5. Summary

This study examined the role of growth factors and one of their receptors in pituitary tumor growth, as assessed in a rat pituitary cells line (GH_3 cells) and/or in primary human pituitary adenoma cells (PP). In summary, the following findings were revealed:

- ^{3}H-thymidine incorporation of GH_3 cells was decreased by bFGF, IGF1 and IL2, and increased by EGF and IL6, suggesting a role of these growth factors in modulating the proliferation of GH_3 cells.
- Apoptosis of GH_3 cells was decreased by bFGF, EGF, IGF1 and IL6. These growth factors also modulated apoptosis of PP (augmenting, decreasing or no effects), demonstrating that growth factors can also influence the growth of pituitary tumor cells by modulating their rate of apoptosis.
- GH secretion of GH_3 cells was increased by bFGF, EGF, IGF1, IL2 and IL6. PRL secretion was increased by bFGF and EGF. Together such data indicate that some growth factors play a role in modulating hormone secretion of pituitary tumor cells.
- Growth factor-induced ^{3}H-thymidine incorporation and hormone secretion (GH and PRL) of GH_3 cells could be neutralized with anti-growth factor antibodies but not their isotypic controls, suggesting that the observed events were specific.
- Different molecular weight fractions of human pituitary adenoma extracts contained proliferation- and hormone secretion-augmenting activities. This was suggestive of the presence of endogenous growth and secretion modulating substances in human pituitary adenomas.
- These proliferation- and hormone secretion-augmenting activities could not be neutralized with anti growth factor antibodies, most likely due to prolonged storage of tumor fractions, resulting in loss of stimulatory activities.
- Further evidence for the presence of endogenous growth factors was demonstrated in PP from several human pituitary adenomas, were in the absence of exogenous growth factors neutralizing growth factor antibodies variably modulated apoptosis (augmenting, decreasing or no effect).

- The effects of growth factors on apoptosis of PP did not correlate with tumor subtype, histology, patient age or sex. Similarly, the proliferation and hormone secretion-augmenting activities, separated from human pituitary tumor extracts did not correlate with tumor subtype, histology, patient age or sex. Together such data suggest that the diversity of pituitary tumor subtypes may not be simply explained by different actions of paracrine or autocrine growth factors on pituitary tumor cell growth and secretion, but that substances other than growth factors may also play a role
- IGF1R expression in PP from several human pituitary adenomas was increased after serum deprivation. High ligand concentrations decreased the IGF1R expression. The ligand effects were time- and dose dependent. Together, these data show for the first time that in pituitary tumor cells the IGF1R can be up and down regulated.
- In other cell systems the IGF1R is necessary for optimal growth. Further experiments are necessary to prove that the decrease of apoptosis following serum deprivation, which is observed analogous to an increase of the IGF1R expression, is suggestive of a growth-modulating role for the IGF1R in human pituitary tumor cells.