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MedGenome suggests personalized cancer vaccine approach for Lynch Syndrome

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Lynch Syndrome (LS), also known as hereditary non-polyposis colorectal cancer (HNPCC) is caused by mutations in genes involved in the repair of DNA replication errors.



A breakthrough study on ‘cancer vaccine approach for personalized treatment of Lynch Syndrome’ by MedGenome was published in Scientific Reports this month. The published study in collaboration with Kailash Cancer Hospital and Research Centre (KCHRC), Goraj, examines the feasibility of treating Lynch syndrome using a personalized cancer vaccine approach by identifying potential immunogenic tumor specific alterations.

Lynch Syndrome (LS), also known as hereditary non-polyposis colorectal cancer (HNPCC) is caused by mutations in genes involved in the repair of DNA replication errors such as MLH1, MSH2, MSH3, MSH6, PMS2, and EPCAM. LS increases the life-time risk of developing cancers of other organs, such as cancers of the colon, stomach, small intestines, liver, kidney, uterus, brain, pelvis and prostate among others.

LS is the most common hereditary CRC syndrome accounting for 2–5% of all CRCs. In the developed world, the estimated number of affected individuals range from 0.3-0.5% of the population. Accurate prevalence details are sparse from developing countries. In India, while the overall incidence of CRC is comparatively lower (4.4 per 100,000 in men and 3.9 per 100,000 in women) than in the west, a large percentage of patients develop CRC before the age of 45 with a higher proportion (10–15%) of LS-CRC cases as confirmed through microsatellite instability (MSI). Statistics says that 12-17% of all colorectal cancers have MSI but only 3 % of these are due to Lynch syndrome.

MedGenome study reported a germline heterozygous frame-shift mutation in the mismatch repair MLH1 gene which was identified in members of two unrelated LS families. Dr. Rakshit Shah, Surgical oncologist, KCHRC, Vadodara stated, *“The screening for genetic mutation in colorectal cancer patients especially those with familial history could help in identifying those that are vulnerable to the disease. Such genetic based screening could be an efficient way of preventing colorectal cancer. Families with history for colorectal cancer like lynch syndrome should be advised to undergo genetic screening and if they carry mutations like MLH1 they are likely to develop colorectal cancer before the age of 50. Our study is unique as genetic screening in familial colorectal cancer has not been widely reported in our country.”*

To this end, MedGenome used its proprietary neoepitope prioritization pipeline OncoPeptVAC to select potential immunogenic peptides from whole-exome and RNA-seq data generated from the patient tumor. From a list of over fifty predicted neoepitopes, three neoepitopes were tested in an ex vivo CD8+ T cell activation assay confirming their immunogenicity.

The MedGenome study reports many potential immunogenic peptides from a Lynch syndrome-affected individual who has progressed to develop colon cancer using OncoPeptVAC. The immunogenicity of several peptides derived from somatic mutations in AXIN2, PIGO and MSH6 was validated using T cells from affected individuals, as well as HLA-matched healthy donors. Additionally, the study also analyzed the tumor microenvironment using a transcriptome-based tumor microenvironment analysis platform OncoPeptTUME, uncovering high infiltration of CD8+ T cells that lack expression of markers of activated phenotype. The potential mechanism of immune suppression, the study suggests may arise as a result of high T-regulatory cell (Treg) and myeloid-derived suppressor cell (MDSC) infiltration. It is possible that the development of CRC in the affected individual was contributed by the lack of anti-tumor immune response. Taken together, this study provides a basis for considering the use of a cancer vaccines to treat or delay the onset/relapse of LS-CRC.

“*Given that Lynch syndrome has limited treatment options, this study provides a basis for considering a cancer vaccine approach that could be used either as monotherapy or in combination with established immuno-oncology or chemotherapy drugs”*, added Dr. Amit Chaudhuri, VP R&D, MedGenome and a Senior author of this study.