

## Ian Frazer

**Research Director of the Translational Research Institute, Brisbane; 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 used the funds available from his 2008 Balzan Prize to support two fellowships. The two fellows were based with Frazer's group at the University of Queensland in Brisbane, and worked 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 were 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 investigated how pathogens are recognized by the immune system, how appropriate inflammatory responses are initiated and regulated, and how this instructs adaptive immune responses that are critical to control chronic infections. Together with Professor Frazer, she directed research that aimed to understand mechanisms of immune suppression and cancer development in the skin and cervix. The fellowship also supported the establishment of Dr Blumenthal's independent research program on regulatory mechanisms that control inflammation and pathogen control during infection. Her work addressed important knowledge gaps on endogenous regulators of the nature and strength of immune responses. This is likely to pioneer new concepts of mechanisms of immune regulation with the potential for the identification of novel therapeutic targets.

Supported by the fellowship, Dr. Blumenthal established a dynamic research group and attracted independent research funding from major national and local sources. She established and maintained strong collaborative ties within the UQ Diamantina Institute and the University of Queensland, as well as at a national and international level. Furthermore, the fellowship has accelerated the maturation of Dr Blumenthal's national and international profile through presentations at conferences and institute seminars, contributions to conference organization, research leadership within the Institute and University as well as peer-review for international journals and the main national funding agency for biomedical research.

#### **Dr. Steven Mattarollo**

Dr. Mattarollo has experience in the cellular mediators of innate immunity in cancer. He was 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 these two years as a Balzan Fellow he 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, where he established an independent group consisting of 6 personnel, focusing on immune-based therapies for blood cancers. He was awarded 3 years' NHMRC project funding commencing in 2013 to continue this research. In January, 2013 he attended the Cancer Immunology and Immunotherapy Keystone Meeting in Vancouver, Canada, where he was selected to present his recent findings in developing a therapeutic vaccine against B cell lymphomas.

#### **Publications:**

##### **Journal Articles Arising from the Research**

Skalamera D, Dahmer M, Purdon AS, Wilson BM, Ranall MV, Blumenthal A, Gabrielli B, Gonda TJ. 2012. Generation of a Genome Scale Lentiviral Vector Library for EF1a Promoter-Driven Expression of Human ORFs and Identification of Human Genes Affecting Viral Titer. PLoS ONE 7(12): e51733.

- Blumenthal A, Nagalingam G, Huch JH, Walker L, Guillemin GJ, Smythe GA, Ehrst S, Britton WJ, Saunders BM. 2012. Mycobacterium tuberculosis induces potent activation of IDO-1, but this is not essential for the immunological control of infection. *PLoS ONE* 7(5): e37314.
- Paget C, Chow MT, Duret H, Mattarollo SR, Smyth MJ. 2012. Role of  $\gamma\delta$  T Cells in  $\alpha$ -Galactosylceramide-Mediated Immunity. *J. Immunol.* March 12 (2012).
- Rahimpour A, Mattarollo SR, Yong M, Leggatt GR, Steptoe RJ, Frazer IH. 2012.  $\gamma\delta$  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.
- Nicol AJ, Tokuyama H, Mattarollo SR, Hagi T, Suzuki K, Yokokawa K, Nieda M. 2011. Clinical evaluation of autologous gamma/delta T cell-based immunotherapy for metastatic solid tumors. *Brit J. Cancer* Sep. 6; 105(6): 778-86.
- Mattarollo SR, Yong M, Gosmann C, Choyce A, Chan D, Leggatt GR, Frazer IH. 2011. NKT cells inhibit antigen-specific effector CD8 T cell induction to skin viral proteins. *J. Immunol.* Jul. 8; 187(4):1601-1608.
- Mattarollo SR, Loi S, Duret H, Ma Y, Zitvogel L, Smyth MJ. 2011. Pivotal role of innate and adaptive immunity in anthracycline chemotherapy of established tumors. *Cancer Res.* Jul. 15;71(14): 4809-4820.
- Ma Y, Aymeric L, Locher C, Mattarollo SR, Delahaye NF, Pereira P, Boucontet L, Apetoh L, Ghiringhelli F, Casares N, Lasarte JJ, Matsuzaki G, Ikuta K, Ryffel B, Benlagha K, Tesnière A, Ibrahim N, Déchanet-Merville J, Chaput N, Smyth MJ, Kroemer G, Zitvogel L. 2011. Contribution of IL-17-producing gamma/delta T cells to the efficacy of anticancer chemotherapy. *J. Exp Med.* Mar 14;208(3): 491-503.
- Mattarollo SR, Yong M, Tan L, Frazer IH, Leggatt GR. 2010. 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.
- Mattarollo SR, Rahimpour A, Choyce A, Godfrey DI, Leggatt GR, Frazer IH. 2010. Invariant NKT cells in hyperplastic skin induce a local immune suppressive environment by IFN-gamma production. *J. Immunol.* 184(3):1242-50.
- Ma Y, Adjemian S, Mattarollo S.R, Yamazaki T, Aymeric L, et al. 2013 – in press. Intratumoral antigen presentation in chemotherapy-induced anticancer immune responses.
- Choyce A, Yong M, Narayan S, Mattarollo SR, Liem A, Lambert PF, Frazer IH, Leggatt GR. 2013. Expression of a single, viral oncoprotein in skin epithelium is sufficient to recruit lymphocytes. *PLoS One.* 8(2):e57798. Epub 2013 Feb 26.

- Mattarollo SR, Smyth MJ. 2013. NKT cell adjuvants in therapeutic vaccines against hematological cancers. *Oncoimmunology* (2013). Jan 1; 2(1). e22615.
- Mattarollo SR, Steegh K, Li M, Duret H, Ngiow SF, Smyth MJ. 2013. Transient Foxp3+ regulatory T cell depletion enhances therapeutic anti-cancer vaccination targeting the immune-stimulatory properties of NKT cells. *Immunol Cell Biol* (2013) Jan; 91(1): 105-14.
- Mattarollo SR, West A, Steegh K, Duret H, Paget C, Martin B, Matthews G, Shortt J, Chesi M, Leif Bergsagel P, Bots M, Zuber J, Lowe S, Johnstone R, Smyth MJ. 2012. NKT cell adjuvant-based tumor vaccine for treatment of myc oncogene-driven B cell lymphoma. *Blood* (2012) Oct 11; 120(15): 3019-3029.

#### **Review Articles, Commentaries and Letters to the Editor**

- Mattarollo SR, Frazer IH. 2012. Response to Comment on “Invariant NKT cells in hyperplastic skin induced a local immune suppressive environment by IFN- $\gamma$  production”. Letter to the Editor, *J. Immunol.* Feb. 1;188(3):931-2 (2012).
- Mattarollo SR, Smyth MJ. 2012. Therapeutic Approaches Utilising NKT Cells. Book Chapter in Terabe M, Berzofsky J, editors. *Natural Killer T Cells: Setting the Balance in the Regulation of Tumor Immunity*. Cancer Drug Discovery and Development, 111-128. New York: Springer. DOI: 10.1007/978-1-46140613-6\_7 (2012).
- Frazer IH, Leggatt GR, Mattarollo SR. 2011. Prevention and treatment of papillomavirus related cancers through immunization. *Annu. Rev. Immunol.* Apr 23;29:111-38.
- Bhat P, Mattarollo SR, Gosmann C, Frazer IH, Leggatt GR. 2011. Regulation of immune responses to HPV infection and during HPV directed immunotherapy. *Immunol. Rev.* 239(1):85-98.
- Mattarollo SR, Smyth MJ. 2010. A novel axis of innate immunity in cancer. *Nature Immunol.* 11(11):981-921.