Molecular Cancer Research

# Highlights

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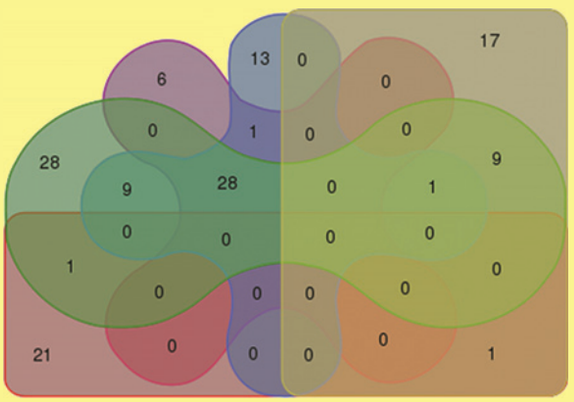
Selected Articles from This Issue




## Gene Profiling of FDC Sarcomas

**Laginestra *et al.*_____Page 541**

Follicular dendritic cell (FDC) sarcomas are rare soft tissue sarcomas with significant metastatic potential. In addition, diagnosis is a challenge due to morphologic and immunophenotypic heterogeneity. To better understand this rare tumor type and uncover potential diagnostic and therapeutic targets, genomic analysis was performed on FDC sarcomas compared to other rare mesenchymal tumors. Based on differential gene expression and pathway enrichment, a number of critical transcriptional programs were identified: signal transduction, cell cycle, metabolism, extracellular matrix (ECM), chromatin organization, and immune system. Further investigation revealed that the PD-1 receptor and its ligands were upregulated in FDC sarcomas and suggests the potential for targeted immunotherapy.

## IDH1-R132H Alters Mouse SVZ and Brain Tumor Progression

**Pirozzi *et al.*_____Page 507**

Mutations in isocitrate dehydrogenase 1 (IDH1) occur in the majority of low-grade gliomas and lead to the production of D-2HG. To determine the effects mutant IDH1 has on neural stem cells (NSCs) and on the microenvironment, Pirozzi and colleagues generated a genetically faithful conditional knock-in mouse model. The data demonstrate that mutant Idh1 confers reduced proliferation of NSCs both *in vitro* and *in vivo*, and results in a disorganized subventricular zone (SVZ). Additionally, this mouse glioma model shows that expression of mutant Idh1 leads to distinct molecular and histological features, and alters the course of tumor progression. Collectively, these findings provide new insights into IDH1-R132H-driven tumorigenesis, and establish a platform for future preclinical investigations focused on mutant IDH1-targeted therapy.

## RNA Hybridization Assay for RNA Pol I Activity

**Guner *et al.*_____Page 577**

Increased nucleolar size and number are common in many cancers. These increases partly reflect increased activity of RNA polymerase I, which catalyzes the synthesis of the precursor rRNA (45S rRNA). Guner and colleagues describe and validate a chromogenic *in situ* hybridization (CISH) assay for the 5′-external transcribed spacer (ETS) of the 45S rRNA in formalin-fixed, paraffin-embedded (FFPE) tissues as a measure of Pol I activity–a therapeutic target in cancer. This 5′ETS/45S signal, restricted to the nucleolus, was attenuated after pharmacological inhibition or RNAi depletion of Pol I. Most invasive prostatic adenocarcinomas and high-grade prostatic intraepithelial neoplasia had increased 5′ETS/45S signals. 5′ETS/45S CISH is a novel, potentially predictive and pharmacodynamic biomarker for Pol I inhibitors in tissue specimens.

## *TRAF6* Expression and Targeting in Multiple Myeloma

**Chen *et al.*_____Page 598**

Bone marrow mononuclear cells from multiple myeloma patients overexpress tumor necrosis factor receptor-associated factor 6 (TRAF6). This protein has been implicated in polyubiquitin-mediated IL1R/TLR signaling through activation of IκB kinase which regulates the NF-κB and JNK signaling pathways. Inhibition of TRAF6 reduces tumor growth and enhances the anti-myeloma effects of proteasome inhibitors. TRAF6 dominant negative peptides also downregulate the RANKL/RANK signaling pathway leading to inhibition of osteoclast cell formation and a reduction in bone resorption. Taken together, these data indicate that targeting TRAF6 is a potential strategy for the treatment of multiple myeloma and its related disease-associated bone loss.



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