Knock down of S100A4 expression by small molecules restricts metastasis formation in colon cancer

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Metastasis formation is the main reason why colon carcinoma is still one of the leading causes of cancer deaths worldwide. Efforts made to identify the main molecular players in metastasis formation revealed the calcium binding protein S100A4. S100A4 is a Wnt/β-catenin target gene [1] which induces migration, invasion and angiogenesis and its overexpression leads to aggressive tumor growth and metastasis formation in many types of cancer. Hence, its suppression bears large potential for therapeutic intervention.

Here we report the identification of a small molecule inhibitor from a high throughput screening of 1,280 drugs, which significantly reduces S100A4 expression in colorectal carcinoma cells. S100A4 suppression is achieved by downregulation of the Wnt/β-catenin pathway. Functional assays revealed that proliferation rates are diminished upon treatment while cell viability is only slightly affected. More strikingly, migration and invasion rates of treated cells are significantly decreased, but rescued by overexpressing S100A4 cDNA. The impact of the small molecule on metastasis formation *in vivo* shows first promising results. In summary, our findings present a new strategy to restrict S100A4 induced metastasis formation in colon cancer.

[1] Stein U., Arlt F., Walther W., Smith J., Waldman T., Harris E. D., Mertins S. D., Heizmann C. W., Allard D., Birchmeier W., Schlag P. M., Shoemaker R. H. (2006): The metastasis-associated gene S100A4 is a novel target of β-catenin/T-cell factor signaling in colon cancer. Gastroenterology 131, 1486-1500