MONASH University | ARMI AUSTRALIAN REGENERATIVE MEDICINE INSTITUTE

Lieschke Group

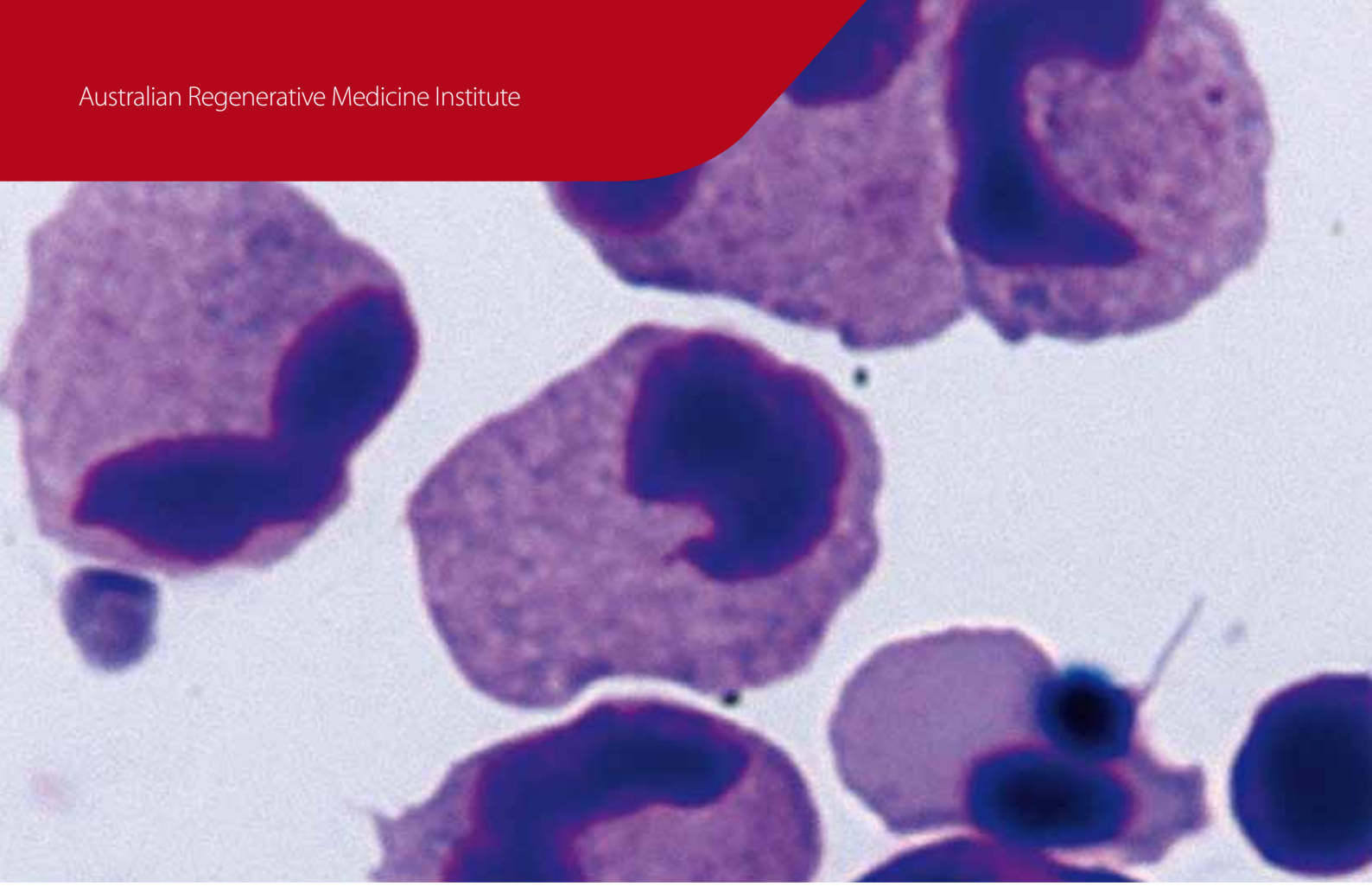
The haemopoietic system makes blood cells and is the archetypal regenerative tissue, constantly supplying blood cells throughout life. It is capable of large bursts of replenishment following injuries such as chemotherapy. White blood cells (leukocytes) are a key cellular player in host defense and as effectors of inflammation. Their function plays a major role in determining the balance between ongoing tissue injury, scarring, healing and regeneration.

The Lieschke group uses zebrafish as the model organism for studying blood development and function. The team was one of the first groups in the world to take advantage of the genetic flexibility and live imaging capacity of zebrafish for white blood cell research. Mutants with faulty blood cell development provide handles on genes regulating the haemopoietic system. Several mutants have proven useful for studying the role of particular leukocytes in inflammation and healing. The Group has also developed an infection model to investigate the role of leukocytes in the host-pathogen response.

Prof Graham Lieschke
Professor Lieschke is internationally recognised for his research into blood disorders and cancer using zebrafish and mice. He is also a clinical haematologist at the Royal Melbourne Hospital, where he treats people with leukaemia and lymphoma.

He established his zebrafish-based research program at the Ludwig Institute for Cancer Research, and continued this as a Laboratory Head in the Cancer and Haematology Division of the Walter and Eliza Hall Institute.

His awards include: the John Maynard Hedstrom Research Fellowship of the Cancer Council of Victoria, a Howard Hughes Postdoctoral Research Fellowship for Physicians, a Wellcome Trust Senior Research Fellowship, an NHMRC Senior Research Fellowship, and the inaugural Ludwig Institute George Hodgson Medal for Medical Science.



Research Projects

The focus of the Lieschke Group is on the development and function of white blood cells (leukocytes). There are two major types of white blood cells: granulocytes (neutrophils) and macrophages. They are important in host defence, are the cellular effectors of inflammation, and are the cell type that grows without control in leukaemia.

Development of white blood cells

To discover new genes critical for white blood cell development we have conducted a forward genetic screen of chemically-mutated zebrafish with defects in blood cell development. We are characterising these mutants and cloning the mutated genes underpinning the phenotypes. These mutants point to new critical steps in the genetic and biochemical regulation of blood cell development in health and disease.

MicroRNAs in blood cell development

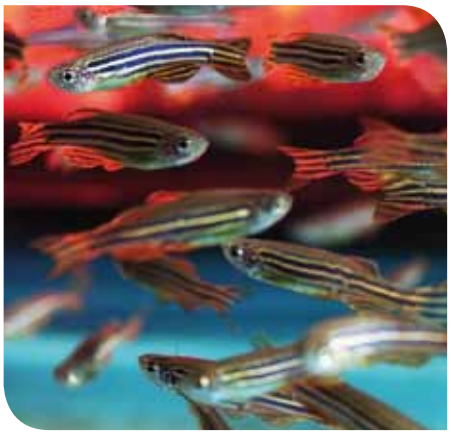
One of our mutants had a surprisingly specific defect in expression of a pair of microRNAs important for red blood cell maturation (miR-144/451). We are studying the role of these microRNAs in regulating blood cell-specific genes during their development. We have cloned the defective gene in this mutant and are trying to understand what this is telling us about microRNA biogenesis.

Inflammation

How is the inflammatory response is regulated? While inflammation is important to protect the body in the face of tissue damage, turning inflammation off is important to minimise unnecessary damage. We are aiming to discover new pathways that initiate and turn off the contribution of white blood cells to inflammation. These studies take advantage of the ability to image inflammation in transparent zebrafish embryos, using transgenic strains with fluorescent white blood cells. They involve sophisticated microscopy and quantitative image analysis.

Infection

An important function of white blood cells is host defence—keeping out and containing invading micro-organisms. To study this role of white blood cells, we have established a zebrafish model of infection with Penicillium marneffei, an opportunistic human pathogen. To facilitate these studies, we have made several transgenic lines that enable



macrophages, one particular type of white blood cell, to be seen and manipulated.

Regeneration

When a tissue is injured, the outcome of healing can be either scarring or regeneration. White blood cells and the inflammatory response are important determinants of the balanced outcome. We plan to extend our work in inflammation to ask how modulating the inflammatory white blood cells might tip the outcome to favour regeneration rather than scarring.

For further information, contact graham.lieschke@monash.edu

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