

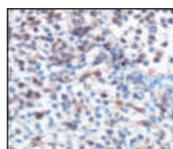
Oxygen Regulates Tumor Cell Immunogenicity

Olin *et al.* _____ Page 4800

Oxygen levels can dictate the expression of many genes, potentially altering immunogenic properties important for tumor cell-based vaccines. In this issue, Olin and colleagues demonstrate that in murine models of glioma and breast carcinoma, 5% O₂-derived vaccines could enhance *in vivo* tumoricidal activity, resulting in extended survival. In the glioma cavity of mice treated with lysate vaccines from 5% O₂, the induction of caspase-3 in glioma cells by multiple CD3⁺ lymphocytes was observed. These findings have important implications for the development of cancer vaccines, which are typically taken from cells cultured in atmospheric oxygen (about 20% O₂).

Roles of HIF-1 α and HIF-2 α in Oral Cancer

Zhu *et al.* _____ Page 4732



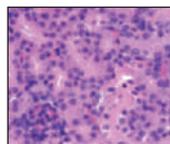
A better understanding of the functional differences between HIF-1 α and HIF-2 α in oral squamous

cell carcinoma (OSCC) is needed. Zhu and colleagues evaluated correlations between HIF-1/2 α expression and clinical-pathological characteristics of OSCC patients, investigated HIF-1 α /2 α -dependent target genes in OSCC cell lines, and examined the contribution of HIF-1 α /2 α to xenograft tumor growth, angiogenesis, and apoptosis. HIF-1 α and HIF-2 α correlated with different clinical-pathological parameters, stabilized at different oxygen levels, and regulated different genes in OSCC. However, both HIF-1 α and HIF-2 α had promoting roles in tumor angiogenesis and growth, suggesting that combined targeting of HIF-1 α and HIF-2 α may improve outcome.

Cisplatin and OCTN2 in Carnitine Wasting

Lancaster *et al.* _____ Page 4789

Carnitine (an essential cofactor for mitochondrial fatty acid oxidation) is reabsorbed by the luminal transporter OCTN2. In humans, cisplatin causes urinary loss of carnitine. To determine the effect cisplatin has on OCTN2 function, Lancaster and colleagues measured carnitine and acetylcarnitine excretion in urine collected from mice with/without cisplatin administration. Cisplatin caused increased urinary excretion of carnitine and acetylcarnitine in wild-type mice but not in Oct1/2(-/-) mice. Gene expression analysis on untreated/treated kidneys showed multiple genes in wild-type mice were downregulated compared to Oct1/2(-/-) mice, including those involved in carnitine shuttling. These findings highlight the role of Oct1/2 in cisplatin-related disturbances in carnitine homeostasis.



Lung SCC mRNA Expression Subtypes

Wilkerson *et al.* _____ Page 4864

Lung squamous cell carcinoma (SCC) has broad clinical, genetic, and morphologic heterogeneity.

Wilkerson and colleagues developed a robust SCC subclassification to describe this variability. They analyzed gene expression arrays from over 400 patients to detect and validate novel gene expression subtypes. The subtypes were found to have significantly different survival outcomes, patient populations, biological processes, and similarities to normal lung cell types. Further, the subtypes stratified heterogeneous SCC into multiple discrete diseases, which could lead to more precise patient prognosis and management, and to advances in basic research.

