Ian Frazer

Research Director of the Translational Research Institute, Brisbane and Research Group Head, The University of Queensland Diamantina Institute

2008 Balzan Prize for Preventive Medicine, including Vaccination
For his outstanding scientific achievement and lasting contribution to preventive medicine through his role in the development of a vaccine that promises to prevent virus-induced carcinoma of the cervix, which claims 250,000 lives every year.

Institution Administering Funds: Diamantina Institute, University of Queensland

Adviser for the Balzan General Prize Committee: Werner Stauffacher

Immune Regulation and Therapeutic Immunisation

Ian Frazer is using the funds available from his 2008 Balzan Prize to support two fellowships. The two fellows are based with Frazer's group at the University of Queensland in Brisbane, and are working on individual projects in the frame of Professor Frazer's program aimed at the development of a "therapeutic vaccine" against HPV-induced cervical cancer. They have been given the opportunity to visit other labs in Australia and internationally as part of their research projects.

Dr. Antje Blumenthal
Dr. Blumenthal has extensive experience in studying the role of the innate immune system in chronic infections. She investigates how pathogens are recognised by the immune system, how appropriate inflammatory responses are initiated and regulated, and how this instructs T cell responses that are critical to control chronic infections. Together with Professor Frazer she directs research that aims to understand mechanisms of immune suppression and cancer development in the skin and cervix. The fellowship also supports the establishment of her own research program that includes investigations into how a novel class of immune molecules, the family of Wnt proteins, shapes innate immune responses and regulates T cell functions. Her work addresses an important knowledge gap regarding the functions of Wnt proteins as novel regulators of the nature and strength of immune responses. These highly innovative research fields

are likely to pioneer new concepts of mechanisms of immune regulation and hold the potential for the identification of novel therapeutic targets.

Supported by the fellowship, Dr. Blumenthal is establishing an independent research group and is currently supervising four Ph.D. students, a Research Assistant and undergraduate students. Since her relocation to Australia, she has already attracted more than $220.000 of additional research support. Dr. Blumenthal has established strong collaborative ties within Professor Frazer's group, the UQ Diamantina Institute and within the University of Queensland. Her growing reputation in immune responses to infection is further evidenced by her strong network of international and national collaborators, invitations to speak internationally and nationally at conferences and institute seminars, peer-review invitations for international journals, and the extent to which her publications have been cited.

Dr. Steven Mattarollo

Dr. Mattarollo has experience in the cellular mediators of innate immunity in cancer. He has been funded for 2 years to work in Melbourne, Australia with Professor Mark Smyth, an acknowledged world expert on the role of NKT cells in control of cancer cell growth. During the first two years as a Balzan Fellow he has pursued two main lines of research:

- Development of a therapeutic cancer vaccine against melanoma and non-hodgkins B cell lymphoma that induces innate and adaptive immunity by targeting the immune adjuvant properties of NKT cells.
- Determining the immune constituents that are important for the therapeutic effectiveness of chemotherapies, and assessing combination chemo-immunotherapy strategies for treating solid tumours.

In May 2012 he returned to Brisbane to continue this research within Professor Frazer's group.

Lectures/Presentations:

Antje Blumenthal:

2012 TLROz, Melbourne, Australia – Invited Speaker
2012 University of Melbourne, Institute Seminar Speaker
2012 2nd Lorne Infection and Immunity Conference, Victoria, Australia – Selected Speaker
2011 ComBIO, Cairns, Australia – Invited Speaker
2011 1st Lorne Infection and Immunity Conference, Victoria, Australia – Selected Speaker

2011 Ludwig Institute, Melbourne, Institute Seminar Speaker
2011 14th Australian Autoimmunity Workshop – Session Chair
2011 Australasian Society for Immunology Annual Meeting – poster presentations (4)
2010 Australasian Society for Immunology Annual Meeting – Selected Speaker (speaker award)
2010 Institute for Molecular Bioscience, University of Queensland, Institute Seminar Speaker
2010 Brisbane Immunology Group Annual Conference – Invited Speaker

Researchers:
Antje Blumenthal
Steven Mattarollo

Publications:
Journal Articles Arising from the research
- Paget C., Chow M.T., Duret H., Mattarollo S.R., Smyth M.J. *Role of γδ T Cells in α-Galactosylceramide-Mediated Immunity*. J. Immunol. March 12 (2012).
- Rahimpour A., Mattarollo S.R., Yong M., Leggatt G.R., Steptoe R.J. and Frazer I.H. *γδ T Cells Augment Rejection of Skin Grafts by Enhancing Cross-Priming of CD8 T Cells to Skin-Derived Antigen*. J. Invest Dermatol. Feb. 23 doi: 10.1038/jid.2012.16 (2012).
- Nicol A.J., Tokuyama H., Mattarollo S.R., Hagi T., Suzuki K., Yokokawa K. and Nieda M. *Clinical evaluation of autologous gamma/delta T cell-based immunotherapy for metastatic solid tumors*. Brit J. Cancer Sep. 6; 105(6): 778-86. (2011).
- Mattarollo S.R., Yong M., Gosmann C., Choyce A., Chan D., Leggatt G.R., Frazer I.H. *NKT cells inhibit antigen-specific effector CD8 T cell induction to skin viral proteins*. J. Immunol. Jul. 8; 187(4):1601-1608 (2011).
- Mattarollo S.R., Loi S., Duret H., Ma Y., Zitvogel L., Smyth M.J. *Pivotal role of innate and adaptive immunity in anthracycline chemotherapy of established tumors*. Cancer Res. Jul. 15;71(14):4809-4820 (2011).
- Ma Y., Aymeric L., Locher C., Mattarollo S.R., Delahaye N.F., Pereira P., Boucontet L., Apetoh L., Ghiringhelli F., Casares N., Lasarte J.J., Matsuzaki G., Ikuta K., Ryffel B., Benlagha K., Tesnière A., Ibrahim N., Déchanet-Merville J., Chaput N., Smyth M.J., Kroemer G. and Zitvogel L. *Contribution of IL-17-producing gamma/delta T cells to the efficacy of anticancer chemotherapy*. J. Exp Med. Mar 14;208(3):491-503 (2011).
- Mattarollo S.R., Yong M., Tan L., Frazer I.H. and Leggatt G.R. *Secretion of IFN-gamma but not IL-17 by CD1d-restricted NKT cells enhances rejection of skin*

grafts expressing epithelial cell-derived antigen. J. Immunol. 184(10):5663-9 (2010).
- Mattarollo S.R., Rahimpour A., Choyce A., Godfrey D.I., Leggatt G.R. and Frazer I.H. *Invariant NKT cells in hyperplastic skin induce a local immune suppressive environment by IFN-gamma production*. J. Immunol. 184(3):1242-50 (2010).

Review Articles, Commentaries and Letters to the Editor
- Mattarollo S.R. and Frazer I.H. *Response to Comment on "Invariant NKT cells in hyperplastic skin induced a local immune suppressive environment by IFN-γ production"*. Letter to the Editor, J. Immunol. Feb. 1;188(3):931-2 (2012).
- Mattarollo S.R. and Smyth M.J. *Therapeutic Approaches Utilising NKT Cells*. *Book Chapter in Natural Killer T Cells: Setting the Balance in the Regulation of Tumor Immunity. Cancer Drug Discovery and Development*. Editors: Terabe M and Berzofsky J. Publisher: Springer New York. pp. 111-128. DOI: 10.1007/978-1-4614-0613-6_7 (2012).
- Frazer I.H., Leggatt G.R. and Mattarollo S.R**.** *Prevention and treatment of papillomavirus related cancers through immunization*. Annu. Rev. Immunol. Apr 23;29:111-38. (2011).
- Bhat P., Mattarollo S.R., Gosmann C., Frazer I.H. and Leggatt G.R. *Regulation of immune responses to HPV infection and during HPV directed immunotherapy*. Immunol. Rev. 239(1):85-98 (2011).
- Mattarollo S.R. and Smyth M.J. *A novel axis of innate immunity in cancer*. Nature Immunol. 11(11):981-921 (2010).