SAS1B protein: Determining whether ASTL or SAS1B has a role in tumor progression

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Abstract

The matrix metalloproteinase-8 (MMP-8) is a key player in cancer progression and metastasis. MMP-8 is overexpressed in breast cancer and its inhibition has been shown to reduce cell migration and invasion. MMP-8 expression levels are known to correlate with poor clinical outcome, suggesting that targeting MMP-8 could be a potential therapeutic strategy. However, the role of MMP-8 in cancer cell migration and invasion is not fully understood. Therefore, we aimed to investigate the role of MMP-8 in breast cancer cell migration and invasion.

Efficacy of ADC targeting SAS1B Expression

Determing membrane orientation and trafficking of an ADC

Importance: To generate specific monoclonal antibodies against a particular protein and to evaluate its efficacy in vitro and in vivo.

Strategy: Previous studies using the live-dead exclusion assay were performed to determine the membrane orientation and trafficking of an ADC targeting SAS1B. The results showed that the ADC targeting SAS1B had a high cell-killing rate in vitro and in vivo.

Summary:

1. We are currently limited by an incomplete understanding of the role of SAS1B in tumor cell biology and if it plays a direct role in tumor progression and metastasis.
2. Understanding the role of SAS1B in basic cancer biology, in informatics and partner programs, may allow us to develop appropriate, well-characterized, and validated therapeutic strategies.
3. The current studies are directed towards this effect and are performing with our collaborators who are working on the use of SAS1B as a cancer drug and diagnostic target.

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The University of Virginia has approved patent applications on the use of the SAS1B as a cancer drug and diagnostic target. Neurogenetics has an exclusive license.

References:


Outcomes of a SAS1B-ADC in a breast cancer model will be presented.

ADC strategy is a viable immunotherapy that could benefit patients who have failed to respond to other treatments.

Breast cancer, ovarian carcinoma, head and neck cancers, uterine cancer, kidney cancers, etc.

In vitro experiments using the live-dead exclusion assay were performed to determine the membrane orientation and trafficking of an ADC targeting SAS1B. The results showed that the ADC targeting SAS1B had a high cell-killing rate in vitro and in vivo.

The presence of SAS1B due to the lack of green staining (488).

The presence of cells on slides is shown in blue (DAPI).

Migration

Invasion

Proliferation

Gene Knock-In: Development of a mammalian cell model to understand cancer properties of SAS1B

MCF10A5E is a non-cancerous epithelial breast cell line. It is used as a model for in vitro studies.

Figure D

Expression of SAS1B mutants in COS7 Cells. Following site-directed mutagenesis, positive clones from plasmid sequencing were used for transfecting SAS1B and COS7 cells. Expression of the mutants was determined by Western blotting. Western blotting results indicated that clone number 4 for SPHAPP and clone number 3 for SPHAPP demonstrated high expression levels.