Loss of Myosin Vb in colorectal cancer is a strong prognostic factor for disease recurrence

Running title: MYO5B is a prognostic marker in CRC

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Abstract

Background: Selecting the most beneficial treatment regimens for colorectal cancer (CRC) patients remains challenging due to a lack of prognostic markers. Members of the Myosin family, proteins recognized to play a major role in trafficking and polarization of cells, have recently been reported to be closely associated with several types of cancer and might thus serve as potential prognostic markers in the context of CRC.

Methods: We used a previously established meta-analysis of publicly available gene expression data to analyse the expression of different members of the Myosin V family, namely *MYO5A*, *5B*, and *5C*, in CRC. Using laser-microdissected material as well as tissue microarrays from paired human CRC samples, we validated both RNA and protein expression of MYO5B and its known adapter proteins (RAB8A and RAB25) in an independent patient cohort. Finally, we assessed the prognostic value of both *MYO5B* and its adapter-coupled combinatorial gene expression signatures.

Results: The meta-analysis as well as an independent patient cohort study revealed a methylation-independent loss of MYO5B expression in CRC that matched disease progression. Although MYO5B mutations were identified in a small number of patients, these cannot be solely responsible for the common down-regulation observed in CRC patients. Significantly, CRC patients with low *MYO5B* expression displayed shorter overall, disease- and metastasis-free survival, a trend that was further reinforced when *RAB8A* expression was also taken into account.

Conclusions: Our data identifies MYO5B as a powerful prognostic biomarker in CRC, especially in early stages (stages I and II), which might help stratifying patients with stage II for adjuvant chemotherapy.