Preclinical in vitro and in vivo models as an efficient tool to identify Multi-Omics Biomarker Signatures for Pancreatic Cancer Precision Medicine

Focus on Pancreatic cancer organoids

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Pancreatic Cancer Organoids

Organoids recent history

Differentiated

Undifferentiated
Focus on Pancreatic Cancer Organoids

Organoids in PDAC chemosensitivity prediction

**Organoids in clinical trials**

**Too much time for pancreatic cancer**
Resectable 15%  
Resection Yes  
Resectable No  
Biopsy 85%  

Preclinical models  
Organoids  
Cells  
PDX  

> 250 Organoids  
> 150 PDX  
> 60 Primary cell cultures  

Serum Plasma Blood Clinical data  

PaCaOmics Clinical Trial  
NCT01692873  

INSTITUT PAOLI-CALMETTES  
Centre régional de lutte contre le cancer Provence-Alpes-Côte d’Azur  

Translational Research Projet  
Systematic Generation of models and Multi-Omics Characterization  

Patients from:
Resectable

Pancreatic Cancer

Resection

Biopsy

15%

Yes

No

85%

Drug Chemosensitivity analysis

- Bioinformatic Analysis

- Biomarkers, targets and signatures identification

PDX

Primary cultures

Organoids

Translational Research Projet

Systematic Generation of models and Multi-Omics Characterization
Translational Research Project
Molecular Gradient System for PDAC

Stratification of 76 PDX from PaCaOmics cohort

Relative risk (decrease)

\[ p = 4.97 \times 10^{-7} \]
Translational Research Project

Model comparison by transcriptome

- Dim1 (27%)
- Dim2 (9.9%)
- Density
- Mol. Grad.

- Cells
- PDX
- Organoids

***

- Mol. Grad.

- PDX
- Organoids
- Cells
Cells
Organoids
PDX
Gemcitabine sensitivity score

IRINOTECAN sensitivity score

5-FU sensitivity score

Oxaliplatin sensitivity score
Translational Research Projet
Predicting chemotherapy sensitivity

Integration of PDAC models

Patient derived primary cell cultures

Patient derived xenografts

Organoids

Gemcitabine response

RNA expression in cell cultures

GemPred algorithm

1. Gemcitabine Response
2. Proliferation
... [other]

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Stratified by adjuvant Gemcitabine & *GemPred*

Validation in a cohort of 435 operated patients

Survival probability

Time (in months)

Number at risk

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Conclusions

• The perfect model to study PDAC chemosensitivity do not exist

• Organoids, PDX and primary cell cultures can be used in a complementary manner

• Different models derived from the same patient do no present always the same chemosensitivity

• Validating and refining predictive transcriptomic signatures using a combination of these models is fundamental to achieve clinical applicability