**A Patient-derived Xenograft Model for Pancreatic Neuroendocrine Tumors**

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**Purpose**

Patients with pancreatic neuroendocrine tumors (PNETs) commonly have extensive metastatic disease and therefore require a drug therapy. However, treatment options remain limited as there is a lack of experimental models that reliably reflect PNET disease. We therefore developed a patient-derived xenograft model of PNET (PDX-PNET), and then evaluated two mTOR inhibitor drugs in this model: FDX-approved everolimus and the investigational new drug sapanisertib.

**Experimental Design**

A patient with PNET liver metastases producing insulin underwent surgery to ameliorate refractory hypoglycemia. PNET tissue was implanted subcutaneously into nude mice, successfully passaged for several generations, and then histologically and genetically characterized. Mice bearing PNET xenografts were treated with everolimus or sapanisertib.

**Results**

1. **Generation and characterization of the patient-derived xenograft model of PNET (PDX-PNET).**

2. **PDx-PNETs harbor mutations in genes commonly associated with PNETs and mTOR pathway activation.**

3. **Response of PDX-PNETs to mTOR inhibitor drugs—everolimus and sapanisertib.**

4. **Sapanisertib causes tumor shrinkage in most everolimus-resistant PDx-PNETs.**

5. **Everolimus-sapanisertib double-resistant PDx-PNETs maintain mTOR pathway activation.**

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**Conclusions**

The PDX-PNET model is the first valid and available PDX model for PNET, and predicts that sapanisertib may serve as an effective new treatment option for patients with PNET or everolimus-resistant PNET.