Molecular Cancer Research **Highlights**

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Selected Articles from This Issue

Integrin α3β1 Promotes Metastasis

Zhou *et al.* **Page 143**

The laminin receptor α3β1 integrin promotes primary breast cancer growth, but its role in cancer metastasis is unclear. Zhou and colleagues reveal that RNAi-mediated depletion of α3 integrin in a murine model of advanced breast cancer strongly suppressed both spontaneous metastasis and lung-specific colonization. An additional study, using *in vitro* growth assays, implicated an autocrine growth mechanism in which α3β1 interacts with tumor-secreted laminin. Importantly, analysis of human breast cancer specimens revealed reduced survival when both α3 integrin and its ligand laminin-α5 are overexpressed. Thus, α3β1 integrin or its effectors are potential therapeutic targets, especially for those cancers that retain laminin expression.

Significance of FBXW7 in Lung Cancer

Yokobori *et al.* **Page 32**

Lung cancer is a leading cause of mortality, and non–small cell lung cancer (NSCLC) represents a large percentage of all lung cancer cases. In this Rapid Impact article, Yokobori and colleagues report on their study that uncovered the clinical significance of the F-box containing ubiquitin protein ligase FBXW7 in NSCLC. Critically, it was determined that NSCLC cells with suppressed expression of *FBXW7* acquired resistance to taxane-based therapeutics. Interestingly, this acquired resistance was eliminated by treatment with the histone deacetylase inhibitor MS-275. As such, MS-275 has clear clinical ramifications and may be used as a therapeutic tool to treat aggressive taxane-resistant NSCLC tumors that lack FBXW7 expression.

CXCR4 and CXCR7 in Lung Cancer Metastasis

Choi *et al.* **Page 38**

The CXCL12/CXCR4 axis is important for promoting either tumor metastasis or tumor-associated angiogenesis. However, reconciling the most relevant of these functions has been difficult due to the discovery that CXCR7 also binds CXCL12. Thus, the function of CXCR4 versus CXCR7 in mediating CXCL12 needs elucidation. Choi and colleagues demonstrate in NSCLC that CXCR4 is necessary and sufficient to mediate metastasis, whereas CXCR7 is dispensable. Moreover, the magnitude of CXCR4 expression, not CXCR7, in the tumor microenvironment competes for CXCL12, limiting endothelial cell progenitor recruitment and tumor-associated angiogenesis. Thus, the CXCL12/CXCR4 axis mediates tumor metastasis and tumor-associated angiogenesis, and the magnitude of CXCR4 expression is important in modulating this biology.

Inhibition of SCLC Metastasis by miR-355

Gong *et al.* **Page 101**

Small cell lung cancer (SCLC) is a rapidly progressing, incurable cancer that frequently spreads to bone. Gong and colleagues investigated the pathological role of microRNAs in preclinical models of SCLC that metastasize to bone. Selective downregulation of miR-335 was observed in a human SCLC cell line (SBC-5) that homes to skeletal sites in mouse xenograft models. Mechanistically, miR-335 inhibited SCLC metastatic skeletal lesions via deregulation of IGF-1R and RANKL pathways, suggesting miR-335 as a candidate therapeutic target to mitigate bone metastases. This study is the first to associate miR-335 with human SCLC and to link miR-335 with bone metastases of SCLC.