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

Simona Falletta1, Teresa Gagliano1, Erica Gentilin1, Carmelina Di Pasquale1, Katiucia Benfìni1, Vanessa Polenta1, Massimo Falconi2, Stefano Partelli2, Ettore degli Uberti1, Maria Chiara Zatelli1

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 epithelium. The role of transforming growth factor beta-1 (TGF-β1) in NET biology is largely unknown. TGF-β1 signaling pathway is tumor suppressive in most non-transformed epithelial 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

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.

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

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.