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Modulation of Wnt signaling pathway, a strategy in urothelial carcinoma progression

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Bladder cancer is the fourth most common cancer in men and the most common malignancy of the urinary tract. When the diagnosis is made at an early stage urothelial carcinoma (UC), the five-year survival rate is high, but when detected after local metastasis the rate is only 50%. Our group has reported a positive correlation between the expression of Wnt5a, a member of the Wnt proteins family, and histopathological grade and stage of UC and recently, the expression of major components of Wnt5a / planar cell polarity (PCP) signaling pathway in UC human tissue samples and UC cell lines. The Wnt proteins have been described in late 80's, and are best known for their association with a number of embryonic functions with critical role in developmental biology and homeostasis of tissues. The aberrant Wnt signaling activation has been described as critical in the pathogenesis of cancer, as tumor suppressor or tumor promoter, in variety of malignancies. A publication on the Wnt family has nearly doubled since 2008 and is exponentially increasing. Recently, Wnt signaling pathways have been associated with metastatic cancer via activation of epithelial mesenchymal transition (EMT) genes transcription suggesting a potential therapeutic use by interference of these pathways. The purpose of this study is to dissect the role of Wnt5a signaling in the pathogenesis/progression of UC. Our findings support that Wnt5a-Ror2 signaling plays a role in UC with potential application as a prognostic marker but most interesting provide evidence that Wnt5a signaling may be used as an effective molecular target for novel therapeutic tools. In conclusion, the correlation between Wnt5a /Ror2 and pathological grade suggests that Wnt5a/Ror2 signaling pathway could play a role in the aggressiveness of this cancer, promoting the EMT and metastasis process. Further studies are needed to determine the underlying mechanism of Wnt5a/Ror2 action in UC for targeting the Wnt signaling pathways as potential treatment for UC, as well as their application as biomarkers for UC.

Biography

Ramiro Malgor is an Associate Professor of Pathology in the Department of Biomedical Sciences at Ohio University. He graduated as MD at Universidad de la Republica in Uruguay and his first area of research was orientated to the development of novel diagnostic method for *E. granulosus* infected dogs. In 2005, he moved to Ohio University, where his new area of research was focused on Wnt5a and its relationship with inflammation and cancer. In last 10 years, his research has been focused on two main goals, to analyze the role of Wnt5a signaling pathway in atherosclerosis, a chronic inflammatory disease; to understand the role of Wnt5a signaling in atherosclerosis to develop novel, safe, and cost-effective strategies for treatment; and to dissect the expression pattern of Wnt5a in urothelial carcinoma, to find a novel molecular biomarker, as well as potential new targets for diagnosis and treatment to this cancer.

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