Diabetes is steeply rising worldwide, and as India leads at the second position with around 70 million diabetic individuals, the condition is quite alarming for us. Unfortunately, the available treatment and/or interventional strategies are not sufficient to combat with the rising prevalence of the disease. Thus, early diagnosis and/or detection of the people at high risk of developing T2D and DR is strongly required. Available strategies for early diagnosis depend mainly on the identification of individuals harboring various environmental risk factors. However, from the review literature, it is evident that genetic factors enhance the risk of T2D and DR by interacting synergistically with other non-genetic factors. Such genetic factors mainly include single nucleotide polymorphisms (SNPs) and less frequently observed insertion/deletion polymorphisms and variations in microsatellites.

So far, many genome-wide association studies (GWAS), candidate genes studies and familial studies have reported increased predisposition to T2D and DR attributed by genetic variations. However, the consistency in results and/or validation of such studies lack in different populations. Genetic association studies are ethnicity dependent since ethnicity influences the allele frequencies of SNPs and their linkage disequilibria. Moreover, environmental and cultural variations are found among different populations. Therefore, validation of such studies in various populations is very much essential.

This approach of studying the genetics of the disease may help in understanding the genetic predisposition as well as the unrevealed etiology of the T2D and DR in our targeted Western Indian population. The study would assist in identifying individuals at high risk of T2D or DR, which would, in turn, facilitate the early disease management and provision of appropriate preventive treatments for delaying the onset or severity of DR.

It is evidently shown in many populations that genetic polymorphisms of CAPN10 increase T2D risk. Hyperglycemia is known to alter the charge across the cell membranes leading to the increased influx of calcium ions to maintain the charge across the membrane. The increased Ca2+ concentration induces the CAPN 10 production that ultimately known to drive apoptotic change in the cell. CAPN 10 evidently induces such an apoptotic destruction of β pancreatic cells. Similarly, retinal pericytes may also undergo damage during severe DR since they express CAPN10.
However, the SNPs of CAPN10 gene is rarely studied in association with DR. VEGF genetic variants especially located in the promoter and UTR regions have shown strongest association with DR in many ethnicities, till now. Although, VEGF plays a vital role in the DR pathology the mechanism is not entirely understood. Hyperglycemia-induced oxidative stress and ischemia in the retinal vessels stimulate VEGF production that it is known to cause hyperpermeability of neovasculature.

Hence, we thought to investigate the previously reported intronic genetic variations of Calpin 10 and VEGF genes in association with T2D and DR in the Western part of India, i.e., Gujarat, which has been yet to report as per our knowledge. Further, we studied genetic variations in the promoter and UTR regions of the VEGF gene due to its highly polymorphic nature and evaluated their association with DR.