“Assessment of anti-cancer drugs against patient-specific pancreatic cancer organoid cultures”

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There is an urgent need for new therapies to treat pancreatic cancer. Among cancers, it recently became second only to lung cancer as a killer of Americans. Unfortunately, the models currently used for pancreatic cancer drug development are either difficult to work with or cannot represent individual patient tumor characteristics.

In this proposal, these issues are addressed with a collection of tumor-derived 3D organoid cultures. Cancer organoids are highly proliferative 3D structures initiated by stem cells recovered from patient tumors during surgery. Organoid cultures retain the specific genetic characteristics of the tumor from which they were initiated and can be adapted to medium-throughput drug screening. Since they represent the stem cell component of the tumor thought to be critical for its resilience, drugs, which kill these cells may be especially useful. Ten different OHSU patient tumor-specific organoid lines will be cultured and treated with panels of known and proposed anti-cancer drugs. The first goal will be to optimize culture conditions for handling by automated instruments for medium-throughput testing. Drugs already approved for the treatment of pancreatic cancer patients will be evaluated first, followed by novel compounds.

These experiments will determine the most efficient ways to evaluate human cancer organoid drug responsiveness, assess the suitability of current drugs for killing cancer stem cells, and will evaluate novel drugs for efficacy against this important cell type. These results will be applicable to future testing of other cancer organoids such as those from lung or colon, and to additional compounds and targeted inhibitors.