Molecular Cancer Research

Highlights

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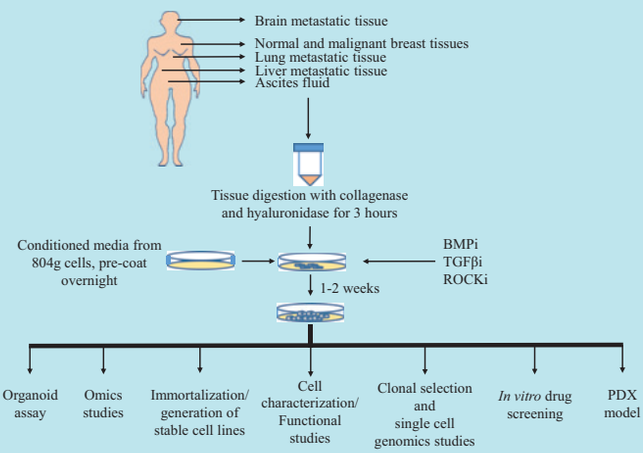
Selected Articles from This Issue



In Vitro Propagation of Primary Epithelial Cells

Prasad *et al.* Page 1556

Mechanistic studies of patient-derived tumor tissues are often limited by sample size and tumor cell content. Methods for culturing primary cells *ex vivo* over a feeder layer are suitable for certain applications, but lack utility in highly sensitive assays like single cell sequencing due to potential contamination by cells from the feeder layer. Here, Prasad and colleagues detail a novel method of propagating dissociated primary cells in tissue culture using defined growth medium with inhibitors of ROCK, TGFβ, and BMP signaling. This method supports the expansion of a variety of cell types, including stromal, luminal, basal, and stem cell subpopulations that are compatible with cell sorting applications and downstream -omics analysis. This method maximizes the utility of primary tissue samples, and broadens the horizon for *ex vivo* analyses.

Subtyping HCC Mouse Models

Friemel *et al.* Page 1493

Mouse models of hepatocellular carcinoma (HCC) often fail to capture the intricacies of human disease, which may influence the clinical applicability of data derived from these models. Here, Friemel, Frick, and colleagues demonstrate the feasibility of using genomic, morphologic, and immunohistochemical analyses to stratify genetically engineered mouse models along eitiologic criteria, matching them with phenotypes observed in human HCC. The authors posit that this data will allow for better alignment of mouse models with HCC subtypes, thereby increasing their clinical relevance.

Energy Profiling in Hypoxic Cancer Cells

Valli *et al.* Page 1531

Hypoxia-inducible factor (HIF)-1α is a key regulator of the cellular response to hypoxia. HIF-1α plays a major role in hypoxic tumor metabolism and owns the potential to be targeted for therapy. However, the mechanism by which cancer cells can adapt to HIF-1α deletion is poorly understood. Integrated metabolomic, proteomic, and transcriptomic analysis by Valli and colleagues has now revealed that HIF-1α-knockout colon cancer cells upregulate creatine metabolism and glucose transporter GLUT14 in response to hypoxic stress. Their data elucidate that colon cancer cell hypoxic metabolism can bypass HIF-1α deletion, provide new insight into the mechanisms underlying hypoxic stress responses, and highlight potential avenues for targeted therapy in colorectal cancer.

p21 Promotes Tumor-Initiating Potential via Wnt/TCF1/Cyclin D1 Upregulation

Benard *et al.* Page 1571

The cell cycle inhibitor p21CIP1 has well-known roles in regulating cellular proliferation, but previous work has shown that it also exerts pro-metastatic effects in mammary tumor models via an unknown mechanism. Here, Benard and colleagues have defined the role of p21CIP1 in promoting cancer stem cell-like phenotypes, demonstrating that its expression is associated with increased Wnt/β-catenin pathway activity through TCF1 and Cyclin D1. Knockout of p21 was concordantly associated with reduction of cancer stem cell properties, inhibition of tumorsphere formation, and suppression of tumor-initiating potential in vivo. The data suggest that, despite its classical role in suppressing cell cycle progression, p21 is also a strong promoter of cancer stem cell properties in mammary cells.

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