Endocrine Abstracts

September 2020 Volume 70
ISSN 1479-6848 (online)

22nd European Congress of Endocrinology

5-9 September 2020, European Society of Endocrinology

eECE 2020
22nd European Congress of Endocrinology

published by
bioscientifica

Online version available at
www.endocrine-abstracts.org

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Therefore, we conclude thatEMT occurs in some somatotropinomas, but it does not seem to explain their response to SRL in this subset of tumors. However, in the rest of somatotropinoma *SNAI1* and *RORC* may predict the response to SRL treatment.

DOI: 10.1530/endoabs.70.AEP729

AEP730

Global methylation-demethylation status in pituitary neuroendocrine tumors as potential therapeutic target

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Background
The altered DNA methylation of certain genes in Pituitary Neuroendocrine Tumors (PitNETs) are well known. However little information is available regarding global methylation changes and the process of demethylation in these tumors. In addition, influencing global methylation-demethylation could be a potential new therapeutic option especially in clinically non-functional PitNETs.
Material and methods
Overall, 44 fresh frozen pituitary adenoma tissues (29 gonadotroph, 12 somatotroph, 3 corticotroph) were collected and characterized according to the 2017 WHO classification. Decitabine was used to alter global methylation-demethylation status on *in vitro* GH3 and RC-4B/B cell lines. In tissue samples 5-hydroxymethylcytisone (5 hmC), UHRF1-2 protein and Ki-67 were assessed by immunohistochemistry; gene expression of DNA Methyl-transferase (DNMT1), methyl-cytosine dioxygenases (TET1-3) and ubiquitin-like with PHD and ring finger domain (UHRF1-2) were investigated by RT-qPCR. 5-methylcytosine (5 mC) and 5 hmC level were determined by HPLC-MS/MS method.
Results
Decitabine decreased 5-methylcytosine (5 mC) and increased 5 hmC levels *in vitro* in both pituitary cell lines. Parallel, cell proliferation and viability were decreased significantly. UHRF1-2 were also altered upon decitabine treatment *in vitro*. Interestingly, in PitNET tissue samples 5 hmC was gradually decreased in samples with higher Ki-67 index. In samples with different histology UHRF2 showed different expression, while UHRF1 showed gradual increase in adenoma samples with higher Ki-67 index. Additionally, UHRF2 positively correlated with 5 hmC level in pitNET tissues and both UHRF1 and UHRF2 showed significant positive correlation with DNMT1 and TET1-3 expression.
Conclusion
Our results showed that methylation-demethylation process (5 hmC, DNMT1, TET1-3 and UHRF1-2) is closely linked to proliferative behaviour of PitNETs. Altering global 5 mC and 5 hmC level can be a potential, new therapeutic target in therapy resistant pituitary tumors.
Grants and financial support
This work has been funded by the National Program of Bionics (Program Medical Bionics lead by Attila Patócs) and Semmelweis Innovation Found (STIA_19) to Henriett Butz. Henriett Butz is a recipient of Bolyai Research Fellowship of Hungarian Academy of Sciences and ÚNKP-18-4-SE-8 New National Excellence Program of The Ministry of Human Capacities.

DOI: 10.1530/endoabs.70.AEP730

AEP731

The expression of oxytocin receptor (OXTR) in metastatic pancreatic neuroendocrine tumors (PNETs)

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Introduction
Pancreatic neuroendocrine tumors (PNETs) are rare malignant neoplasms which incidence is continually increasing. They are characterized by diverse biological behaviour and impact on the patients' prognosis, ranging from clinicaly indolent to very aggressive. Oxytocin receptor (OXTR) is a member of the family of G-protein receptors and is present on the cell-surface of the gastrointestinal organs. Unfortunately, theimpact of OXTR signaling on the development of PNETs and its underlying molecular mechanisms involved in gastrointestinal oncogenesis remains unsufficiently researched. Theaim of our study was to assess the expression of OXTR in a group of patients diagnosed with metastatic PNETs.
Material and methods
Metatatic PNETs (liver metastases) specimens ($n=24$) matched control (normal) tissue were surgically collected and mRNA expression was determined by Real-time polymerase chain reaction (Real-time-PCR). OXTR expression for tumor and control tissue was additionally analysed by immunohistochemistry.
Results
Compared to normal tissue, the OTXR showed significant overexpression in metastatic PNETs. Moreover, significant overexpression of OXTR in tumor tissue was confirmed by immunohistochemistry.
Conclusion
Our findings highlight the possibility of making OXTR a promising novel molecular target for imaging and different therapeutic approach in patients diagnosed with metastatic PNETs.

DOI: 10.1530/endoabs.70.AEP731

AEP732

Metastatic insulinoma managed with lutetium (177LU) and somatostatin analog

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Background
Insulinoma is a rare tumour representing 1–2% of all pancreatic neoplasms and it is malignant in only 10% of cases. Locoregional invasion or metastases define malignancy, whereas dimension (> 2 cm), CK19 status, tumor staging and grading (Ki67 > 2%), and age of onset (> 50 years) can be considered elements of suspect.
Case presentation
We report a case of malignant insulinoma in a 80 year old woman presenting symptoms compatible with hypoglycemia. Low blood glucose levels (< 40 mg/dl) were documented during of these episodes. Symptoms regressed with food intake and intravenous glucose administration. No abnormality was detected in the biochemical evaluation. Prolong fasting test was performed, and the patient underwent symptomatic hypoglycemia at the 5th hour. Plasma glucose level was 39 mg/dl, insulin level 36.4 uIU/mL and C-peptide 9.28 ng/ml. Glucagon responce was measured 10 min. intervals, 85 mg/dl, 95 mg/dl and 113 mg/dl respectively. These results were suggestive of endogenous hyperinsulinemia. Magnetic resonance imaging revealed a invasive mass in the pancreatic tail location ~ 63×40 mm in size and multiple metastatic nodules in the the liver. Ga–68 DOTATATE PET-CT, which showed a lesion located in the pancreatic tail location and multıpl metastatic lesion in the liver, with a high somatostatin receptor density. Tru-cut biopsy made from liver lesions revealed the insulinoma tumour metastasis. Synaptophysin, pancytoceratine and chromogranin were positive. The histopathological diagnosis was suggestive of a neuroendocrine, grade-2 tumour (mitotic rate 1/10 HPF, KI-67 proliferative index 15%). Lanreotide 120 mg IM was started an every 28 days basis. The patient received 2 infusions of radiolabeled somatostatin analog lutetium (177LU) 8 weeks apart and denied any hypoglycemia. After the second administration of the lutetium, Ga–68 DOTATATE PET-CT had shown objective metabolic and radiologic response to treatment. Lutetium treatment was given as 8 cycles. Treatment of the patient with metabolic and radiological responses continues with lanreotide 90 mg/every 28 days.
Conclusions
We report a case of metastatic insulinoma treatment with somatostatin analog and Lutetium. Due to previous glycemic control reports and objective responses in unresectable cases, we decided to use Lutetium together with lanreotide. The patient's hypoglycaemia improved immediately after treatment. Unresectable metastatic insulinomas may present as a major therapeutic challenge for the physician. Treatment with landreotide and Lutetium