

Establishment and Characterisation of a New Well-Differentiated Pancreatic Neuroendocrine Tumor Cell Line

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Background: The development of new therapeutic strategies for patients with pancreatic neuroendocrine tumours is impaired by the paucity of suitable pre-clinical models. Although the two available tumour cell lines BON and QGP have a neuroendocrine phenotype, the proliferation rates are far too high for a well differentiated neuroendocrine tumour. Hence, there is great need for the development of new neuroendocrine tumor cell lines.

Methods: We successfully established a new primary human neuroendocrine tumor cell line from a lymph node metastasis of a patient with a pancreatic neuroendocrine tumor. The expression profile, growth characteristic and treatment response in this cell line was analyzed in comparison to the established BON and QGP cells.

Results: The new cell line („NT-3“) has now been cultured for more than 18 month with a stable neuroendocrine tumor phenotype assessed by chromogranin A, synaptophysin and SSTR expression. The cells have a doubling time of 8 days in comparison to a doubling time of less than 2 days in the BON and QGP cells. In soft agar the NT-3 cells form small colonies after an incubation period of 8 weeks with a colony frequency

of ~2% of plated cells. The expression of SSTR subtypes 1, 2, 3 and 5 is at least 10-fold higher in NT-3 cells compared to BON and QGP. Likewise, the expression of the pro-angiogenic factors VEGF A, VEGF B and Angiopoetin 2 is more than 5-fold higher in NT-3 cells. As a marker of functionality the NT-3 cells express and secrete insulin. The IC₅₀ for treatment with streptozotozin was ~1mM and >10mM and with 5-FU was ~100µM and >500µM in NT-3 and QGP cells, respectively.

Conclusion: In summary, we have established a new slow growing, functional active pancreatic neuroendocrine tumour cell line with a well differentiated phenotype and high expression of pro-angiogenic factors.