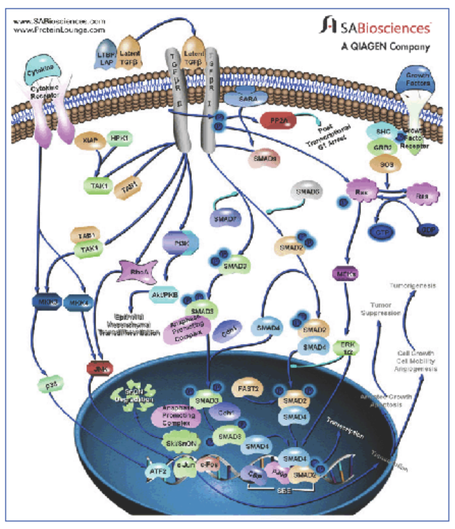
Role of TGF beta-1 in regulating pancreatic neuroendocrine tumor cell viability

Simona Falletta[1], Teresa Gagliano[1], Erica Gentilin[1], Carmelina Di Pasquale[1], Katiuscia Benfini[1], Vanessa Polenta[2], Massimo Falconi[2], Stefano Partelli[2], Ettore degli Uberti[1], Maria Chiara Zatelli[1]

[1] Department of Medical Science, Section of Endocrinology and Internal Medicine, University of Ferrara, Ferrara, Italy
[2] Pancreatic Surgery Unit, San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy

BACKGROUND

Pancreatic neuroendocrine tumors (pNETs) are neoplasms arising from neuroendocrine cells spread in the gastro-entero-pancreatic ephitelium. The role of transforming growth factor beta-1 (TGF-β1) in NET biology is largery unknown. TGF-β1 signaling pathway is tumor suppressive in most non-transformed ephitelial cell lines. In contrast, many human carcinomas are refractory to the growth-inhibitory effects of TGF-β1

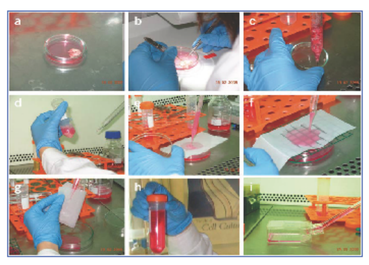


AIM

To investigate if TGF-β1 may modulate cell viability and apoptosis in NET of the pancreas and to understand whether TGF-β1 may influence the effects of therapeutic molecules currently used in the management of pNETs

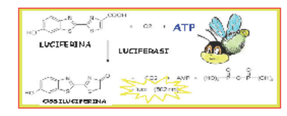
MATERIALS AND METHODS

20 primary cultures obtained from surgical samples of pNETs were treated with TGF-β1 and/or Everolimus, a mTOR inhibitor. Cell viability and caspase activity were evaluated



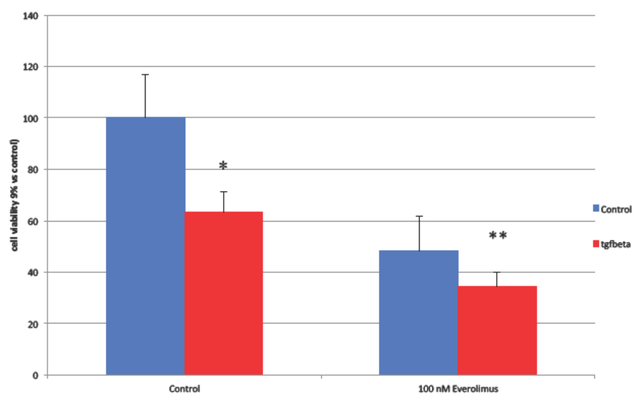
RESULTS

CELL VIABILITY ASSAY

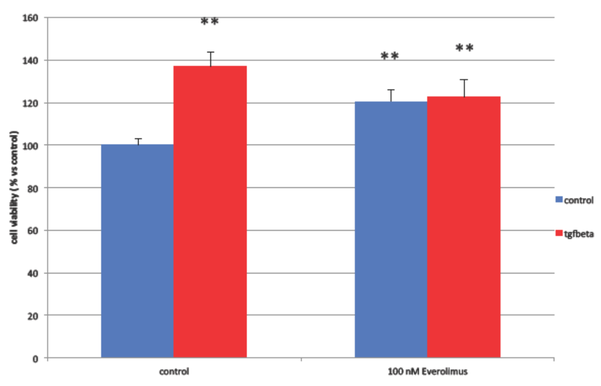


TGF-β1 reduced cell viability by 40% in "responder" pNETs.
In this group, TGF-β1 and Everolimus induced a significant decrease in cell viability by 65%, which was not observed under treatment with Everolimus alone

RESPONDERS pNETs



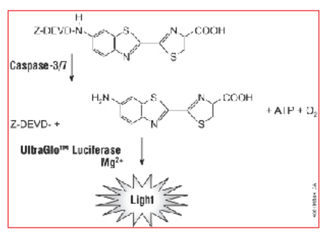
NON RESPONDERS pNETs



*p<0.05 vs. control

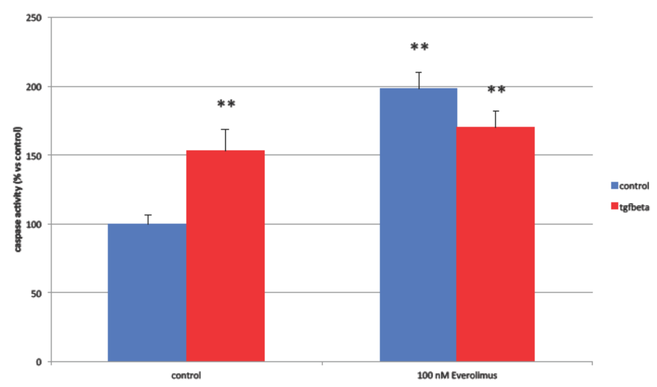
TGF-β1 induced an increase by 37% in "non responder" pNETs and didn't influence the effect of Everolimus when used in combination.

CASPASE ACTIVITY ASSAY



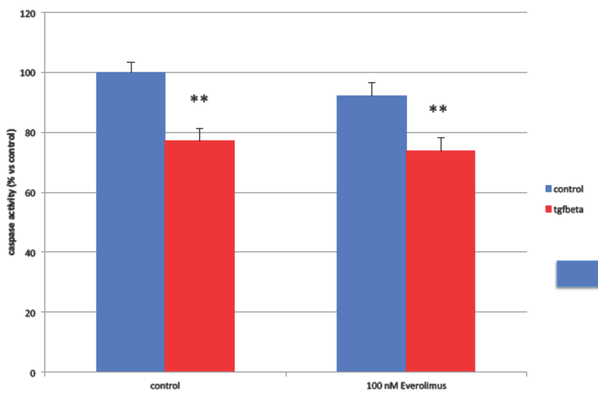
TGF-β1 increased caspase activity by 53% in "responder" pNETs.

RESPONDERS pNETs



** p<0.01 vs. control

NON RESPONDERS pNETs



** p<0.01 vs. control

TGF-β1 decreased caspase activity by 30% in "non responder" pNETs.

CONCLUSIONS

TGF-β1 reduces cell viability of a pNETs sub-group and may cooperate with Everolimus in inducing growth arrest. Further studies are necessary to understand TGF-β1 related functional context in pancreatic neuroendocrine tumors

17 ECE
171--EP
Reproduction, endocrine disruptors and signalling
Simona Falletta
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY
PosterSessionOnline.com