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Editorial

Toll-Like Receptor (TLR) Gene Polymorphisms as "Immuno-Inflammatory Triggers" in Human Papillomavirus-Mediated Cervical Cancer Susceptibility in HPV Vaccines (Gardasil/Cervarix) Era: Global Priorities in Molecular Medicine, Cancer Therapeutics and Public Health in Asian-Indian and American Ethnicity Women

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Demystifying the physiological intricacies associated with the complex etiopathogenesis of Human Papillomavirus-mediated cervical cancer in HPV vaccines (Gardasil/Cervarix) era warrants dynamic global collaborations for cost-effective management of cervical cancer in Asian-Indian and American ethnicity women of varying lifestyles; in this context, the enigmatic array of Toll-like Receptors 1-13 have emerged as pivotal "Immuno-Inflammatory Triggers" in early and advanced/fulminant stage(s) of HPV-mediated cervical carcinogenesis in the present Covid-19/Omicron pandemic era for development of clinically validated predictive biomarkers. Single nucleotide polymorphisms are the most common forms of genetic variants in human genome, some of which have potential functional influence on the susceptibility to human diseases including gynecological cancers; TLR gene polymorphisms have considerable causal role in disease susceptibility, including cancers as evident in elegantly designed TLR-genetic association case-control prospective statistically-powered epidemiology studies in Asian-Indian population primarily North Indian cohort [1-3]. Analysis of potentially functional polymorphisms in candidate genes has emerged as a powerful approach in understanding the complex causal relationship between genotype and phenotype; genetic association analyses are pragmatic public health-oriented models to explore the potential role of genetic polymorphisms in susceptibility to various cancers, including HPV-mediated cervical cancer. TLR-biomarker immunogenetics merits further clinical research experimental innovative evidence-based investigation; cervical cancer is a multifactorial disease and viral persistence and/or clearance in the susceptible host may vary at diverse stages: FIGO I/II/III/IV of tumorigenesis in ethnically disparate population-pools. The GA genotype of TLR 9 showed borderline association (P = 0.056, OR = 0.31, 95% CI = 0.09 - 1.03) with FIGO stage II of cervical cancer; however, there was no significant association between TLR 9 polymorphism and FIGO stages III and IV while TLR 9 AA genotype was observed to be marginally associated (P = 0.053, OR = 2.63, 95% CI = 0.99 - 7.01) with advanced stages of cervical cancer [4]. Pandey conducted an innovative HPV-mediated cervical cancer survey-based study in a clinical setting in North India wherein the unbiased response regarding cervical cancer awareness in terms of "yes", "no" and "no response" in 103 women residing in Lucknow and adjoining

areas was 43.7, 44.7 and 11.6%, respectively, while the response to knowledge of HPV vaccine Gardasil was 28.1% ("yes"), 37.9% ("no") and 34.0% "no response", implicating the effectiveness of HPV-cervical cancer-vaccines' awareness programs for overall cervical cancer management [5].

Racial and ethnic disparities in cervical cancer management and health care utilization are emerging as thrust areas of public health policy-related research in contemporary times; cost-effective predictive research models with biomarkers are warranted to decrease the increasing burden of HPV-mediated cervical cancer amongst disease-susceptible at-risk individuals of ethnically disparate populations. Surveillance of HPV-mediated cervical cancer risk and outcomes-based timeline based immunotherapeutic strategies may be developed for prevalence and disease outcome assessments involving risk factors, Gardasil/Cervarix vaccination and patient-care/management for gynecological cancer control and prevention globally. TLR-cancer immunotherapeutics certainly offers fascinating translational and clinical research avenues in the ever-expanding onco-fertility and public health field.

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