

Investigation of potential risk factors of Human Papillomavirus (HPV) 18 infection among women with cervical lesions

M. Martinelli¹, C. Villa¹, C. Giubbi¹, I. Sechi², N. Moresu², F. Sina³, M. Di Meo³, A. Piana², R. Fruscio^{1,3}, F. Landoni^{1,3}, C. Cocuzza²

¹ Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy.

² Department of Medical Surgery and Experimental Sciences, University of Sassari, Sassari, Italy

³ San Gerardo Hospital, ASST Monza, Monza, Italy

Introduction: High-risk Human Papillomavirus (hrHPV) persisting infection is known to be associated with cervical lesions although only few of them will progress to cancer. Recent studies have reported other potential risk factors for cancer progression such as co-infections with multiple hrHPV types and/or infection with specific intra-type variants. HPV-18, although less prevalent among the female population, together with HPV-16, is responsible for almost 70% of all cervical cancers worldwide.

The aim of this ongoing study is to investigate HPV-18 intra-type variants and its co-infections with other high-risk HPV genotypes in women with cervical lesions as potential indicators of risk of cervical disease.

Methods: Cervical samples (L-shaped Endocervical/Esocervical FLOQSwab, Copan) were collected from 326 women referred to colposcopy at San Gerardo Hospital (Monza, Italy). All samples were tested using Anyplex™II HPV on MicroLab Nimbus platform (Seegene). HPV-18 positive samples were further analysed using previously described PCR protocols to obtain sequences for intra-type variants' determination. Phylogenetic analysis was conducted using specific bioinformatics software.

Results: Preliminary results showed that 6.1% (20/326) of women enrolled in the study were HPV-18 infected. Most of the women were of Italian nationality (17/20). In 55% (11/20) of cases HPV-18 was found in co-infection with other hrHPV genotypes. A Cervical Intraepithelial Neoplasia of grade 2 or worse (CIN2+) was diagnosed in 7 women (7/20, 35%) with HPV-18 infection. Multiple hrHPV infections were found in 5 (5/7, 71.4%) of these women (Table 1).

Sample ID	Cytology	Histology	HR-HPV genotype
MO03	HSIL	/	16, 18
MO30	LSIL	/	18, 31
MO31	LSIL	CIN3	18, 59
MO83	ASCH	CIN3	16, 18
MO100	AGC	CC	18
MO102	LSIL	/	18, 33, 51, 66
MO113	LSIL	/	16, 18, 52, 58
MO114	HSIL	CIN3	18, 35, 51
MO188	LSIL	/	18
MO196	ASCH	CIN2	18
MO202	ASCH	/	18, 33, 68
MO204	LSIL	/	18
MO210	LSIL	/	18
MO215	LSIL	/	18
MO219	ASCUS	/	18, 33
MO249	LSIL	/	18
MO252	LSIL	/	18
MO293	ASCUS	/	18
MO317	HSIL	CC	18, 58
MO326	HSIL	CIN3	16, 18

Table 1: Results obtained from HPV detection with clinical data

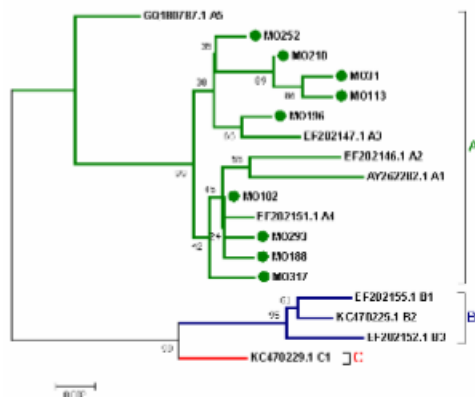


Figure 1: Phylogenetic tree of LCR sequences of HPV-18

From the phylogenetic analysis all obtained sequences clustered into the A lineage, in particular into sub-lineages A3 and A4 (Figure 1).

Conclusion: Data obtained from these preliminary results have confirmed a low prevalence of HPV-18 among women referred to colposcopy. A high prevalence of hrHPV multiple infection was found in HPV-18 infected women, especially among women with high grade lesions. All sequences analysed up to now were found to belong to A lineage. The analysis of a larger number of samples together with the analysis of other viral risk factors such as viral load will permit in future to better understand the possible role of these potential biomarker of cervical lesion progression.

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