prognostic factors. This result was also validated in an independent validation cohort (n=53).

Conclusions: Our results demonstrated that Robo4 expression was correlated with surface antigen expression of leukemic cells, cytogenetics, and molecular mutation. Further, high Robo4 expression indicates an unfavorable prognosis in de novo AML patients. It may be used as a biomarker for risk-stratification of AML patients.

PP-14

Deregulated microRNA genes in triple-negative breast cancer revealed by deep sequencing

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Background and aims: Triple-negative breast cancer is a subtype of breast cancer that lacks of immunohistochemical (IHC) expression of estrogen receptor (ER), progesterone receptor (PR), and Human Epidermal Growth Factor Receptor 2 (HER2). Disease outcome of triple-negative breast cancer patients is relatively poor and currently there is no miRNA expression profiling available for elucidating the molecular mechanisms underlying the aggressiveness of triple-negative breast cancer.

Materials and Method: Twenty-four triple-negative breast cancer and 14 adjacent normal tissues were collected from breast cancer patients during surgeries at National Taiwan University Hospital (NTUH, Taipei, Taiwan) from 2004 to 2007. All triple-negative breast cancer samples were invasive ductal carcinomas (IDC). Total RNA was extracted from each triple-negative breast cancer or adjacent normal tissue for SOLiD small RNA ligation sequencing (Applied Biosystems). All small RNA reads were aligned to human miRNA reference using the Small RNA Analysis Tool V0.5 (Applied Biosystems) for quantification of miRNA expression reads. The reference databases used for alignment were miRBase (version 17.0) and human genome RefSeq Hg19.

Results: A total of 113,412,568 miRNA reads were identified from all 38 samples after sequence alignment with the human miRNA reference, yielding a median of 2,670,242 miRNA reads from our sample data (range: 393,305-7,906,634). By using the Student's t-test with the Holm step down procedure for multiple comparisons, a list of 25 significantly expressed miRNAs (adjusted P <0.05) was identified in this study. Hierarchical cluster analysis of the samples using the 25-miRNA signature showed that all triple-negative breast cancer and adjacent normal tissues were classified into two major clusters with 100% accuracy. Moreover, miRNA components within seven genomic miRNA clusters, including the miR-301b-130b cluster at 22q11.21, the miR-497-195 cluster at 17p13.1, the miR-17-92 cluster at 13q31.3, etc., were all found to be differentially expressed in triple-negative breast cancer.

Conclusions: A novel set of 25-miRNA signature identified in this study was an effective classifier for triple-negative breast cancer and adjacent normal tissues. Further investigations of the deregulated miRNA genes may provide insights into the etiology of triple-negative breast cancer at the level of global transcriptomic regulation.

PP-15

Fenofibrate suppresses oral tumorigenesis via reprogramming metabolic processes

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Background and Aim: In Taiwan, oral squamous cell

carcinoma (OSCC) is the most common head and neck cancer with poor prognosis due to frequent lymph node metastasis and local invasion. Most cancer cells rely on a metabolic/cell signaling basis of Warburg effect to generate the energy needed for cellular processes. Metabolic and anti-inflammatory effects induced by peroxisome proliferator-activated receptors (PPARs) are reported to interfere with Warburg effect. Fenofibrate, an agonist of PPAR, is a potent and effective clinical lipid-lowering reagent. Our previous study demonstrated that fenofibrate reduced the tumor incidence rate, decreased the tumor size, and suppressed the tumor progression into squamous cell carcinoma in an oral-specific 4-nitroquinoline 1-oxide (4-NQO)/arecoline mouse model. We also found that fenofibrate inhibits the invasion and migration of CAL27oral cancer cells, which were correlated with adenosine 5'-monophosphate-activated protein kinase signaling. The aim of this study was to explore the antitumor effects and mechanisms of fenofibrate on metabolic reprogramming and molecular signaling.

Materials and methods: We used SAS (high-grade malignant cells) and OECM1 (low-grade malignant cells) to explore the effect of fenofibrate on metabolic reprogramming. Primary cultured cells from mouse tongue cancer were used to examine the metabolites in glycolysis and tricarboxylic acid cycle. The preventive and therapeutic efficacy of fenofibrate was evaluated in an oral-specific 4-NQO/arecoline mouse model.

Results: We found that fenofibrate induced metabolic reprogramming by changing the protein expressions of hexokinase II (HK II), pyruvate kinase, pyruvate dehydrogenase, and voltage-dependent anion channel (VDAC), which are associated with Warburg effect. In addition, fenofibrate inhibited the binding of HK II to VDAC and increased metabolites in tricarboxylic acid cycle. In oral-specific mouse model, we found fenofibrate had both preventive and therapeutic efficacy on oral tumorigenesis. Fenofibrate treatment suppressed the incidence rate of tongue lesions, reduced the tumor multiplicity, decreased the tumor size, and decreased the immunoreactivity of mTOR.

Conclusions: Fenofibrate demonstrated both preventive and therapeutic efficacy on oral tumorigenesis. The molecular mechanisms involved in inducing the dissociation of HK II from the mitochondria and promoting metabolic reprogramming. Our findings provide a molecular rationale, whereby fenofibrate exerts anticancer effects and additional beneficial effects for the treatment of cancer patients.

PP-16

Direct identification of drug-selected cancer stem-like cells from tumor xenografts by molecular imaging technique

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Background and aims: Cancer stem cells (CSCs) are a small subset of cancer cells capable of self-renewal and tumor maintenance and able to escape chemotherapy and metastasis. Although CSCs can be generated in vitro by non-adherent suspension culture in serum-free medium, the biologic characteristic of tumorspheres was far from CSCs in real tumors due to the distinct environmental factors, such as stromal cells, inflammation and hypoxia within tumor, which may -