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# BRC Diabetes & Metabolism Theme

https://oxfordbrc.nihr.ac.uk/research-themes-overview/diabetes-and-metabolism/

The long-term primary strategic aims of the **Diabetes & Metabolism Theme's** research are **(i)** understanding, preserving and restoring normal pancreatic islet and liver function; **(ii)** identifying biochemical, genetic and genomic biomarkers for precision medicine; **(iii)** evaluating novel therapeutics and devices to restore islet and liver function and **(iv)** developing translational pipelines to rapidly assimilate this knowledge into integrated clinical care pathways. Four closely linked inter-disciplinary subthemes will achieve our aims using BRC-supported core infrastructure.

***Subtheme 1. Translational Physiology, Therapeutics and Medical Innovation***

Mechanistic and interventional studies will be performed in adults and children to characterise metabolic dysfunction related to impaired islet function (*Gloyn, Rorsman, McCarthy, Todd*), insulin resistance (*Karpe, McCarthy, Tomlinson, Gloyn*), non-alcoholic fatty liver disease (NAFLD) (*Hodson, Neubauer, Tomlinson*), and altered immunity (*Todd, Johnson, Besser, Owen*). The **Oxford BioResource** and the **OCDEM CRU** will provide the crucial BRC-supported infrastructure to enable in-depth physiological analysis of human subjects recruited on the basis of genotype and/or phenotype using sophisticated, system-specific approaches. These studies will typically provide the translational perspective for large separately-resourced, international, discovery projects and will benefit from collaborations with all 4 cross-cutting themes.

***Subtheme 2. Translational Islet and Metabolic Tissue Biology***

We will exploit our unique opportunities offered by integrating local access to human islets with world-leading expertise in islet biology (*Rorsman, Gloyn*) and genomics (*McCarthy, Gloyn, Todd*) to: define molecular mechanisms for islet dysfunction; repurpose small molecules to improve islet function, and compare genetic, genomic and electrophysiological signatures of human islet-cells with alternative sources for clinical islet-cell replacement. A major focus will be the development of pharmacological approaches to restore normal insulin and glucagon secretion (*Rorsman*). We will use *in vitro* liver cell models to identify mechanisms driving NAFLD progression and potential therapeutic targets (*Tomlinson, Hodson*).

***Subtheme 3. Pancreas and Islet-Cell Transplantation***

Oxford, with the world's most active clinical service (>800 patients over 12 years), has integrated programs in solid organ and islet pancreas transplantation and is uniquely placed to develop beta-cell replacement therapies. The subtheme also co-leads a national project to identify reliable clinical, histological, radiological, biochemical and proteomic markers that identify viable/non-viable organs: Two thirds of UK donor pancreases meeting national criteria are declined/discarded because of fears of post-operative pancreatitis or non-function. This will be supplemented with analyses and outcome data from the Oxford-based QUOD biobank *(Friend, Ploeg, Johnson, Gloyn).*

***Subtheme 4. Service Innovation and Evaluation***

This subtheme will evaluate the impact of novel service models in diabetes care. The work will include modelling and analysis of clinical outcomes, research into patient experience and self-management, economic evaluation and creation of an environment where research and innovation flourish within routine clinical pathways. The theme also manages the Patient Public Involvement meetings *(Owen, Rea, Tan, Lumb, Fitzpatrick, Sharpe)*.