TrialNet Prioritization for Mechanistic Studies

TrialNet will review concept proposals for mechanistic studies according to the priorities defined below. Only those concept proposals identified as being of high priority and outstanding scientific interest will be pursued for access to stored samples.

Tier 1. Established biomarkers (i.e., biomarkers that have been validated in the sense that reproducibility data is known and correlation with defined outcomes is known) that inform the clinical trial from which the samples were collected.

a. Does the proposed assay identify subgroups that have a different outcome (e.g., rate of disease progression)?
b. Does the proposed assay identify whether the drug used in the primary study is having the biologic effect hypothesized (e.g., does an anti-inflammatory actually reduce levels of inflammation)?
c. Does the proposed assay provide insight as to a therapeutic effect that might be seen at different at different time points relative to drug dosing (e.g., can there be an early effect that wanes or a cumulative exposure effect)?
d. Can the proposed assay serve as a surrogate end point for future trials (e.g., can it be measured before the study end point and does it correlate with that end point)?

Tier 2. Established Biomarkers that identify different subpopulations based upon mechanism of disease progression.

a. If we hypothesize that type 1 diabetes is the result of multiple pathways resulting in insulin production sufficient to maintain glycemic control, then does the proposed assay elucidate these different pathways? Currently, TrialNet uses the number of autoantibodies and level of glycemic control as stages of disease development, but perhaps new assays could identify different stages or paths of disease development such as immunologic staging (e.g., immune cell sub-populations).
b. Since it is recognized that age impacts on disease risk, does the proposed assay shed light on differences in immunology that helps explain the age effect that appears to be pervasive across all stages of autoimmunity and extends past diagnosis.

Tier 3. Disease and therapeutic mechanism/pathway studies

a. Proposals seeking to examine hypotheses related to immune or metabolic disease pathways that could provide new insight into pathogenesis (e.g., mechanisms through which tolerance is lost; mechanisms of disease progression; mechanisms by which immune cells cooperate to initiate/drive disease) and therapeutic potential (e.g., new cytokine pathway amenable to blockade)
b. Proposals seeking to examine hypotheses related to mechanism of action of a given therapeutic in terms of immune or metabolic pathways that could provide new insight into mode of action, optimization, biomarker development (e.g., disturbance/depletion of immune cell sub-populations by a biologic)

Tier 4. Biomarker validation studies

a. Proposals seeking to validate assays against TrialNet clinical end points.

Tier 5. Assay development studies

a. Rationale for use of TrialNet subjects (through living biobank) or stored samples are needed.