



McGlinn Group

The McGlinn Group uses the developing limb bud and axial skeleton to understand genetic hierarchies governing patterning mechanisms.

The reiterative use of key signaling pathways across multiple organs has meant that the limb, with its advantages of ease of manipulation and lack of requirement for embryonic survival, has provided fundamental contributions to our understanding of broader developmental processes.

More recently, it has become clear that a comprehensive understanding of these processes requires integration of all levels of gene regulation, including both protein-coding and non-protein coding mechanisms.

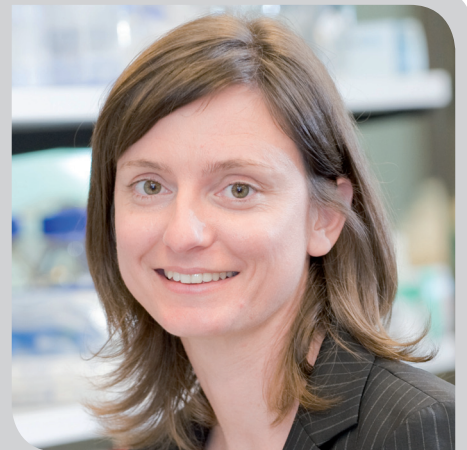
For this reason, we have pioneered a novel approach to investigate the role of microRNAs in development.

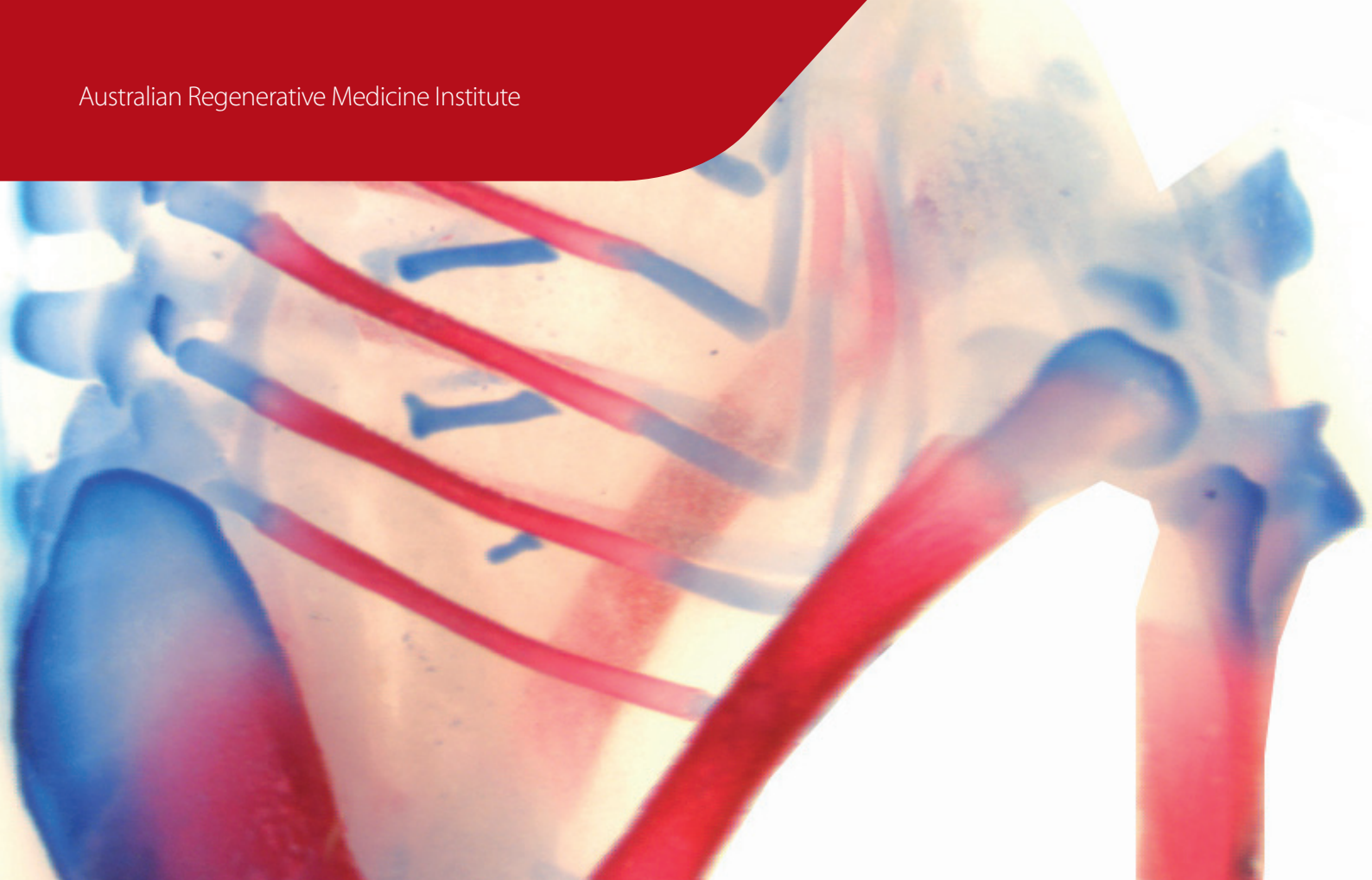
We aim to build a more complete molecular road-map of how the size, shape and number of bones form within the early vertebrate embryo.

Dr Edwina McGlinn

Dr McGlinn is a highly talented young scientist in the area of developmental biology, focusing on formation of the vertebrate skeleton. Her research has contributed significantly to our understanding of how growth and patterning of the limb is coordinated during development and has pioneered novel technologies to address the role of microRNAs during these developmental processes.

Before joining ARMI as the first EMBL Australia Partner Laboratory Network Group Leader, Edwina held the position of Research Fellow in the Department of Genetics at Harvard Medical School.





Research Themes

The molecular basis of proximal-distal positional information in the vertebrate limb bud

Exactly how cells within the upper arm know to form one skeletal element, while cells in the hand form multiple is currently unknown. Accumulating evidence suggests that cells within the very early limb bud already know which skeletal element they will contribute to, however the molecular basis of this early fate specification is unclear.

To address this question, we plan to utilise the strength of the mouse system to genetically label precursor cells of the three limb segments (upper arm, mid arm and hand) with different fluorescent reporters. This will allow us access to these cells throughout development and to molecularly profile them as their identity is being specified.

High throughput screen for miRNAs relevant to limb and axial patterning

For the majority of miRNAs currently annotated, little or no functional information exists creating a major road-block in the field. Our recent success in developing an antagomiR-

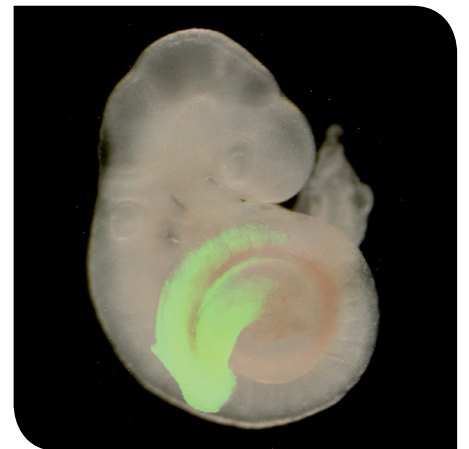
based knockdown strategy in chick now opens the way to perform a high throughput screen to identify additional developmentally relevant miRNAs.

We will generate an updated miRNA expression profile at key time points in development using microarray or deep sequencing based approaches. Functional analysis will include both retroviral based over-expression and antagomiR knockdown in chick. In mouse, we have pioneered an in utero ultrasound guided injection strategy to knockdown miRNA function in the developing embryo.

Full characterisation of miR-196 knockout phenotypes

The miR-196 family of miRNAs exhibits striking developmental expression and its members are predicted to control the expression levels of up to 10 different Hox genes. We have generated knockout mice for the miR-196 genes and a complete analysis of single, double and triple mouse mutant will be a significant focus of this lab.

The expected phenotypic analysis will involve both developmental studies as well as adult homeostasis and disease states.



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