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From bench to bedside: Conquering the translational gap by humanizing type 2 diabetes research

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Obesity and type 2 diabetes (T2D) have reached epidemic proportions worldwide and thus considerable research effort has been dedicated to developing strategies to understand and treat these complex diseases. The two hallmark features of T2D, insulin resistance and pancreatic dysfunction, have been studied extensively using various animal models. Despite the wealth of knowledge hitherto acquired from animal models, many details of human disease pathogenesis remain unknown and pharmacotherapeutic options for humans remain limited, with adverse effects associated with many widely used T2D drugs. From gene regulation to pancreatic cytoarchitecture to glucose sensing and transport to regulation of insulin secretion, emerging human data have raised concern regarding the immutable species differences and the subsequent limitations to translatability. This study addresses the challenges and opportunities in type 2 diabetes research and how it can be transformed with existing and novel future methodologies using human-based data acquisition. We discuss how state-of-the-art in vitro, *in vivo*, and in silico technologies can be utilized to delineate disease mechanisms and drug responses. Insulin resistance and pancreatic dysfunction can be studied at many levels from gene transcription/regulation to functional proteomics to cellular signalling and cell-cell interactions to organ cultures and whole-body glucose regulation to human population-based studies. T2D research is in dire need of a paradigm shift, with increased emphasis on human-based data acquisition and decreased reliance on animal models. With continued support from scientists and funding agencies alike, this is the clear-cut path to address the challenges in the translational barrier and creating opportunities for diabetes research and treatment.

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