Paracrine Signaling between Carcinoma Cells and Mesenchymal Stem Cells Generates Cancer Stem Cell Niche via Epithelial–Mesenchymal Transition…….775
K. Räsänen and M. Herlyn
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Investigating Metformin for Cancer Prevention and Treatment: The End of the Beginning …….778
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BRAF L597 Mutations in Melanoma Are Associated with Sensitivity to MEK Inhibitors …….791
Précis: Non-V600E BRAF mutations that are sensitive to MEK inhibition occur in 8% of “BRAF–wild-type” melanomas.

Proteomic Profiling Identifies Dysregulated Pathways in Small Cell Lung Cancer and Novel Therapeutic Targets Including PARP1 …….798
Précis: Small cell lung cancer cells express significantly higher levels of PARP1 than non-small cell lung cancer cells and are highly sensitive to PARP inhibition.
**DDX5 Regulates DNA Replication and Is Required for Cell Proliferation in a Subset of Breast Cancer Cells**

A. Mazurek, W. Luo, A. Krasnitz, J. Hicks, R.S. Powers, and B. Stillman

**Précis:** DDX5 amplification frequently occurs in breast cancer and promotes cell proliferation by controlling transcription of DNA replication genes.

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**CD36 Repression Activates a Multicellular Stromal Program Shared by High Mammographic Density and Tumor Tissues**


**Précis:** Decreased CD36 expression in mammary stromal cells promotes a pro-oncogenic microenvironment and enhances breast cancer risk.

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**Correction**

**Correction: Gene Signatures Associated with Mouse Postnatal Hindbrain Neural Stem Cells and Medulloblastoma Cancer Stem Cells Identify Novel Molecular Mediators and Predict Human Medulloblastoma Molecular Classification**

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**Cancer-Stimulated Mesenchymal Stem Cells Create a Carcinoma Stem Cell Niche via Prostaglandin E₂ Signaling**

H-J. Li, F. Reinhardt, H.R. Herschman, and R.A. Weinberg

**Précis:** Bidirectional signaling between tumor cells and associated mesenchymal stem cells promotes EMT and enhances cancer stem cell formation.

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Dahlman and colleagues identified a **BRAF**<sup>L597R</sup> mutation in an aggressive **BRAF**<sup>V600E</sup>-negative melanoma, and found that as many as 8% of melanomas classified clinically as “**BRAF** wild type” may actually harbor other less common **BRAF** exon 15 mutations. Importantly, these mutants led to increased MEK/ERK signaling that was readily suppressed by MEK inhibitors, suggesting that patients with these less common **BRAF** mutations may also benefit from MEK inhibitor therapy. Indeed, one such patient with metastatic melanoma enrolled in a phase I trial of an allosteric MEK inhibitor experienced a sustained partial response, indicating that expanded **BRAF** mutational testing may benefit additional patients. For details, please see the article by Dahlman and colleagues on page 791.

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ON THE COVER

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