Generating Patient-Derived Organoid Models of Disease from Pre-treated Patients in a Clinically Certified Laboratory Setting: A Critical Step Towards Precision Medicine in Pancreatic Cancer

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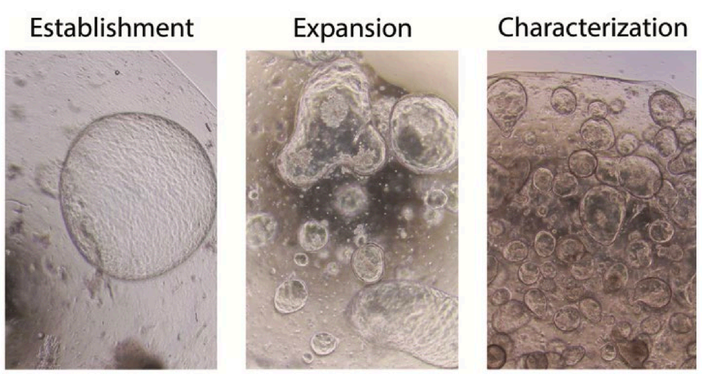
Background

- Despite overall cancer cases declining resulting in 3.2 million fewer deaths since 1991, pancreatic cancer rates are increasing with about 62,000 cases predicted in 2022[1].
- Antiquated 2D cell lines do not adequately represent the disease therefore research progress is often thwarted.
- Patient Derived Organoids (PDOs) are ex-vivo 3D tumor models that recapitulate individual patient tumors.
- With treatment naïve tumors, PDO success rate is approximately 70% and can be achieved within weeks in a research laboratory.

Objectives

- Does exposure to neoadjuvant chemotherapy affect the establishment, expansion or characterization rate of PDOs?
- Can PDOs be established utilizing a standard operating procedure in a CLIA certified cell culture facility?
- How quickly can PDOs be successfully characterized?



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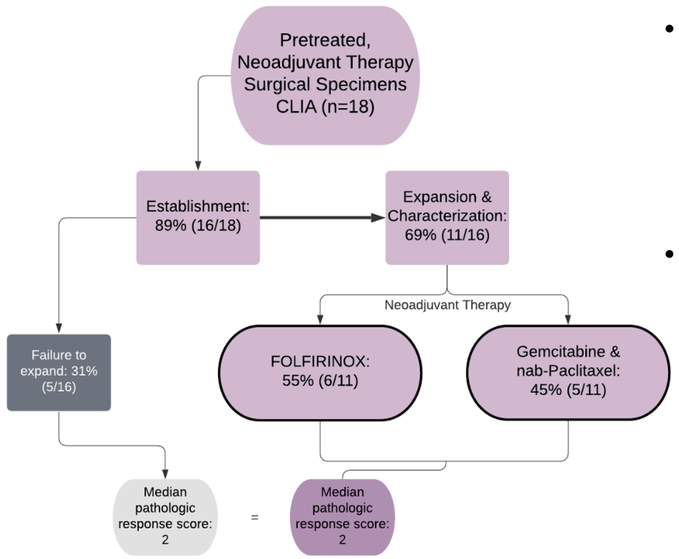
Methods

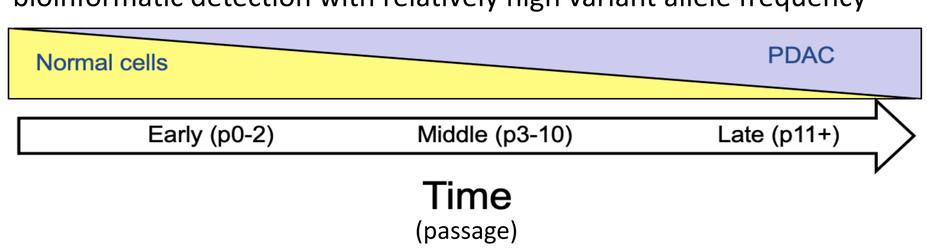
- PDOs were established in a CLIA lab from 18 patients undergoing pancreatectomy who had received neoadjuvant chemotherapy.
- Primary outcome of interest included rates of successful establishment, expansion and characterization.
- Additional outcomes included affects of neoadjuvant regimen, pathologic response score and very early passage (p0-p1) characterization success.

Results



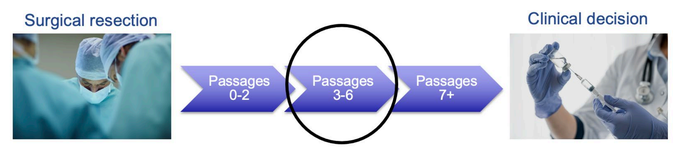
- Successful organoid generation is possible after neoadjuvant chemotherapy.
- Chemotherapeutic regimen and pathologic response score do not affect success rate.

- Very early characterization is possible, however malignant cells can expand in later passages.
- 50% (4/8) detect PDAC mutations: KRAS, CDKN2A, SMAD4, TP53 at p0-p1
- 50% (4/8) were not ***yet*** enriched for cancer at p0-p1
- However, at later passages (p6+) PDAC mutations cross the threshold for bioinformatic detection with relatively high variant allele frequency



Conclusions

- Organoids can be successfully established, expanded and characterized from pre-treated tumors in a CLIA setting.
- Early characterization is optimized around passages 3-6 within a “Goldilocks” Zone in order to have malignant cell proliferation within a clinically meaningful timeframe



This is the first example of PDO utilization in a high-volume academic center for precision medicine approaches.

Questions?

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1. Siegel, RL, Miller, KD, Fuchs, HE, Jemal, A. Cancer statistics, 2022. *CA Cancer J Clin*. 2022.