The UCD Diabetes Complications Research Centre (DCRC) investigates the microvascular complications of diabetes. Our work focuses on identifying novel drivers of disease progression, regression and genetic susceptibility with a view to identifying and developing innovative therapeutic paradigms and biomarkers.

The DCRC comprises a multidisciplinary research group with expertise in molecular cell biology, genetics, bioinformatics, pharmacology, systems biology, chemical pathology and clinical medicine. Investigators at the UCD Conway Institute and the Mater Misericordiae University Hospital work closely with international collaborators in academia and industry. Research programmes are funded by national and international sources including Science Foundation Ireland (SFI), The European Union, Wellcome Trust, the National Institute of Health (NIH), the Juvenile Diabetes Research Foundation (JDRF), European Renal Association (ERA) and bio pharma industry.

Over the past decade we have applied differential gene expression technologies to identify novel genes expressed in vitro and in vivo models of diabetic nephropathy (DN) and, importantly, in human renal tissue. Current efforts focus on mining these datasets and probing the regulation of expression and actions of specific molecules. We have identified novel roles for molecules such as the BMP antagonist Gremlin, induced by high glucose-1, IHG-1, a protein that amplifies fibrotic responses in the context of DN and Connective Tissue Growth Factor, a growth factor which drives scarring in the kidney and other organs. As part of an international consortium with investigators at Harvard, Massachusetts Institute of Technology (MIT) and Queen’s University Belfast (QUB) we have used genome wide association studies to identify genetic polymorphisms linked to DN, which will help understand the genetic susceptibility to this devastating condition. We have explored the potential of the anti-inflammatory eicosanoid lipoxin to promote resolution and inhibit pathologic responses in models of disease. Thus, we have identified factors that may influence progression of DN and are potential targets for novel therapies including IHG-1, CTGF and Gremlin which exacerbate renal injury and protective lipid mediators such as lipoxins which are protective. These agents target distinct cell types and processes and may also implicated in the pathogenesis of diabetic retinopathy. We have further characterised these and related modulators in order to define the molecular mechanisms underlying DN. Our access to human samples including blood, urine and renal biopsy materials facilitates our efforts to identify those targets most relevant to human disease.

In 2012 noteworthy achievements for DCRC investigators included Prof le Roux’s highly prestigious President of Ireland Young Researcher Award, NIH funding for the Diabetes Complications Consortium, EU Marie Curie Outgoing fellowship award to Dr Emma Borgeson to UC San Diego. Investigators were invited to make presentations at several important international conferences including the Keystone Conference on Diabetic Complications (USA), the International Society for Nephrology Conference on Systems Biology of the Kidney (USA), and the International Society for Nephrology Conference on Tubulointerstitial Fibrosis (Australia).
early detection of renal disease and as therapeutic targets for treatment of kidney injury.

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My research team is primarily focused on understanding the underlying mechanisms regulating microvascular complications of diabetes as a result of longstanding hyperglycaemia. New concepts on therapeutic intervention have begun to take hold in particular the idea that populations of cells within the kidney have the capacity for self-renewal and that by exploiting these stem-cell-like properties researchers can aim for effective clinical regression. Evidence suggests that this process involves renewal of cells from a resident “stem cell-like” niche. We are using TGF receptor silencing RNAs and receptor targeting extracellular antagonists to manipulate epithelial cell fate and determining the mechanism through which resident cells can be reprogrammed to effect repair. We work closely with industry partners and clinical colleagues in the University hospitals in a programme that is significantly translational in its ambition, rescoring data from gene expression studies, animal models of disease and cell biology to inform the development of de novo therapeutics.

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My research focuses on differential gene expression in diabetic nephropathy with a view to identifying novel therapeutic targets and mediators of disease progression. Our most recent discoveries include novel fibrosuppressant biomolecules.

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I am a consultant nephrologist at the Mater Misericordiae University Hospital. My research interests include diabetic nephropathy, the biology of inflammation and fibrosis, and chronic kidney disease. I am a co-supervisor of both MD and PhD students. Our efforts form an important part of the critical link between the bedside and the bench, helping to further the goals of translational research and improving the care delivered to our patients.

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Title: The molecular mechanisms underlying the initiation progression and GWAS in Diabetic Nephropathy
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Amount: €378,208


