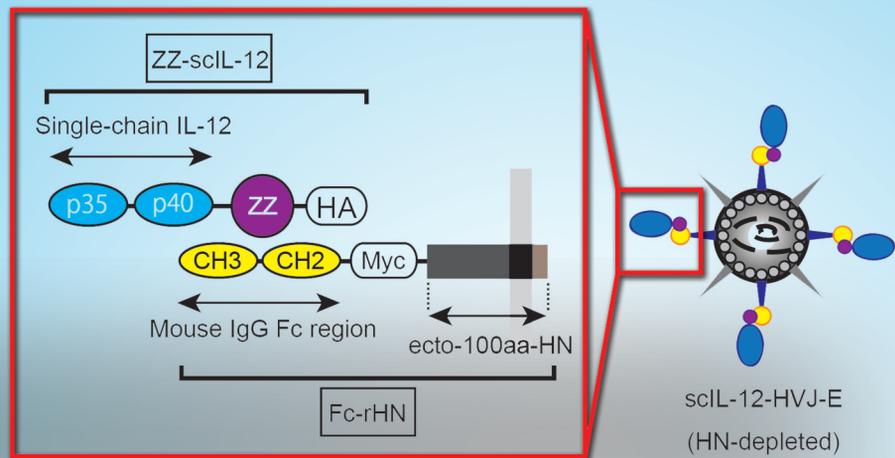


Immune-Stimulatory Pseudovirion for Cancer Therapy

Saga *et al.* _____ Page 668

Sendai virus-envelope (HVJ-E) induces multiple antitumor immunities. However, the limitations of current HVJ-E are the lack of IFN- γ production and the inability to be systemically administered. To overcome these limitations, Saga and colleagues developed single-chain interleukin-12-conjugated HN-depleted HVJ-E (scIL-12-HVJ-E). scIL-12-HVJ-E with high production of IFN- γ eradicated tumors by robust induction of cytotoxic T cells. The particle could be systemically administered because of the lack of hemagglutinating activity. Systemic administration of scIL-12-HVJ-E significantly reduced the number of metastatic foci of melanoma in the lung by regionally inducing IFN- γ . Thus, scIL-12-HVJ-E will be a promising tool to treat metastatic cancers.



BRAF Inhibition Modulates Programmed Death-1-Ligand 1 Expression in Melanoma

Jiang *et al.* _____ Page 598

Jiang and colleagues identify a molecular mechanism that provides the basis for BRAF inhibitor-resistant melanoma cells to evade the immune system via upregulation of the inducible ligand programmed death-1-ligand 1. In addition, a potential molecular means to reverse this through MEK inhibition is described. These findings have implications for therapeutic strategies in the development of targeted combinations as well as combinations of targeted small molecules and immune checkpoint blockade.

Interleukin-8 Regulates Human Breast Cancer Stem Cell Activity

Singh *et al.* _____ Page 643

Interleukin-8 (IL-8) is upregulated in poor prognosis breast cancer, but its role in regulating patient-derived breast cancer stem cell (BCSC) activity remains unknown. Singh and colleagues investigated IL-8 and its receptors, CXCR1/2, in the regulation of BCSCs isolated directly from HER2-positive and -negative patients. Metastatic pleural effusion and ascites fluid IL-8 levels correlated with BCSC activity *ex vivo*. IL-8/CXCR1/2 was shown to regulate BCSC activity via SRC kinase, EGFR/HER2, AKT, and ERK1/2 signaling. For HER2-positive BCSC activity, blockade of CXCR1/2 added to the efficacy of inhibiting EGFR/HER2. However, EGFR/HER2 blockade alone prevented CXCR1/2-induced activity in HER2-negative BCSCs.

EGF Receptor Mutations in Bronchoalveolar Lavage and Pleural Fluids

Buttitta *et al.* _____ Page 691

Assessment of *EGFR* mutations in non-small cell lung cancer patients is required for appropriate selection of treatment. In some cases, the only material available to assess mutations is represented by poor cytologic specimens unsuitable for molecular analysis with conventional techniques. Buttitta and colleagues analyzed a series of cytologic samples with a low rate or absence of neoplastic cells by deep next-generation sequencing (NGS) and Sanger sequencing (SS). NGS allowed the detection of *EGFR* mutations in many cases negative by SS. The authors conclude that NGS may open up the possibility to detect mutations in patients otherwise doomed to rebiopsies or nontargeted therapies.

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