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A unified pathophysiological construct of diabetes and its complications, including cancer, based on the beta-cell classification of diabetes: Value of biomarkers in order to implement precision medicine in diabetes

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We have previously presented a proposal for a new, beta-cell centric classification of diabetes based on a consilience of genetic, metabolic, and clinical research that have accrued since the current classification was instituted . It recognizes that the beta-cell is THE core defect in all patients with diabetes. Differences in the genetics (and epigenetics), insulin resistance, environment and inflammation/immune characteristics resulting in the damage to the beta-cell in each individual will determine the phenotypic presentation of hyperglycemia and allow for a patient-centric, precision-medicine therapeutic approach , part of which we labeled 'the Egregious Eleven'. We now recognize the same pathophysiologic mechanisms that account for damage to the beta-cells govern the susceptibility of the cells involved in the complications of diabetes to damage by the now well-defined abnormal metabolic environment that typifies beta-cell dysfunction. This abnormal metabolic environment is typified by oxidative stress which alters metabolic pathways a la Brownlee's Hypothesis model, alterations in gene expression, epigenetics, and inflammation. This Unified Pathophysiologic Approach to The Complications of Diabetes in The Context of the B-cell–Classification of diabetes allows us to understand the varied risk of developing complications of diabetes, including malignancies, with similar levels of glycemic control, how non-glycemic effects of some medications for diabetes result in marked complication risk modification and the value treating co-morbidities of diabetes in modifying complication risk. Principles we outlined in using 'the Egregious Eleven' model- use agents that preserve beta-cell function, treat with least number of agents that treat most number of mechanisms of hyperglycemia- can be extended to use those agents, in combination, that also engender weight loss, and decrease CV outcomes. this approach allows for a more accurate assessment of each patient's disease and effecting true precision medicine. A MAJOR corollary of our construct is that 'bio-markers' of disease, for example, cardiovascular disease in patients with Diabetes, will allow us to determine those at undue risk, allow us to determine best therapies for each individual (patient-centric-precision medicine), and provide direction for future research.

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