PO-116  INCREASE IN PROTHYMOSIN ALPHA EXPRESSION WITH HISTOLOGICAL AGGRESSIVENESS OF GLIOMA
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Introduction Gliomas are the most common primary brain tumours accounting for 2.5% of the total cancer deaths worldwide. c-Myc is a proto-oncogene, it plays an important role in initiation and progression of gliomas. It upregulates expression of nuclear onco-protein prothymosin alpha (PTMA). PTMA is a transcription factor with a spectrum of functions ranging from cell cycle regulator to immunomodulatory function depending upon its distribution. Its overexpression is reported in malignancies of breast, liver, lung and bladder.

Material and methods This study was conducted on patients who underwent elective surgery for glioma (n=176). The histological grading and MIB1 labelling index was recorded from surgical pathology reports. Expression levels of PTMA in these tissues were assessed by immunohistochemistry.

Results and discussions Our study population consisted of 30 (17%) Grade I, 56 (31.8%) Grade II, 45 (25.6%) Grade III and 45 (25.6%) Grade IV glioma cases. PTMA expression was significantly associated with the histological grades of glioma (p<0.0001, Kruskal-Wallis test) and proliferative capacity assessed by MIB1 labelling index (p=0.0125, Kruskal-Wallis test). PTMA expression was not associated with age, sex and the site of the glioma. Though c-Myc expression was not done in this study previous studies showed its expression was associated with the histological grades of glioma.

Conclusion Our study demonstrates the involvement of PTMA overexpression in the pathogenesis of glioma and its association with histological grading and proliferation. Differential expression of this protein suggests its potential utility in histological grading and prognosis of glioma.

PO-118  THE EXPRESSION OF THE CALCIUM-SENSING RECEPTOR IN COLON ORGANOID
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Introduction The calcium-sensing receptor (CaSR) is a heterotrimERIC G protein-coupled receptor that was firstly identified as a key regulator of Ca++ homeostasis in the blood. Ubiquitously expressed in the body, the CaSR controls also cell proliferation, differentiation and apoptosis. In colorectal cancer the CaSR slows cell proliferation and induces apoptosis, however, it is down-regulated during tumorigenesis due to unclear mechanisms. Moreover, a common view on CaSR localization within normal intestinal crypts is still missing.

We hypothesise that restoring CaSR expression inhibits tumour progression. Therefore, it is of paramount importance to understand the mechanisms that regulate CaSR expression in normal colonic epithelia and in tumours.

Our aim is to find ways to restore CaSR expression by inducing differentiation in colonic organoids.

Material and methods We used a 3D cell culture methodology, culturing colon organoids in matrigel. The organoids were generated extracting colonic crypts from the intestine of the mice and were kept in standard stem cell media to guarantee stem cell poll.

We induced lineage-specific differentiation of colonic organoids either into enterocytes or goblet cells by altering the composition of the culturing media. We assessed CaSR expression by RT-qPCR and immunofluorescence, testing also specific differentiation markers such as FABP2 for enterocytes and MUC2 for goblet cells.

PO-117  ROLE OF NFE2L3 IN COLON CANCER BY REGULATING CANCER CELLS PROLIFERATION
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Introduction Dysfunctional transcriptional and signalling networks play a fundamental role in colorectal cancer (CRC), one of the most common and fatal malignancies worldwide. Different molecular CRC subtypes have been identified, and understanding of the underlying pathogenesis of CRC formation is crucial for predicting prognosis and treatment response. Constitutive NF-kB activation is a hallmark of colon tumour development. In this study, we aimed to unravel the cellular network governing NFE2L3 regulation and function. We report that NFE2L3 acts as a central player in a newly identified NF-kB signalling pathway that controls colon cancer cell growth.

Material and methods We analysed the level of NFE2L3 in colon cancer samples extracted from patients. We compared by qPCR and immunohistochemistry the level NFE2L3 expression in normal and tumour tissues. We performed a knockdown of NFE2L3 in different colon cancer cell lines. We characterised the phenotype associated to its depletion in vitro and in vivo. Then, we used a CHIP sequencing analysis to identify the targets of NFE2L3 in our models and we validated by qPCR the direct link between NFE2L3 expression and targets discovered. Finally, by using a strategy of immunoprecipitation associated to mass spectrometry analysis, we identified potential proteins implicated in the pathway of NFE2L3 in colon cancer.

Results and discussions Firstly, we observed that the expression of NFE2L3 in colon cancer samples is significantly higher compared to in normal colon tissues. Moreover, the expression of this protein directly correlated to the survival of patients and could be used as a prognostic marker in colon adenocarcinoma. After that, we depleted the expression of NFE2L3 and we observed that the proliferation of colon cancer cells was slow down. Then, we identified NF-kB pathway as a key regulator of NFE2L3 expression by regulating promoter region. Finally, we demonstrated that NFE2L3 controls the cell cycle in cancer cells by modulating the expression of negative regulators of proliferation.

Conclusion Taken together, based on our observations, we propose the existence of a novel oncogenic pathway, comprising the NF-kB, NFE2L3 and cell cycle regulators, that controls cancer cell growth. Our study establishes a key role for the NFE2L3 transcription factor that regulates cell cycle progression in colon cancer cells.