Natural product silvestrol helps shrink pancreatic tumors in mice

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is one of the most common causes of cancer-related death globally and is increasing in incidence. While some cancers can be effectively treated with immune checkpoint blockade (ICB) therapy, no such treatments currently exist for PDAC, and no effective biomarkers of this disease have been identified. Recently, researchers demonstrated the ability to shrink PDAC tumors in mice using the drug silvestrol. PDAC is associated with mutations in the KRAS gene that cause the excessive production of proteins involved in normal cell functioning, such as ARF6, AMAP1, and MYC. Interestingly, while silvestrol tended to promote tumor growth in mice with PDAC when administered alone, when combined with anti-PD-1 therapy, a form of ICB treatment, silvestrol reduced the size of PDAC tumors by disrupting the ARF6-AMAP1 pathway in KRAS-mutated cells. These results highlight not only the potential for KRAS mutations in cancer cells to serve as biomarkers in patients with drug-susceptible disease but also the potential benefits of silvestrol in ICB therapies targeting PDAC.