Influence of mTOR and ERK 1/2 pathways on the IGF-1 negative feedback in GH secreting pituitary adenoma cell line

Carmelina Di Pasquale, Mariaenrica Bellio, Erica Gentilin, Teresa Gagliano, Simona Falletta, Katiuscia Benfini, Maria Rosaria Ambrosio, Ettore degli Uberti, Maria Chiara Zatelli.

Department of Medical Science, Section of Endocrinology and Internal Medicine, University of Ferrara, Italy

Background: Gigantism and Acromegaly are the main consequences of GH excess, mainly due to a pituitary adenoma. Surgery is the first therapeutic option, but also medical therapy is employed, being mostly represented by somatostatin analogues (SSA), that reduce both tumor mass and GH hypersecretion. However about 10% of patients is resistant to SSA.

PI3K/Akt/mTOR pathway, activated by growth-factors such as IGF-1, is important in regulating many cellular processes.

Aim: To understand whether PI3K/Akt/mTOR and ERK 1/2 pathways can influence IGF-1 feed-back in GH secreting pituitary adenoma cell line, we employed three inhibitors: Everolimus (mTOR inhibitor), NVP-BEZ235 (mTOR and PI3K inhibitor) and SCH772984 (ERK 1/2 inhibitor), evaluating their effects in presence or in absence of IGF-1.

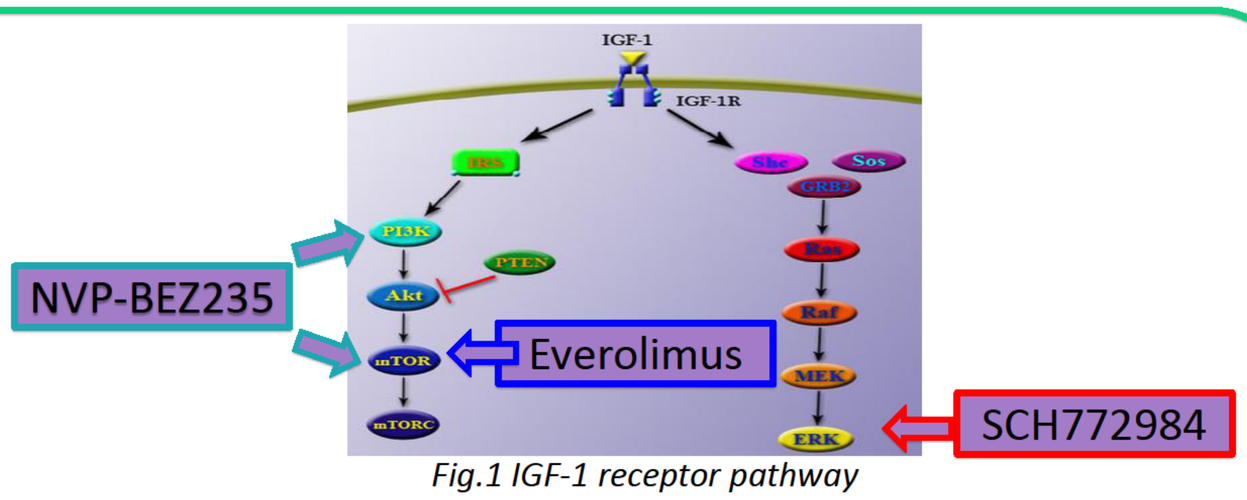
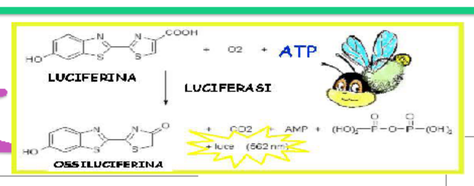


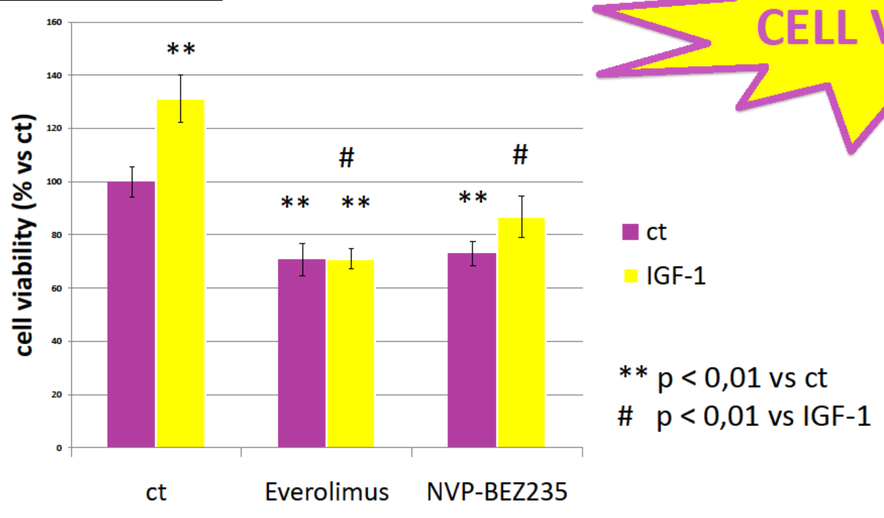
Fig.1 IGF-1 receptor pathway

Material and methods: Cell viability and GH secretion assays have been performed in the GH3 cell line (rat GH-secreting pituitary adenoma cell line).

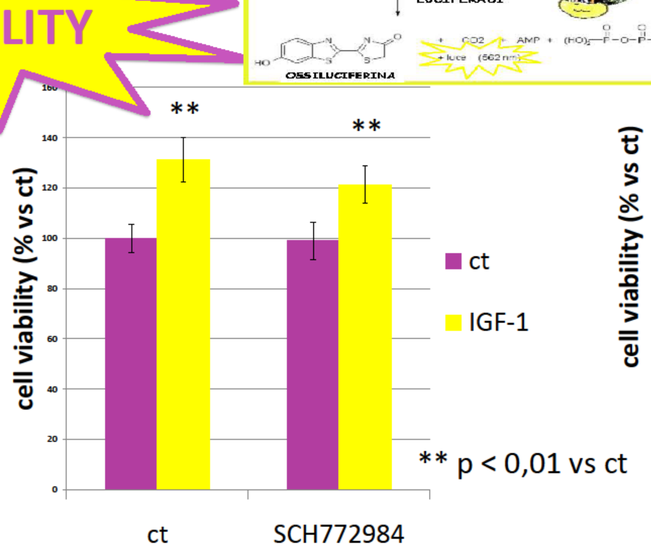
Results:

CELL VIABILITY

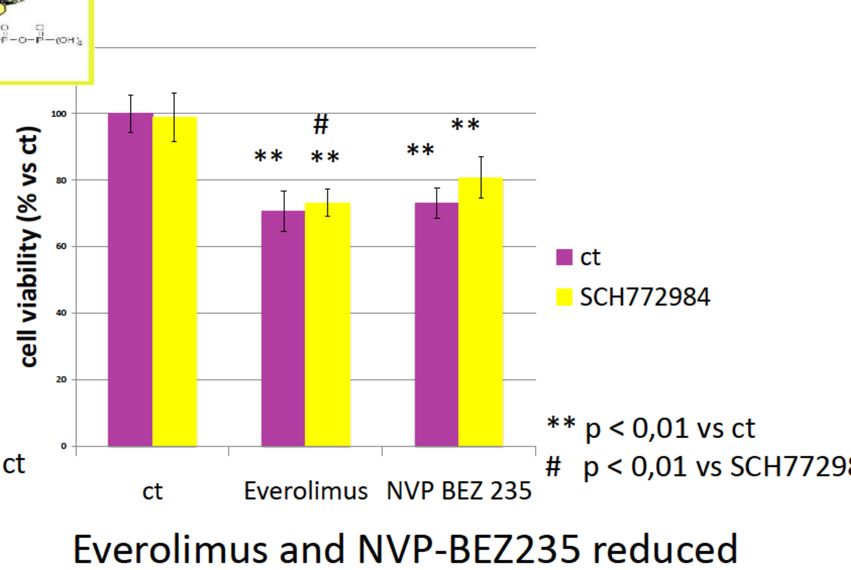




IGF-1 induced cell viability by 30%. Everolimus reduced viability up to 30% and this effect was not counteracted by IGF-1. NVP-BEZ235 reduced cell viability and IGF-1 counteracted this effect

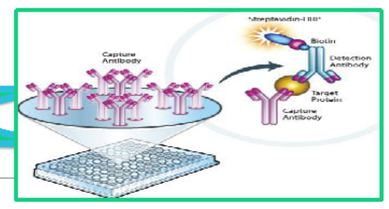


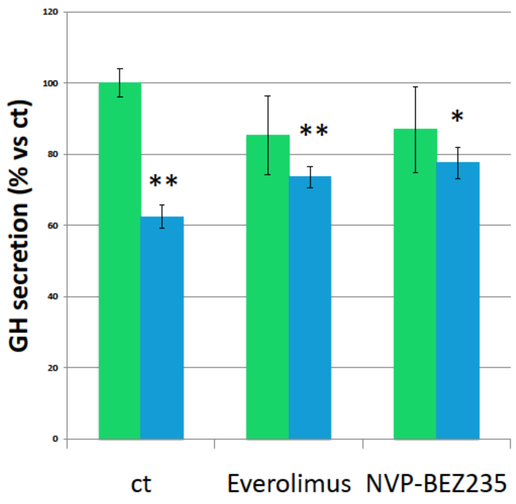
SCH772984 did not influence viability and not counteracted the effect of IGF-1



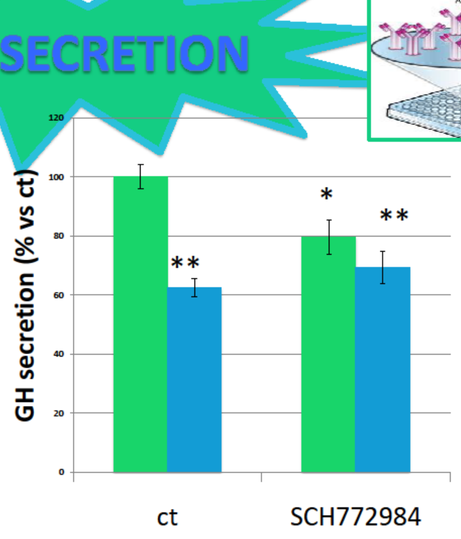
Everolimus and NVP-BEZ235 reduced viability up to 30%, and this effect was not counteracted by SCH772984

GH SECRETION

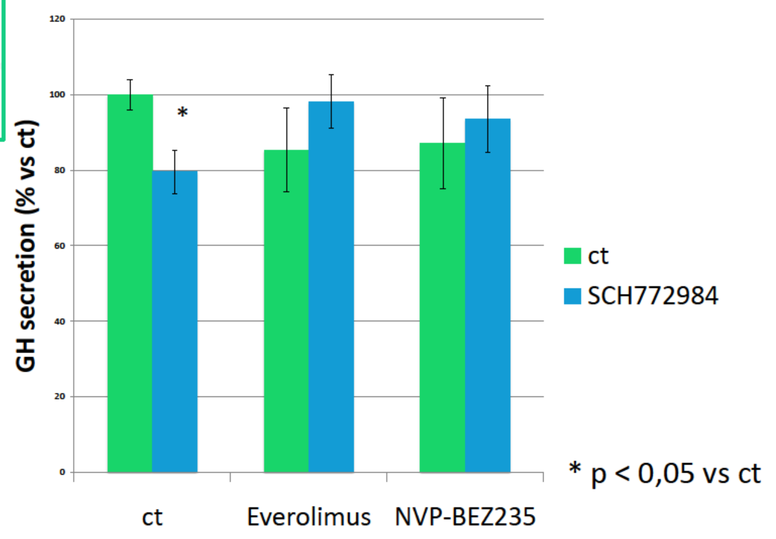




GH secretion was reduced by IGF-1 (40%); Everolimus and NVP-BEZ235 did not affect GH secretion and these compounds did not enhance the negative feed-back of IGF-1



SCH772984 reduced GH secretion up to 20% without enhancing IGF-1 negative feed-back



Everolimus and NVP-BEZ235 did not influence SCH772984 effects on GH secretion

Conclusions: These data indicate that IGF-1 is important in regulating proliferation and GH secretion in GH3 cells. mTOR blockade reduces viability without affecting GH secretion. ERK 1/2 affects secretion but not IGF-1 negative feed-back. In conclusion, our data suggest that mTOR and ERK 1/2 pathways are not involved in IGF-1 feed-back on GH secretion.

17 ECE
170--EP
Reproduction, endocrine disruptors and signalling
Carmelina Di Paquale
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND
PosterSessionOnline.com