Multiple Sclerosis and Gene Polymorphisms: are we Groping in the Dark?

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Till date, the etiology of multiple sclerosis (MS) remains convoluted and many recent studies have added some startling findings to the existing literature on MS. There have been some noticeable developments in dissecting genetics of MS, but the results remain controversial due to divergence in geographic prevalence of MS across different populations. By and large this may be attributed to the enigmatic genetic and environmental background in its etiopathogenesis. By unlocking the missing link between these two components, some advancement can be achieved in devising better treatment options for MS management. This commentary highlights the outcome of our recent study aimed at exploring the association between MS susceptibility and EIF2B5 Ile587Val polymorphism in a subset of Indian population [1].

The nature of MS is very heterogeneous, a single factor cannot be assigned as definite reason for its causation. Although, MS has become a burning issue and the subject for extensive research across the globe; still there is no fully established cause and cure for it. It is believed that environmental factor like an infection modifies the risk of MS development in an individual in diverse ways [2]. It seems that MS primarily results due to complex interactions between genetic and the environmental components but genetic risk factors seem to preponderate in its development [3-5]. From this perspective, current efforts have been focused to uncover the genetic components behind its development. One of the studies carried out on MS patients from Italy by Ungaro et al., has reported Ile587Val (rs843358) polymorphism of the eukaryotic translation initiation factor-2B (EIF2B5) gene to be responsible for an increased susceptibility for developing MS [6]. EIF2B5 belongs to the EIF2B gene family and it encodes the catalytic epsilon subunit of the EIF2B complex involved in translation initiation [7]. It is uncertain whether this polymorphism is associated with MS across different populations and in order to evaluate the same, we screened EIF2B5 exon 13 and introns flanking it in the first ever investigation in an Indian subset of MS population, covering patients from its Kashmir region [1].

Our preliminary findings did not provide evidence for the contribution of Ile587Val in MS development in Kashmiri population, even though the study by Ungaro et al., has suggested a role of this SNP in MS susceptibility. The role of EIF2B5 as a susceptibility factor in MS development however remains controversial [8-10]. The data from our study provide crucial insights into etiology of MS by suggesting the role of local geographic factors in selective predominance of genetic variants among MS patients from different populations there by further complicating the genetics of MS. In fact, we could not find any significant association between Ile587Val distribution and gender bias. Although the sample size in our study was nominal, but considering an increase in the number of persons with MS in the Indian subcontinent (Atlas of MS 2013, http://www.atlasofms.org), results of our study provide significant contribution in understanding the pattern of susceptibility genes particularly in Kashmir region of India.

A large global sample of MS patients need to be studied to discern the role of racial differences on the selective prevalence of sequence variants in a particular population and thereby determine the ultimate impact on MS susceptibility and its proper diagnosis. The recognition of different allelic variants across globe can help in designing new personalized therapeutic interventions for MS patients. Therefore, there is an urgent need for cross continental collaborations to get better insights about the MS etiology.

References


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