Novel Small Molecule Inhibitor of Notch1 Activation

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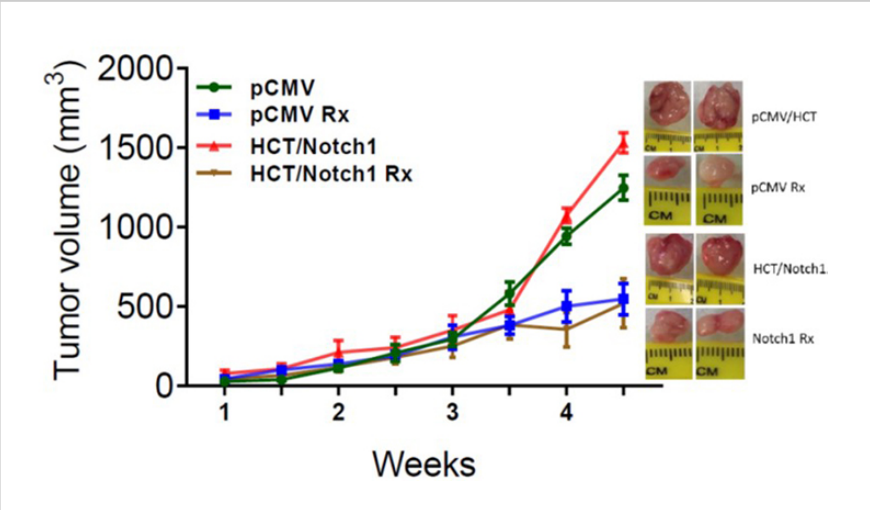

ASR490 inhibits CRC tumor growth

Technology Summary

In colorectal cancer (CRC), Notch1 signaling is a major pathway that governs cancer cell differentiation and proliferation. Its dysregulation is associated with CRC pathogenesis, the second leading cause of cancer death among US men and women combined. Although recent advances in CRC treatment have resulted in dramatic reductions in CRC-related death, CRC-related morbidity in young adults and chemoresistance to existing therapies remains a major challenge.

The inventors have developed a novel suite of small molecule inhibitors, including ASR490, that demonstrate efficacy in both in vitro and in vivo CRC models. Results demonstrate that ASR490 effectively suppresses Notch1 signaling and inhibits epithelial-to-mesenchymal (EMT) transition, which is critical for metastasis. Results further demonstrate that ASR490 significantly reduces cell proliferation and tumor burden in xenograft models.

Application & Market Utility

While screening can significantly improve survival, most patients are diagnosed with CRC at an advanced stage. High toxicity profile and development of chemoresistance are current limitations to pharmacological therapy for CRC. Increasing incidence of chemoresistance to existing CRC therapies and the importance of Notch1 signaling in the maintenance of oncogenic phenotypes suggests that novel therapeutics targeting aberrant Notch1 activation may help to overcome current limitations in the field.

Next Steps

Seek a commercial partner for continued development.

TECHNOLOGY READINESS LEVEL 4-7

Seeking

Licensing |

Keywords

- Notch1
- Colorectal Cancer
- Small Molecule Inhibitor
- Chemoresistance
- EMT Transition Inhibition

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