pipeline, based on fitted beta distributions, to accurately quantify and compare alternative splicing across different types of senescent cells, relying both on public and in-house RNA-seq datasets.

Results and discussions Our analyses reproducibly identified, at a transcriptome-wide level, the alternative splicing changes specifically related with replicative and different types of induced senescence in multiple types of cells. For instance, Ras-induced senescence appears to associate with alterations in the splicing of genes involved in the secretory pathway and intracellular trafficking.

Conclusion Differential splicing analyses based on beta distribution modelling contribute to elucidate the specific alternative splicing signatures of different types of senescent cells, providing insights for targeting senescence in cancer therapies.

Cancer Cell Metabolism

PO-212 MORPHOLOGICAL HETEROGENEITY OF HEPATOSPLENIC GAMMA/DELTA T-CELL LYMPHOMA

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Introduction Hepatosplenic gamma/delta T-cell Lymphoma (HSTL) is a systemic extra-nodal lymphoma originating from cytotoxic T-cells expressing the gd receptor. We report clinical, morphologic and phenotypic characteristics of 3 patients with HSTL.

Material and methods All patients were male and presented at a mean age of 23 years. One was treated with azathioprine for inflammatory bowel disease, the two others had no history of immunosuppression. All patients were admitted to the hospital with high fever and hepatosplenomegaly. Two presented severe abdominal pain and lymphadenopathy.

Laboratory studies of the three patients were different:

- Case 1: thrombopenia and bone marrow infiltration with 69% of large lymphomatous blast cells and minimal peripheral blood infiltration.
- Case 2: pancytopenia without excess of blasts in the peripheral blood and moderate bone marrow infiltration in cytometry. Morphological and immune-phenotypical studies of the spleen (after splenectomy) showed a massive infiltration by lymphocytic small cells.
- Case 3: pancytopenia with 25% and 45% of blast cells in the peripheral blood and bone marrow aspirate respectively.

Immuno-phenotyping showed a T lymphocytic population double negative (CD3pos CD4neg CD8neg to dim) with gamma-delta expression, CD1a- CD2 +CD5 CD7+CD56 +CD57 in all 3 patients.

Two patients underwent an initial treatment with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone: the first died after 4 months, and there is no response to treatment in the second patient. Treatment was recently initiated in the third patient.

Results and discussions In our series, HSTL confirmed a predilection to develop most often in young men with hepatosplenomegaly. Variable degrees of hematologic abnormalities were observed. Thrombocytopenia was the most striking finding in all. Bone marrow involvement is described in approximately two thirds of patients but was observed by immunophenotyping in our 3 cases. We show that immunophenotyping seems to be the best method for the rapid characterisation of the lymphoma cells morphologically heterogeneous and difficult to identify.

Conclusion HSTL is an infrequent, rare aggressive tumour. The diagnosis is difficult. There is no treatment consensus and the prognosis remains poor.

PO-213 HIGH GLUCOSE AFFECTS ER +BREAST CANCER CELL METABOLISM

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Introduction *In vitro* high glucose (HG) level, mimicking hyperglycemia condition *in vivo*, has been reported to influence breast cancer cells growth, proliferation and survival suggesting glucose as being crucial for breast cancer progression and response to therapy in diabetic patients. Diabetes, in turn, might have a direct effect on breast cancer prognosis. This study investigated the impact of HG on MCF-7 breast cancer cell metabolism and phenotype.

Material and methods MCF-7 breast cancer cell line were cultured in DMEM with high glucose (HG 25 mM) and low glucose (LG 5 mM). Metabolic fluxes analyses were performed with Seahorse Bioanalyzer. Live cell imaging for reactive oxygen species (ROS) content was performed by confocal microscopy by using DCF-DA as selective probe. Mitochondrial DNA (mtDNA) and protein expression were evaluated by qPCR and western blotting respectively.

Results and discussions Using a metabolic fluxes analyses, we showed a significant reduction of the mitochondrial oxygen consumption rate (OCR) and glycolysis-related extracellular acidification rate (ECAR) in MCF-7 cultured in HG- as compared in LG-medium. According with these results, MCF-7 in HG displayed lower mtDNA amount and increased ROS level. Furthermore, the analysis of stemness markers revealed a significant upregulation of Nanog, Lin28 and Myc thus suggesting an increased stem-like phenotype due to growth in HG.

Conclusion Overall our results indicate that glucose may foster breast cancer progression promoting stem cell-like phenotype strongly affecting the metabolic profile in MCF-7 cell line. Further investigations are ongoing to define the mechanism underlying the switch towards an undifferentiated state to be exploited as therapeutic target.

PO-214 COMBINATION OF MOLECULAR HYDROGEN (H2) AND 5-FLUOROURACIL (5-FU) IN CANCER TREATMENT

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Introduction Oxidative stress is clearly recognised as involved in cancer development, as H_2 is clearly recognised as a patent