DIFFERENTIAL ANTIBODY RESPONSE AGAINST CONFORMATIONAL AND LINEAR EPITOPES OF THE L1 PROTEIN FROM HUMAN PAPILLOMAVIRUS TYPES 16/18 IS GENERATED IN VACCINATED WOMAN OR WITH DIFFERENT EXPOSURES TO THE VIRUS.

Gutierrez-Xicotencatl L. Research Center for Infection Diseases, & Center for Research in Population Health, National Institute of Public Health, Cuernavaca, Morelos, Mexico;
Pedroza-Saavedra A, Chihu-Amparan L, Maldonado-Gama M, Salazar-Piña DA, Research Center for Infection Diseases, & Center for Research in Population Health, National Institute of Public Health, Cuernavaca, Morelos, Mexico;
Rodríguez-Ocampo AN, Cruz-Valdez A, Academic Unit of Chemical Biology and Pharmaceutical Sciences, Autonomous University of Nayarit, Mexico;
Carmona-Balandrano E, Esquivel-Guadarrama F, Faculty of Medicine, Autonomous University of Morelos Estate, Mexico.

Antibodies against human papillomavirus (HPV) L1 protein are associated to past infections and related to the evolution of the disease, while antibodies against L1 virus like particles (VLPs-L1) are used to follow the neutralizing immune response in vaccinated women. In this study, sera antibodies against conformational and linear epitopes of L1 protein from HPV16/18 were evaluated to discriminate HPV vaccinated women from those naturally infected or with uterine cervical lesions. The VLPs-L1 from HPV16/18 generated in baculovirus were purified by CsCl gradient and linear L1 protein obtained by denature VLPs. Serum antibodies against VLPs-L1 and L1 from vaccinated women or with different exposures to the virus were measured by ELISA. Regresion and ROC analysis were carried out to evaluete the test performance to discriminate the different women populations. The results showed that antibodies against VLPs-L1-16/18 highly associated with vaccinated women (OR=2.11e+08 and 57.74, respectively), but not associations were observed with natural infected women or with cervical lesions. However, antibodies against L1-16/18 showed high associations with vaccinated women (OR= 101.33 and 37.91, respectively) (*p≤ 0.05*), but also associations of these antibodies were observed with the cervical cancer (CC) group (OR= 3.33 and 5.65, respectively). The ROC analysis showed that antibodies against VLPs-L1 and L1 16/18 were highly effective to detect vaccinated women (AUC= 0.96, 0.91. 0.80 and 0.78, respectively), with high sensitivity for HPV16 (100% and 86.3%), and moderate for HPV18 (63.6%). However, anti-L1 antibodies had the best test performance to discriminate the cervical intraepithelial neoplasia grade 3 (CIN3)/CC group from controls (AUC= 0.67 HPV16 and 0.63 HPV18), with low sensitivity (15% to 20%, respectively) and high specificity (96% and 92%, respectively). In conclusion, our results suggested that anti-VLPs-L1 16/18 antibodies are highly efficient to detect vaccinated women, but anti-L1 antibodies are better to discriminate CIN3/CC among the general population.