

Results: The results showed that the studied drugs reduced cell viability in a time-, dose- and cell line-dependent manner, being the 697 cells more sensitive than KOPN-8 cells. B-ALL cells were found to be more sensitive to DAC (697 10 μM ; KOPN-8 > 15 μM) than to 5-AC (697 15 μM ; KOPN-8 > 20 μM), after 72h of treatment. They were also more sensitive to PAN (697 7.5nM; KOPN-8 > 20 nM) than to SAHA (697 750 nM; KOPN-8 1,000 nM). In addition, therapeutic associations of DAC with PAN or SAHA reduced more effectively the cell viability when compared to monotherapy treatments. These drugs induced predominantly apoptosis in 697 cells and apoptosis and necrosis in KOPN-8 cells. Moreover, SAHA induced cell cycle arrest in phase S and G0/G1, respectively in 697 and KOPN-8 cells. Finally, both DNMTi and their association with PAN induced a decrease in 5-mC levels and the demethylation of at least two TSGs (697: TP73, KLLN, MGMT, and CD44; KOPN8: MGMT and STK11).

Conclusions: Our results suggest the therapeutic potential of epigenetic modulators in the treatment of B-ALL in monotherapy and in association with panobinostat.

P38. DETECTION OF *HELICOBACTER PYLORI* IN EXTRAGASTRIC TISSUES: ASSOCIATION OF INFECTION WITH CARCINOGENESIS

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Introduction: *Helicobacter pylori* (HP) is a gram-negative micro-aerophilic bacterium that has been described as the main pathogen of several benign and malignant diseases of the digestive tract, such as gastric and duodenal ulcers, chronic gastritis, hepatobiliary diseases, gastric lymphoma and carcinoma. HP was classified as class I human carcinogen in 1994. The relationship between HP infection and extragastric diseases has been investigated over the years with contradictory conclusions. The objective of this work is to perform a bibliographic review on the association between HP infection and the development of extragastric pathologies, particularly of pancreatic carcinoma. It is also intended to determine the best method for the detection of the bacterium.

Materials and methods: work was based on the literature from the following databases: b-on, PubMed, SciELO, Wiley Online Library and Scientific Repository of the Polytechnic Institute of Lisbon, under the terms "Helicobacter spp.", "Helicobacter pylori", "pancreatic cancer", "extragastric diseases", "risk of pancreatic cancer" and "CagA". From a total of 32 analyzed articles, 18 were selected, excluding those with dubious methods and results, that were not performed in human samples and meta-analysis.

Results: In the selected studies the presence of HP DNA was detected by Polymerase Chain Reaction (PCR) in more than 50% of the pancreatic and hepatocellular cancer samples. There was also an association between the presence of this bacterium and colonic cancer, primary sclerosing cholangitis, primary biliary cirrhosis, cholecystitis and biliary tract carcinoma. However, detection by enzyme-linked immunosorbent assay provided ambiguous results, with 2 of the studies showing no association between infection and pancreatic cancer, while others showed positive results below 50%. There are also 3 studies that related the seroconversion of cytotoxin-associated gene A negative to pancreatic carcinoma. Other methods like histochemical and immunocytochemistry (ICQ) techniques were compared to each other and the results demonstrated that ICQ had the greatest consistency.

Conclusions: The majority of the studies demonstrated an association between HP infection and the development of extragastric diseases. Therefore, HP is a potential risk factor for the etiology of these pathologies. Comparing previous methods, it was possible to observe that PCR was the most sensitive and specific technique for HP detection.

P39. CONSERVED EMBRYONIC SIGNALING PATHWAYS INHIBITORS AS NEW THERAPEUTIC STRATEGIES IN B-CELL NEOPLASMS

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Introduction: B-cell neoplasms are a heterogeneous group of diseases that include B-cell lymphomas and plasma cell disorders. Multiple myeloma (MM) is a malignant neoplasm originated by the proliferation of monoclonal plasma cells that remains incurable. Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma, with a fast growing that is rapidly fatal if untreated. Inappropriate activation of conserved embryonic signaling pathways critical for stem cell self-renewal and differentiation in hematopoiesis, such as WNT/ β -catenin and Hedgehog, has been implicated in these B-cell neoplasms. The main goal of this study was to evaluate the therapeutic potential of WNT/ β -catenin and Hedgehog inhibitors, respectively IWR-1 and vismodegib, alone and in combination in MM and DLBCL cell lines.

Materials and methods: The therapeutic potential of IWR-1 and vismodegib in monotherapy and in therapeutic combination was evaluated in two in vitro models of MM and DLBC, the H929 and FARAGE cell lines, respectively. The metabolic activity was evaluated by resazurin assay and cell death by optical microscopy (May-Grunwald staining) and flow cytometry (FC; Annexin V/7-AAD staining). Cell cycle analysis was evaluated by FC, using a PI/RNase solution. Proteins related to apoptosis (BAX, BCL2, caspases) and some molecules related to WNT and HH signaling pathways (β -catenin and p-ERK) were tested by FC. The results were statistically analyzed considering a level of significance of 95% ($p < 0.05$).

Results: The results showed that IWR-1 and vismodegib reduced metabolic activity in a time- and dose-dependent manner. H929 cells were more sensitive to IWR-1 (IC50 40 μM) than FARAGE cells (IC50 75 μM), while FARAGE cells were more sensitive to vismodegib (IC50 57 μM) compared to H929 (IC50 70 μM). The reduction of metabolic activity was more pronounced in the combination regimens as well as in the fractional administration of drugs compared to single-dose regimens. IWR-1 and vismodegib induced cell death by apoptosis, associated with increased activated-caspases, and G0/G1 cell cycle arrest. In addition, both drugs induced a decrease in β -catenin and p-ERK expression levels, more pronounced in MM cells (H929).

Conclusions: The results suggest that MM cells are more sensitive to WNT/ β -catenin pathway inhibitors and LDGCB cells to Hedgehog pathway inhibitors. However, both drugs may represent potential therapeutic approaches in these lymphoid neoplasms, especially in therapeutic combination.

P40. FADU RESPONSE TO CISPLATIN, DOCETAXEL AND 5-FLUOROURACIL - IN VITRO PRELIMINARY RESULTS

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