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Developing Model Systems of Neuroendocrine Tumors: Cell Lines and Patient-Derived Xenograft (PDX) Tumors

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BACKGROUND: A major barrier to neuroendocrine tumor (NET) research is scarcity of model systems. Only two pancreatic and zero small bowel NET cell lines are available with just one reported patient-derived xenograft (PDX) for pancreatic NET. PDXs are made by directly transplanting human tumors into immunocompromised mice. These preserve the original histological, genetic phenotype and drug response of the patient tumor. Three-dimensional (3D) spheroid cultures are another valuable model that is generally lacking for NETs. Our goal is to establish the first repository of NET PDX models and 3D tumor cell lines using freshly isolated NETs or high grade cryopreserved NET specimens.

METHODS: Fresh pancreatic, small bowel and thyroid NETs were collected immediately following surgery at UI. Tumor fragments were implanted into NSG (Nod-scid-gamma) mice, and when possible digested to establish cultures on ultralow attachment dishes (ULA). Cryopreserved NETs were provided by the LSU team, and high grade tumors from pancreas and small bowel were selected for implantation. Cultured cells from freshly isolated NETs were maintained and those with sufficient growth collected for analyses and cryopreservation.

RESULTS: Establishment of NET PDX models is ongoing with 57 mice currently implanted with fresh or cryopreserved NETs. Significant tumor growth has not yet been observed. Multiple NET cultures have been developed from

surgical specimens, several of which display expression of NET biomarkers (synaptophysin and chromogranin A).

CONCLUSION: Our studies will establish the relative effectiveness of fresh versus cryopreserved NET specimens for generating sustainable PDXs. Successful, models will be characterized at molecular, genetic, pathological and biological levels. Analyses of several NET-derived cultures demonstrated their NET origin. Development of NET PDX and/or cell lines would represent a significant advance in the field that will facilitate NET research and improve patient treatment.