Modulation Of Tff1 Expression In Physiopathological Conditions

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The repair of the gastric epithelium is modulated by several factors included the trefoil factors (TFFs), a family of small peptides characterized by a conserved domain containing six cysteine residues that form a cloverleaf structure. Among these, TFF1 plays a key role in the correct formation of the mucous layer, promotes the epithelial restitution after injury and protects the integrity of the epithelial barrier. TFF1 has a seventh cysteine that allows the formation of homo- and/or hetero-dimers. The peptide is able to bind copper in vitro, favoring its homodimerization. The expression of TFF1 is strongly induced after mucosal injury, and it is frequently lost in gastric cancer or overexpressed in most cases of breast cancer.

Investigating the influence of copper on the expression of TFF1, we established that metal overload negatively modulates TFF1 expression in cancer cell lines. Furthermore we examined the binding of Sp1, a copper sensing transcription factor, on TFF1 promoter and we observed that it was able to bind two different sites with a significant reduction of protein binding after copper treatment.

The expression of TFF1 is also regulated by epigenetic mechanisms. We focused our attention on the optimization of a High Resolution Melting technique for the analysis of DNA methylation pattern in different experimental conditions. The aim of our study is to elucidate the involvement of TFF1 in neoplastic processes and inflammatory diseases, as Helicobacter pylori infection and coeliac disease, in order to gain insight into the pathogenic mechanisms and provide useful tools to interfere and slowing down the disease progression.