numerous small, yellowish-brown colonies scattered across the surface. The petri dish is held at an angle, and the background is slightly blurred. The text 'IMMUNOSUPPRESSION USING TRANSGENIC EXPRESSION OF IMMUNOMODULATORY MOLECULES' is overlaid on the bottom half of the image.

IMMUNOSUPPRESSION USING TRANSGENIC EXPRESSION OF IMMUNOMODULATORY MOLECULES

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Transplantation is now used as a method of choice for the treatment of many diseases due to the advance in surgical and immunosuppressive techniques. However, with a crucial shortage of human donor organs largely due to the reduction of deaths from car accidents, today, only about a quarter of patients receive the transplant they require. Xenotransplantation, the transplantation of organs from one species to another, is now seen as a viable solution to the world wide problem of lack of supply of suitable human organs for patients requiring transplantation. Standard

immunosuppression may not be effective at preventing cell mediated xenograft rejection, nor is it desirable for patients to receive long-term heavy immunosuppression. A better approach is to express transgenes in the donor pig with the ability to modulate the cellular response to xenografts, thus eliminating or reducing the amount of immunosuppression required. This project will use transgenic strategies to reduce cellular xenogeneic responses by expression of molecules, such as CtlA-4Ig, CD40Llg and PD1L-Ig, that can inhibit co-stimulation.

Techniques:

- Molecular Biology
- Cell culture
- Animal models
- Proliferation assays
- Immunostaining
- Western-blots
- FACS analysis
- RT-PCR

Projects

1. Modulation of the cellular response to xenografts by the expression of immunomodulatory molecules

Publications:

Mulley WR, Wee JL, Christiansen D, Milland J, Ierino FL, Sandrin MS. Lentiviral expression of CTLA4Ig inhibits primed xenogeneic lymphocyte proliferation and cytokine responses. *Xenotransplantation*; 13: 248–252, 2006.

Mulley WR, Li YQ, Wee JL, Dodge N, Christiansen D, Simeonovic C, Ierino FL, Sandrin MS. Local expression of IDO, either alone or in combination with CD40Ig, IL10 or CTLA4Ig, inhibits indirect xenorejection responses. *Xenotransplantation*;15(3):174-83, 2008.

Wee JL, Christiansen D, Li YQ, Boyle W, Sandrin MS. Suppression of cytotoxic and proliferative xenogeneic T cell responses by transgenic expression of Indoleamine 2,3-dioxygenase (IDO). *Immunology and Cell Biology*; 86:460-5, 2008.