Abstract:
Insulin autoantibodies (IAA) precede type 1 diabetes, but not all IAA-positive children develop other islet autoantibodies and disease. Diabetes risk can be stratified by laborious IAA affinity measurement using competition with multiple ligand concentrations. Here, we identify a single competitor concentration that discriminates low- and high-affinity IAA. Discrimination was achieved among 122 IAA-positive sera using 7.0 nM competitor which is 54-fold that of the assay radioligand concentration. Relative-binding = 1.0 × 10^(-5) L/mol and none with lower affinities (P<0.0001), and 45 (96%) of 47 multiple islet autoantibody-positive sera (P<0.0001). IAA competition was further tested in a second set of 119 IAA-positive sera. Of these, 99 fulfilled high-affinity competition criteria of < 60% relative-binding at 7.0 nM competitor including 89 (94%) of 95 sera with multiple islet autoantibodies (P<0.0001). Thus, increased IAA specificity can be achieved with simple modification to existing assays.