HPV: Genetic Susceptibility and immunotherapies

Patrícia Savio de Araujo Souza

Instituto Ludwig de Pesquisa sobre o Câncer, São Paulo, Brasil - psas@ludwig.org.br

Cervical cancer is one of the leading causes of death for women in developing countries. Although the greatest risk factor for the development of invasive cervical cancer (ICC) is persistent infection with oncogenic types of human papillomavirus (HPV), several host genes can be involved in genetic susceptibility. Codon 72 polymorphism of p53 gene / gene P53 was investigated but controversial results were found, possibly due to differences in methods of detection and sample sizes. The immune responses to HPV infection in the majority of women are effective, but a small percent are not able to clear the infection. Due to the crucial function of HLA class II molecules in antigen presentation to CD4+ T cells, the role of the polymorphisms of HLA genes in the outcome of HPV-associated diseases has been intensely investigated. Positive associations of ICC with HLA-DRB1*15 and HLA-DQB1*03 were found in different populations, while negative associations with HLA-DRB1*13 alleles were also observed. Despite the differences observed in immune response to naturally acquired infections, vaccination studies showed promising results. ICC and other HPV-associated malignancies might be treated or prevented by HPV vaccines. As E6 and E7 genes are necessarily expressed in HPV associated lesions, they are the major target of therapeutic vaccines. Protocols using different vaccine delivery systems are being tested. Successful results in animal models led to clinical trials of prophylactic vaccines in humans. Data from clinical trials of prophylactic vaccines using HPV 6, 11, 16 or 18 L1-virus like particles showed reduction of HPV infections and clinically associated diseases and suggest that they may be controllable by vaccination.