

Vitamin D receptor and type 2 diabetes mellitus: Growing therapeutic opportunities

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Type 2 diabetes mellitus (T2DM) is a complex, polygenic, and multi-factorial disease. Both genetic predisposition and environmental factors contribute in the development and pathogenesis of T2DM. Several reports in literature have already been shown that Vitamin D deficiency may persuade to glucose intolerance, tainted insulin secretion, and finally results T2DM, suggesting the role for vitamin D in the pathogenesis of T2DM.^[1] Expression and nuclear activation of the Vitamin D receptor (VDR) are necessary for the effects of vitamin D. Vitamin D plays an important role in insulin secretion. Pancreatic tissue (exclusively the insulin-producing beta-cells) expresses the VDR and allelic variations are involved in vitamin D metabolism and are associated with glucose intolerance and insulin sensitivity.^[2] Interestingly, T2DM patients also have a higher incidence of hypovitaminosis D.^[3] Till date, numerous genetic variations have been identified in the *VDR* gene and variations in this receptor have been linked to several diseases, including T2DM.^[4-9] Previously, we reported that the frequency and distribution of *VDR* gene variants is substantially different in diverse populations and ethnic groups.^[10] Genetic studies with respect to *VDR* gene will definitely offer exceptional opportunities to connect molecular insights with epidemiological data and

may reveal reticent and subtle but true biological effects. Collective evidences from few decades have indicated the association of many polymorphisms that exist in the *VDR* gene with T2DM including ours.^[9] But there is no concrete conclusion or insight from the available literature that we can use the VDR variants as diagnostic tools or as a marker in future in case of T2DM. This is a big question and still a matter of debate. Additional attempts have to be initiated for better understanding of the molecular and cellular variations exaggerated by *VDR* gene variants including multi cohort studies; in bigger populations, special attention should be paid to correlate the effects of all the risk factors for the better understanding of the role of *VDR* gene variants with T2DM risk. Furthermore, the study of the different haplotypes, instead of single variant study, could eliminate some of the discrepancy found so far. Also, there is a need of more randomized clinical trial to explore the effect of Vitamin D and/or calcium supplementation with conciliator endpoints (like glucose tolerance, insulin secretion, and insulin sensitivity) and eventually with the incident of T2DM. One more prospect for better understanding of the physiological role of the vitamin-D system in diabetes is not only the insulin secretion, but also insulin resistance, which needs to be further investigated. This will increase the attention in its budding function in prevention and management of T2DM.

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