Issue Highlights


MiR-143/MSI2/KRAS Cascade Contributes Positively to Carcinogenesis in Human Bladder Cancer.

CADM1 associates with Hippo pathway core kinases; membranous co-expression of CADM1 & LATS2 in lung tumors predicts good prognosis.
A fusion image of matrix-assisted laser desorption/ionization mass spectrometry imaging in the brain tissue section from mice intravenously administrated with eribulin. See also Takahashi et al. (pp. 2247–2257 of this issue).
Cancer Science (formerly Japanese Journal of Cancer Research) is the official journal of the Japanese Cancer Association, and is published monthly. The journal was founded in 1907 as Gann, meaning cancer, by the late Dr. Katsusaburo Yamagiwa, who first produced skin cancer in experimental animals by painting tar on their skin. Cancer Science publishes original articles, editorials, letters to the editor, and reports describing original research in the fields of basic, translational and clinical cancer research. The following subject categories are covered: basic and clinical immunology, carcinogenesis, cell, molecular, and stem cell biology, clinical research, drug discovery and delivery, epidemiology and prevention, genetics, genomics, and proteomics, inflammation and virology, and pathology. The Journal also publishes review articles which may be solicited or submitted.

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1. **EXOSOMES CONTAINING ERBB2/CRK INDUCE VASCULAR GROWTH IN PREMETASTATIC NICHES AND PROMOTE METASTASIS OF BLADDER CANCER**

Locally advanced and metastatic invasive bladder (BC) cancer has a poor prognosis, and no advanced therapies beyond cisplatin-based combination chemotherapy have been developed. Prior studies have shown that CRK, an adaptor protein that mediates the interaction between receptor tyrosine kinases and small G proteins, is overexpressed in BC and induces epithelial-mesenchymal transition (EMT). In this study, Yoshida et al. describes a novel role of exosomes containing ErbB2 and CRK in metastasis. They showed that CRK induced the expression of ErbB2/3 in BC cells and that ErbB2-containing exosomes derived from those cells increased proliferation, invasion and lung metastasis of low grade BC cells in a CRK-dependent manner. They also showed that the ErbB2/CRK unit was transferred from host BC cells to metastatic recipient cells through exosomes, leading to vascular leakiness and proliferation and contributing to metastasis. This suggests that CRK may be a feasible target for patients with ErbB2-overexpressing advanced BC.

https://doi.org/10.1111/cas.14080

2. **MICRORNA-143/MUSASHI-2/KRAS CASCADE CONTRIBUTES POSITIVELY TO CARCINOGENESIS IN HUMAN BLADDER CANCER**

Recent studies have shown that there is a high frequency of mutations in the RAS signaling networks in bladder cancer. Prior studies have shown that the microRNA 3 specifically miR-143 can target KRAS signaling and impede 4 KRAS driven tumorigenesis. miR-143 has been found to be severely down-regulated in several cancers. In this study, Tsujino et al. developed a synthetic miR-143 (syn-miR-143) with a potent RNase-resistant anti-cancer activity, which they used to clarify the mechanism by which miR-143 negatively regulates KRAS signaling. They showed that miR-143 silenced the RNA-binding protein Musashi-2 (MSI2) in bladder cancer cell lines. MSI2 was found to directly interact with KRAS mRNA and post transcriptionally enhance translation of KRAS. This study helps to clarify the complex nature of KRAS networks and offers a novel therapeutic target in bladder and other cancers.

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3. **CADM1 ASSOCIATES WITH HIPPO PATHWAY CORE KINASES; MEMBRANOUS CO-EXPRESSION OF CADM1 & LATS2 IN LUNG TUMORS PREDICTS GOOD PROGNOSIS**

Lung adenocarcinoma is the most common primary lung cancer and is the leading cause of death in developed countries. Cell adhesion molecule-1 (CADM1), which is responsible for cell-cell attachment, has been found to be a critical tumor suppressor in lung adenocarcinoma. Cell contact inhibition is known to play an important role in tumor suppression and members of the Hippo pathway have been increasingly associated with this inhibition. In this study, Ito et al. clarifies the association between CADM1 and core Hippo pathway kinases like MST1/2 and LATS1/2. By immunoprecipitation, they suggested that CADM1 recruited MST1/2 and LATS1/2 to the cell membrane via scaffold protein complexes. This recruitment activates a kinase cascade reaction that induces contact inhibition, which is important for tumor suppression. Furthermore, they showed that co-expression of CADM1 and LATS2 in the membrane projected longer disease free survival. These clinically applicable data warrant further investigation.

https://doi.org/10.1111/cas.14040