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TGFB-INDUCED PROTEIN IG-H3 IS ESSENTIAL FOR THE GROWTH OF HUMAN LIVER METASTASES. V. Castronovo (1), A. Blomme (1), P. Delvenne (1), O. Detry (2), A. Turtoi (1). (1) University of Liege, Liège, Belgium ; (2) Centre Hospitalier Universitaire de Liège, Liège, Belgium.

**Introduction** : Transforming growth factor-beta-induced protein ig-h3 (TGFBI) is extracellular matrix component known to be important for cell-collagen interaction. We and others have reported elevated expression of TGFBI in several human cancers, where its role remains controversial. **Aim** Current study aims at clarifying the function of TGFBI in colorectal carcinoma liver metastases (CRC-LM), a frequently encountered malignancy with no satisfactory treatment to date.
**Methods &Results** : Employing immunohistochemistry we have confirmed that TGFBI is highly expressed in human CRC-LM and in liver metastases originating from breast, lung and pancreatic tumors. We have next focused on functional aspects and have silenced TGFBI expression in SW1222 human colorectal carcinoma cells. The suppression of TGFBI protein led to a marked decrease in cell migration (-70%) and proliferation (-30%) *in vitro*. To study the effects *in vivo* we have developed a novel animal model of colorectal carcinoma based on chicken chorioallantoic membrane (CAM) that mimics human CRC-LM. TGFBI silencing resulted in 50% reduction of tumor volume in the CAM tumor model. Notably, the tumors displayed a marked inhibition of vascularization, suggesting an additional anti-angiogenic effect. Indeed, SW1222 cells silenced for TGFBI expression secreted lower levels of VEGFA *in vitro*. Finally, we have investigated if TGFBI can be used as systemically reachable target for antibody-drug delivery. For this purpose we have produced a fluorescently labeled anti-TGFBI monoclonal antibody and have injected it in mice bearing liver metastases. The *in vivo* data demonstrated that TGFBI is an accessible tumor target.
**Conclusions** : **T**aken together, the present study shows that TGFBI is essential for promoting the development of CRC-LM and therefore represents a promising target for designing novel therapeutic approaches.

- O06 -

STUDY OF GENOMIC ALTERATIONS IN COLON CARCINOMA BY ARRAY COMPARATIVE GENOMIC HYBRIDIZATION. E. Mampaey (1), A. Fieuw (2), T. Van Laethem (2), N. Van Roy (2), L. Ferdinande (1), W. Ceelen (1), P. Pattyn (1), Y. Van Nieuwenhove (1), K. De Ruyck (2), K. Geboes (1), S. Laurent (1). (1) Ghent University Hospital, Gent, Belgium ; (2) Ghent University, Gent, Belgium.

**Introduction** : Colorectal cancer is characterized by the presence of deletions and amplifications of several genes. Large genomic profiling studies however, have not been conducted in colorectal carcinoma. Since the number of genetic aberrations in a tumour sample can be correlated with recurrence or survival, these analyses can be used as biomarker for therapeutic decision making or even restaging of patients.
**Methods** : High resolution DNA copy number alterations of 102 colon carcinoma samples were studied using array CGH analysis. These data were combined with other parameters such as *KRAS* mutation status, MSI status and clinical data for data mining purposes.
**Results** : Both large and small (SRO) chromosomal deletions, gains and amplifications were identified in our sample cohort. Our results were consistent with data presented in the literature, but we also identified new recurrent chromosome alterations in interesting regions. The deletion of the *RBFOX1* gene is recently being described as associated with a poor clinical outcome in one study. We could not confirm this finding, but we found a significant correlation between *RBFOX1* deletion and *KRAS* mutation status ($p = 0,05$). We also found a correlation between the number of chromosomal alterations and the overall survival of patients with colon cancer ($p = 0,001$). The presence of chromothripsis in a number of patients was significantly correlated with the colon disease stage ($p = 0,038$).
**Conclusions** : In this study, we identified a number of new recurrent chromosome alterations in colon cancer. Furthermore, we found a significant correlation between the number of copy number alterations and the 3-year overall survival of colon cancer patients.