SUPPLEMENTARY DATA

Supplementary Table S1. Consensus recommendations on research gaps to address precision medicine for diabetes

Research Gaps Related to Demographics
Establish drivers of increased risk for type 2 diabetes in individuals of low socioeconomic status.
Define factors associated with race/ethnicity and geography that differentially increase risk for type 1 diabetes and for type 2 diabetes.
Research Gaps Related to Genetics
Determine genetic influences that affect rate of progression of diabetes.
Define phenotypic subtypes of diabetes and investigate specific genetic associations.
Develop precision medicine and tests to predict response to—and side effects of—therapies.
Research Gaps Related to Environmental Influences
Define public health interventions that successfully reduce the levels of consumption of energy dense foods and/or reduce sedentary time and increase time spent in physical activity; determine whether these interventions reduce type 2 diabetes incidence at a population level.
Determine the role of gene-environment interactions.
Determine the role of the intestinal microbiota in pathogenesis of type 1 and type 2 diabetes and response to therapies.
Determine causal environmental etiologies of type 1 diabetes and their relative contribution to onset of autoimmunity and progression to symptomatic disease.
Research Gaps Related to β-Cell Mass and Function
Determine the role of β-cell dedifferentiation in type 1 diabetes and type 2 diabetes.
Ascertain the extent to which insulin resistance contributes to glycemia and the complications of type 1 diabetes.
Define the molecular basis for the glucose-specific insulin secretory defect in type 2 diabetes.
Determine the point at which β-cell dysfunction becomes irreversible.
Establish whether common etiologic factor(s) are the basis for abnormal insulin secretion patterns in type 1 diabetes and type 2 diabetes.
Develop biomarkers and imaging to assess β-cell mass and loss and functional mass and to monitor progression and responses to therapeutic interventions.
Determine mechanisms by which β-cells can overcome an insulin resistant environment.
Determine whether increased β-cell activity, stimulated by insulin resistance, enhances or accelerates the β-cell lesion.
Research Gaps Related to Autoimmunity and Inflammation
Determine whether different antigenic targets, single antibody positivity, or other contributing factors have different prognostic, genetic and environmental correlates that can be used to better develop and apply stage-appropriate personalized therapies
Develop inexpensive, specific and sensitive assays to identify β-cell autoimmunity on a population-wide level and beyond the confines of specialized laboratories.
Develop biomarkers and imaging to define reversion or stable autoimmunity versus active or flaring autoimmunity, and to monitor responses to therapeutic interventions.
Understand how β-cells die or fail in the presence of β-cell autoimmunity.
Define the role of inflammatory factors in the pathophysiology of type 1 and type 2 diabetes.
Research Gaps Related to Therapeutics
Determine appropriate immune therapies to be used in combination (sequentially or simultaneously) to target the β-cell specific immune response, islet inflammation, and more global defective immunoregulation.
Develop evidence-based targets to avoid cardiovascular complications in type 1 diabetes. Current treatment recommendations for management of cardiovascular risk factors predominantly come from data in type 2 diabetes, or in populations that did not discriminate between diabetes type.

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Develop combinations of immune and β-cell targeted therapies for type 1 diabetes.
Determine rationale for early combination of glucose lowering agents in type 2 diabetes.
Define the impact and durability of specific therapies on β-cell function and mass.
Determine whether weight loss medication and bariatric surgery should be used to support treatment goals in people with diabetes who are overweight and obese.
Perform studies in vulnerable populations, including the elderly and children.
Research Gaps Related to Complications
Delineate mechanisms of complications in type 1 diabetes and in type 2 diabetes and the differences between them to drive the development of new therapeutics
Identify better predictors of kidney disease progression.
Determine whether environmental exposures or genetics drive development of diabetic complications
Develop the evidence base for preventing and treating complications through randomized clinical trials to: • determine the clinical benefits of screening and early treatment to normalize glucose levels in people with presymptomatic diabetes; • examine effective glucose control in various populations with co-morbidities and complications and compare different strategies to achieve glucose control; • identify how complications of diabetes affect one another and treatment approaches to each; • determine whether fibrates modify the natural history of retinopathy, and, if so, what the mechanisms are; • determine appropriate lipid targets in type 1 and type 2 diabetes.