Diabetic complications in genetic and epigenetic variations

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Description

The predominance of diabetes (DM) is continuously increasing universal at an alarming rate. According to the International Diabetes Federation in 2015, an estimated 415 million people globally were suffering from this condition. Difficulties of DM account for increased sickness, disability, and mortality and represent a threat for the economies of all countries, especially the developing ones. The present special issue has been devoted to the recent progress in our understanding of diabetic complications, including the underlying molecular mechanisms, new diagnostic tools that facilitate early diagnosis, and novel treatment options. It consists of 5 thematic areas: (a) epidemiology and pathogenesis of diabetic complications, (b) microvascular complications, (c) macrovascular complications, (d) miscellaneous complications, and (e) treatment options.

There is increasing evidence that the fundamental appliances in the pathogenesis of diabetic complications include certain genetic and epigenetic modifications, nutritional factors, and sedentary lifestyle. In a paper of this special issue entitled "Epigenetic Lessons Point to DNA Repetition/Repair Genes as a Basis for the Heritable Nature of Long Term Complications in Diabetes," A. A. Leontovich et al., using a zebrafish diabetic model, have explored the role of epigenetic mechanisms on the persistence of diabetic complications even after euglycemic control is achieved, a condition known as metabolic memory. They found that DNA-methylation, in or near genes going to the DNA replication/DNA metabolism process group, might play a key role in this process. Concerning basic risk factors for macro- and microvascular complications, the Irish Longitudinal Study on Ageing (TILDA), as M. L. Tracey et al. describe in their article "Risk Factors for Macro- and Microvascular Difficulties among Older Adults with Diagnosed Type 2 Diabetes: Discoveries from The Irish Longitudinal Study on Ageing," has recognized ageing, male gender, smoking, low level of physical activity, and high cholesterol as independent predictors of macrovascular complications. Conversely, smoking, hypertension, and duration of DM over 10 years proved to be predictive features for microvascular complications.

A large number of studies have focused on the factors involved in the pathogenesis of diabetic complications, most looking for actual therapies, but the exact cellular or molecular basis of these complications has not yet been fully elucidated. Hyperglycemia is still well-thought-out the principal source of diabetes complications. Its deleterious effects are attributable, among other things, to the formation of sugar-derived substances called advanced glycation end products (AGEs). AGEs form at a constant but slow rate in the normal body, starting in early embryonic expansion, and accumulate with time. However, their formation is markedly accelerated in diabetes because of the increased availability of glucose.

AGEs are a heterogeneous group of molecules shaped from the nonenzymatic reaction of reducing sugars with free amino groups of proteins, lipids, and nucleic acids. The original product of this reaction is called a Schiff base, which spontaneously rearranges itself into an Amadori product, as is the case of the well-known hemoglobin A1c (A1C). These initial reactions are reversible depending on the concentration of

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the reactants. A lowered glucose concentration will unhook the sugars from the amino groups to which they are attached; conversely, high glucose concentrations will have the opposite effect, if persistent. Sequences of subsequent reactions, including successions of dehydrations, oxidation-reduction reactions, and other preparations lead to the formation of AGEs. Numerous compounds, e.g., N-carboxymethyl-lysine, pentosidine, or methylglyoxal derivatives, assist as samples of well-characterized and widely studied AGEs.

The distinguishing organizational changes of diabetic nephropathy, solidified glomerular basement membrane and mesangial expansion, are accompanied by accumulation of AGEs, leading to glomerulosclerosis and interstitial fibrosis. Prolonged distillation of nondiabetic rats with AGEs has led to the development of similar morphological changes and significant proteinuria. Here again, AGE inhibitors such as aminoguanidine prevented diabetic nephropathy in diabetic animal models and were newly shown to do the same in one clinical trial on diabetic patients.