

The Titanium Surface Modulates the Expression of Beta-Catenin and DLX5 Genes in Pancreatic Ductal Carcinoma *in Vitro*. Can the Metallic Stent Increase PDAC Aggressiveness?

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Context Adenoductal pancreas (PDAC) is a fatal cancer. Its aggressiveness is associated in part with the EMT process of metastasis. Two genes specifically involved in these phenomena are β -catenin and DLX5. While the first gene has been widely studied also in pancreatic cancer, few data are associated with DLX5. However, its over-expression has been recently associated with the formation of metastases in breast cancer *in vivo*. An exogenous factor involved in the modulation of the expression of these genes seems to be titanium. This compound is usually employed for the pallia action of patients with PDAC, to reduce choledochal stenosis due to compression. **Objective** The purpose of this study was to assess whether titanium is able to modulate the expression of these two genes *in vitro*. **Methods** We used a primary cell culture of PADC (PP78). The cells were seeded and cultivated in contact with two different titanium surfaces for 10 days. After this period the total mRNA was extracted and the quantification of β -catenin and DLX5 genes was performed by RT-PCR according to the $\Delta\Delta C_t$

analysis. Then cells were stained using the immunofluorescence technique (IF) to quantify the β -catenin protein expression using a computerized high-resolution acquisition system (D-Sight, Menarini, Florence, Italy) The cells were scored evaluating the cytoplasmic positivity as follows (0 absent, 1 low, 2 middle, 3 strong). The experiment was carried out in triplicate and untreated cells (without titanium contact) were used as control. **Results** Quantitative analyses showed that both titanium surfaces positively affected beta-catenin (mean 2.8 fold) and DLX5 (2.0 fold) mRNA expressions with respect to the controls ($P < 0.0007$). Both titanium surfaces also increased the protein score 3 values of β -catenin in treated cells with respect to their controls ($P = 0.0158$). **Conclusion** Our data showed that several titanium surfaces positively modulated the expression of two genes associated with the increase of the aggressiveness of PDAC *in vitro*. Clinical studies are needed to find out which type of stent can be used in the surgical operation with palliative intent.