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Characterization of *LDB1* expression in Colorectal cancer

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Colorectal cancer is the third most common cancer worldwide and fourth highest cause of cancer deaths. Several pathways including Wnt, TGF- β , PI3K/KRAS and p53 were shown to play a major role in Colorectal cancer development. Ldb1 (LIM-domain-binding protein 1) is an adaptor protein shown to interact with the Wnt signaling pathway and has a role in adult intestinal homeostasis. Moreover, *Ldb1* downregulation in the liver induces hepatocellular carcinoma. Therefore, the aim to evaluate the role of *LDB1* in Colorectal cancer development.

Quantitative PCR analysis was performed on 59 tumor samples from Colorectal cancer patients to evaluate the clinical relevance of *LDB1* expression in colorectal cancer. In addition, functional assays were implemented in four different Colorectal cancer cell lines using siRNA and *LDB1*-GFP expressing lentivirus.

Differential *LDB1* expression in Colorectal cancer patients was correlated with a decrease in overall survival and metastasis-free survival, suggesting a role of *LDB1* in Colorectal cancer progression. Additionally, a positive correlation was found between tumor *LDB1* expression and genes involved in the Wnt signaling pathway (*CTNNB1*, *AXIN2*, *MYC* and *CCND1*).

Downregulation of *LDB1* in HCT116 and SW620 cell lines resulted in the upregulation of *CCND1*, but unexpectedly decreased the proliferation *in vitro*. *LDB1* overexpression induced an upregulation of *CCND1* in all Colorectal cancer cell lines. Furthermore, this overexpression increased *MYC* expression in SW480 and SW620 cells and augmented Wnt activation in DLD1 and SW620 cells. Interestingly, it led to a downregulation of *CTNNB1* and *AXIN2* in SW480 cells.

The presently available data shows that *LDB1* expression has a role in Colorectal cancer progression. The experimental data also confirms an influence of *LDB1* on the Wnt signaling pathway and tumor cell proliferation. This influence is not well understood yet, warranting further experiments.