Type 2 diabetes (T2D) and diabetic retinopathy (DR) being a multifaceted disease involves multiple genetic and environmental determinants. For the genetic studies of complex human disease, it has been recognized that the interplay among multiple genetic variants is driving disease phenotype.

Our study reported that rs699947 and rs2142363 of VEGFA gene significantly increase the risk of proliferative diabetic retinopathy as much as by two fold. The haplotype of the five VEGFA SNPs consisting risk allele A of these two polymorphisms indicated the potential association with PDR in the current Indian ethnicity by attributing 4 fold risk. Conversely, haplotype consisting wild alleles for these two SNPs showed significant protection against PDR development. The DNA sequence analysis of upstream VEGFA gene and 3’UTR suggested insight to some rare and novel variations that may play a role in the DR development in the Western Indian population. The analysis showed non-significant p values, which should not be overlooked due to low powered association studies. Though, we did not find an association of the Calpain 10 polymorphisms with T2D or DR, haplotype containing wild alleles of the studied SNPs showed the possibility to give protection against T2D development.

However, future studies massively genotyping these polymorphisms in the larger sample size is recommanded. Identification of these variants in an individual with DR may help in the appropriate medical management, promising its application in the prevention and treatment of DR in term of personalized medicine. Further, the studies would also aid a direction to understand the basis of the DR pathogenesis.