

Localization and distribution of wolframin in human female reproductive tract

Angela Lucariello¹, Angelica Perna¹, Lucrezia Manente¹, Rosanna Palladino², Maria De Falco³, Antonio De Luca¹

¹ Department of Medicine and Public Health, Section of Human Anatomy, Faculty of Medicine, Second University of Naples

² Luigi Curto Hospital, Polla – Salerno

³ Department of Biological Sciences, Section of Evolutionary and Comparative Biology, Faculty of Biology, University of Naples Federico II

Wolframin, a transmembrane glycoprotein of endoplasmic reticulum consisting of 890 amino acids, is encoded by the WFS1 gene, mutated in the Wolfram syndrome. This pathology, also called DIDMOAD, is an autosomal recessive disorder defined by the association of diabetes mellitus, optic atrophy, and further organ abnormalities.

To gain further insight into the pathogenesis of diseases associated with WFS1 mutations, we conducted an immunohistochemical study to investigate its pattern of expression in human female reproductive tract in physiologic and pathologic conditions. For this purpose, samples of physiologic and pathologic endometrium, samples of placenta throughout pregnancy in normal and diabetic pregnant women, were used. In physiologic endometrium, we observed a light increase of wolframin from proliferative to secretory phase where wolframin was localized in the glands, stroma and cells lining blood vessels. In menopause, wolframin expression increased with a glandular and stromal localization. In pathologic endometrium, we observed an increase of wolframin expression from hyperplasia to polyps until a higher expression in carcinoma tissues. In normal placenta there was a modulation of wolframin throughout pregnancy with a strong level of expression during the first trimester and a moderate level in the third trimester. In diabetic women, the wolframin expression was strongly reduced in the third trimester of gestation. In human endometrium, wolframin seems to have a role in differentiation program. Deregulation of these functions may induce the onset of several endometrial pathologies. Moreover, in normal placenta wolframin may be required to sustain normal rates of cytotrophoblast cell proliferation during the first trimester of gestation.

The decrease of wolframin expression in diabetic placentae may hypothesize that this protein is directly regulated by insulin concentration also in the placenta, suggesting that this protein physiologically maintain the glucose homeostasis in this organ.

Keywords: wolframin, placenta, endometrium, immunohistochemistry