ANALYSIS OF RKIP EXPRESSION IN CERVICAL CYTOLOGY SAMPLES AS A MARKER FOR HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

Maíra D. Stein[1], Vânia S. Mariano[1], Cristovam Scapulatempo Neto[1], Guilherme G. Ribeiro[1], Adhemar Longatto Filho[1,2,3,4], Julio Cesar Possati Resende[1], Márcio Antoniazzi[1], Rui Manoel Reis[1], Jose Humberto T. Fregnan[1].

[1]Barretos Cancer Hospital, Pio XII Foundation, Barretos, Brazil.

[2]14, Department of Pathology, Faculty of Medicine, University of São Paulo, São Paulo, Brazil.

[3]Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal.

[4]ICVS/3B's – PT Government Associate Laboratory, Braga/ Guimarães, Portugal.

BACKGROUND: Cervical cancer is the third most common cause of cancer related mortality in women worldwide (530,000 cases and 275,000 deaths), and about 85% of these cases occur in developing countries where organized screening program for precancer lesions detection, early stage cervical cancer diagnosis, and treatment modalities are not commonly available compared to developed countries. In Brazil, cervical cancer affects approximately 15,000 women annually. The implementation of cervical cytology screening strategies (Papanicolaou – Pap test) reduced the number of cervical cancer in developed countries, but the incidence and mortality in developing countries, such as Brazil, was not significantly altered to date. There is well documented evidence in the literature demonstrating that cervical cytology has limitations as an isolated method for cervical cancer screening. Hence, there is a need for developing new biomarkers (as Raf-1 kinase inhibitor protein- RKIP, that modulate intracellular signaling pathways in cancers and is frequently downregulated) to improve the detection of high grade cervical intraepithelial neoplasia (CIN2+).

HYPOTHESIS: To describe and compare Raf-1 kinase inhibitor protein (RKIP) protein expression in cervical cytology samples from women with and without CIN2+.

METHODS: The series was composed of cervical liquid-based cytology (LBC) samples (SurePath™) from 31 women collected just prior to the colposcopy, from January 2014 to April 2015 at the Prevention Department in Barretos Cancer Hospital. The LBC samples were used for RKIP immunostaining with DAB, Ultraview detection kit, Ventana, Roche. The reading of the slides was made by one cytologist and one pathologist in a two heads microscopy, they evaluated the intensity and extension of immunoexpression.

RESULTS: Immunoexpression of RKIP, intensity and extension were not associated with CIN2+ ($p>0.05$). However, expression of RKIP was significantly higher in atypical cells in comparison to normal one (78.3% vs. 12.5%; $p=0.002$). Despite the positive RKIP immunoexpression was mainly found in abnormal cells, we have not found association between intensity and extension of RKIP expression with CIN2+ in these cases.

.