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Development of patients-derived NET organoids

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BACKGROUND

Neuroendocrine tumors (NETs) are clinically and biologically heterogeneous neoplasms with limited representative cell lines. Patient-derived organoids (PDOs) are three-dimensional cell culture models that recapitulate the molecular characteristics of the original tumors. In this study, we aimed to establish PDO from patients with well-differentiated NETs.

METHODS

Patients with a diagnosis of gastrointestinal NETs undergoing surgical resection as part of standard clinical care were prospectively enrolled. Tumor specimens were collected and minced into approximately 1 mm^3 fragments, then embedded in Matrigel and seeded in 24-well plates in culture media containing 30% of Wnt3a conditioned media and 10% R-Spondin-1 conditioned media supplemented with growth factors; hEGF, hFGF, huIGF-1. PDO growth was monitored every 48 hours by light microscopy, and images were acquired.

RESULTS

A total of four patient samples were collected from primary and metastatic sites, and PDO cultures were established. The following samples were collected: patient 1, a liver metastasis from a small bowel NET, grade 2; patient 2, a liver metastasis from a small bowel NET grade 1; patient 3, two liver metastases from a pancreatic, grade 1 NET; patient 4, a primary pancreatic NET, grade 3. All liver metastasis–derived samples demonstrated successful PDO growth, independent of primary tumor site or grade. Notably, patient 3-derived organoids from pancreatic primary liver metastases exhibited the most rapid growth. In contrast, PDO establishment from the primary pancreatic lesion was unsuccessful, and extensive tissue necrosis was observed in the specimen.

CONCLUSIONS

We successfully established PDO from liver metastases of patients with neuroendocrine tumors originating from the small bowel and pancreas, spanning grades 1 to 3. This

model represents a promising platform for preclinical drug testing and for studying NET biology.

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