MRC Mouse Network

Tissue Remodeling and Fibrosis Research Consortium (TeRiFiC consortium)

Consortium led by UCL
Programme Director: Dr Jill Norman

Generation of > 100 conventional and conditional knock-out mice in the next three years

Principal Aims and Objectives:

Fibrotic diseases are a leading cause of morbidity and mortality and are relatively intractable to current treatments. The response of any organ, to tissue damage involves a carefully choreographed series of cellular interactions between immune (haematopoietic) and non-immune stromal cells. Therefore understanding the effect of modifying the biology of leukocytes, endothelium or fibroblasts in terms of their effect on tissue fibrosis is a vital area of research. The aims of this consortium are to define the critical regulatory networks underlying the pathogenesis of organ/tissue-based fibrosis and tissue remodelling processes, delineate the cellular and molecular links between tissue injury, subsequent remodelling and the development of fibrosis, and to identify organ-selective and common anti-fibrotic targets. By combining are expertise we will utilise novel gene knockout mice to discover and develop novel therapies for the treatment of fibrotic diseases translating our findings into the clinical arena to enhance patient management and treatment.
Objectives:

- Utilise a panel of gene knock-out mice generated by IMPC to determine molecular mechanisms initiating spontaneous fibrotic pathology in a range of different tissues using histopathology
- For each gene knock-out mouse line utilise at least one in vivo model of fibrosis initiated by either tissue injury, infectious disease (viral, bacterial or parasitic), surgical manipulation, autoimmune disease, wound healing, cardiovascular and pulmonary inflammation or chemical administration to study the influence of gene deletion in different organs and tissues
- Utilise an integrated research approach combining systems biology approaches with primary human tissues, experimental mouse models and the gene knock-out mice to discover and define pathways underlying the pathogenesis of fibrosis and tissue remodelling
- Where appropriate apply cutting edge image analysis to understand cellular process involved in tissue fibrosis in gene knock-out mice
- To adopt conditional allele deletion to refine our understanding of leading candidate genes in fibrosis and tissue remodelling using tissue specific, temporal or cell specific Cre recombinase mice to micro-dissect the pathogenic process