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    A new tumor suppressor function of the RNA demethylase FTO implicates m^6A RNA modifications in the regulation of cyclic AMP signaling involved in stemness and tumor initiation.

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3215  Obesity/Type 2 Diabetes-Associated Liver Tumors Are Sensitive to Cyclin D1 Deficiency
    Chi Luo, Jiaxin Liang, Kfir Sharabi, Maximilian Hatting,
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    Obesity/diabetes-associated liver tumors are specifically vulnerable to cyclin D1 deficiency and CDK4 inhibition, suggesting that the obese/diabetic environment confers cancer-selective dependencies that can be therapeutically exploited.

MOLECULAR CELL BIOLOGY

3222  Extracellular Vesicles from Cancer-Associated Fibroblasts Containing Annexin A6 Induces FAK-YAP Activation by Stabilizing β1 Integrin, Enhancing Drug Resistance
    Tomoyuki Uchihara, Keisuke Miyake, Atsuko Yonemura,
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    Tadahito Yasuda, Kota Arima, Kazuto Harada,
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    Patrick Tan, Hideo Baba, and Takatsugu Ishimoto
    This study elucidates a novel molecular mechanism through which Annexin A6 in CAF-EV activates FAK-YAP by stabilizing β1 integrin at the cell surface of gastric cancer cells and subsequently induces drug resistance.
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<td>Pharmacokinetic Profiles Determine Optimal Combination Treatment Schedules in Computational Models of Drug Resistance</td>
<td>Itziar Irurzun-Arana, Thomas O. McDonald, Inaki F. Trocóniz, and Franziska Michor</td>
<td>These findings introduce a computational modeling platform and software package for combination treatment strategies with flexible pharmacokinetic profiles and multidrug interaction curves that are estimated from data.</td>
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<td>Senescent Stromal Cells Promote Cancer Resistance through SIRT1 Loss-Potentiated Overproduction of Small Extracellular Vesicles</td>
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<td>Senescent stromal cells produce a large number of sEVs to promote cancer resistance in therapeutic settings, a process driven by SIRT1 decline in stromal cells and ABCB4 augmentation in cancer cells. See related commentary, p. 3193</td>
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<td>Engineering the Human Fc Region Enables Direct Cell Killing by Cancer Glycan-Targeting Antibodies without the Need for Immune Effector Cells or Complement</td>
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<td>NRAS Status Determines Sensitivity to SHP2 Inhibitor Combination Therapies Targeting the RAS–MAPK Pathway in Neuroblastoma</td>
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<td>LDtrait: An Online Tool for Identifying Published Phenotype Associations in Linkage Disequilibrium</td>
<td>AC Shu-Hong Lin, Derek W. Brown, and Mitchell J. Machiela</td>
<td>The new GWAS search tool LDtrait will expedite discovery of shared genetic components underlying seemingly unrelated diseases and may offer novel insights into cancer research.</td>
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Neoadjuvant chemotherapy provides long-term clinical benefits to patients, especially when the primary tumor fully regresses before surgery. However, therapeutic benefits of these anticancer drugs may be limited by tumor-promoting host responses, which are frequently elicited by off-target effects of chemotherapy and are manifested as stromal cell senescence in the tumor microenvironment. Senescent stromal cells produce a large number of small extracellular vesicles (sEV) responsible for development of acquired cancer resistance. With confocal microscopy, active biosynthesis of sEVs by senescent stromal cells can be observed, as evidenced by remarkable expression of CD63 (green), a tetraspanin protein, and TSG101 (red), both typical biomarkers of sEVs. Nuclei were stained with DAPI (blue). For details, see article by Han and colleagues on page 3383.