Modern Genetics in Combating Tuberculosis

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Brief Discussion on Genetics in Tuberculosis

Among all the communicable diseases, Tuberculosis (TB) is a major burden even to the present day. Though it is completely curable and preventable yet an ocean of people are succumbing to this disease every year. It is caused by Mycobacterium Tuberculosis (Mtb). If an infected person coughs or sneezes, the infection is transmitted from one person to another in the form of aerosol droplets. Though many are exposed to the causative bacterium yet only a few are infected. Some of the factors like poverty, malnutrition, smoking and diabetes aggravate the disease [1].

Out of the affected individuals some are able to clear the disease because of adherence to treatment, while in others it remains in latent condition. When this happens there are chances that the disease may again be rejuvenated if the levels of immunity decrease in the host. This shows that not only the bacteria but also host factors like immunity and genetic susceptibility are associated with the expression of the disease. So one of the approach to identify the susceptibility of the disease is the case–control approach, where effected and unaffected are involved. Here screening of genetic markers can be done. The other method is the use of candidate gene approach where entire genetic complement variation is identified. Mutations were detected in genes like NRAMP1, VDR, IFNy, TNFa and IL10. These mutations cause gain and loss of function leading to recessive and dominant form of disease.

Natural Resistance Associated Macrophage Protein 1 (NRAMP1) candidate gene for TB has been extensively studied in many ethnic groups and was found to be predisposed to severe form of TB. NRAMP1 is also known as Solute Carrier family 11 proton-coupled divalent metal ion transporter membranes 1 (SLC11A1). This gene is located on chromosome 2q35. These studies prove that innate immunity plays a major role to protect an individual from the disease.

Another candidate gene of study is VDR gene. Vitamin D induces antimicrobial peptide cathelicidine which is necessary to develop adaptive immunity. It also helps in the growth of different immune cells. The molecular study conducted by using the DNA variants of VDR gene on different ethnic groups reveals that VDR gene is associated with susceptibility to TB [2]. This proves that absorption of Vitamin D through sunlight reduces the risk of TB.

The primary clinical diagnostic techniques like acid-fast staining of sputum smear and radio diagnosis remain as the basic techniques for identification of Mtb. Yet rapid diagnostic techniques like bacterial culture (BACTEC), Nucleic acid hybridisation probes, DNA sequencing, micro arrays, Matrix Assisted Laser Desorption Ionisation-Time Of Flight Mass Spectroscopy (MALDI-TOFMS) which are cost effective and accurate have evolved in time. These techniques help in rapid diagnosis of the disease to the molecular level [3].

Tuberculosis is multifactorial disease both genetic and environmental factors are involved. When favourable conditions for the Mtb increase, then the risk of the disease also increases. So we have to decrease the favourable conditions for the bacteria. Latent TB infected person can reduce the risk of developing active TB by allowing more amount of sunlight and ventilation into the rooms, proper intake of nutrients, eradication of poverty, reducing the risk of diabetes, and pulmonary infections and eradication of habitual smoking. These factors also regulate gene expression. In addition to the above suggestions an infected TB person should adhere to the drug therapy which stops the transmissions of TB from one person to another [1].

BCG vaccination in children acts as a shield against TB. But it does not protect the adults from the disease. TB Awareness have to be inculcated in general population and TB patients have to be educated to adhere to the Directly Observed Treatment Strategy Programme (DOTS) by taking the prescribed drug therapy like Isoniazid, Rifampicin, Pyrazinamide and Ethambutol [3]. The main reason for the increase of TB is presence of HIV co-infection and improper adherence of TB drug therapy. If the patient stops the drug therapy in the middle then it increases the risk of developing Multi-drug resistance TB. Multiplex allele –specific PCR assays can be used to detect the resistance of second–line drug in Mtb [4].

Genome wide and Bioinformatics study on Mtb have helped to identify glycosinc rich proteins of Mtb [5]. These studies are useful to identify the susceptibility of host from the pathogen. It is also useful for site-specific drug target therapy, and improved vaccines. Molecular research on TB can pave way to develop new drugs for the treatment of MDR-TB and also reduce the duration of the treatment therapy of pulmonary tuberculosis [6].

References

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