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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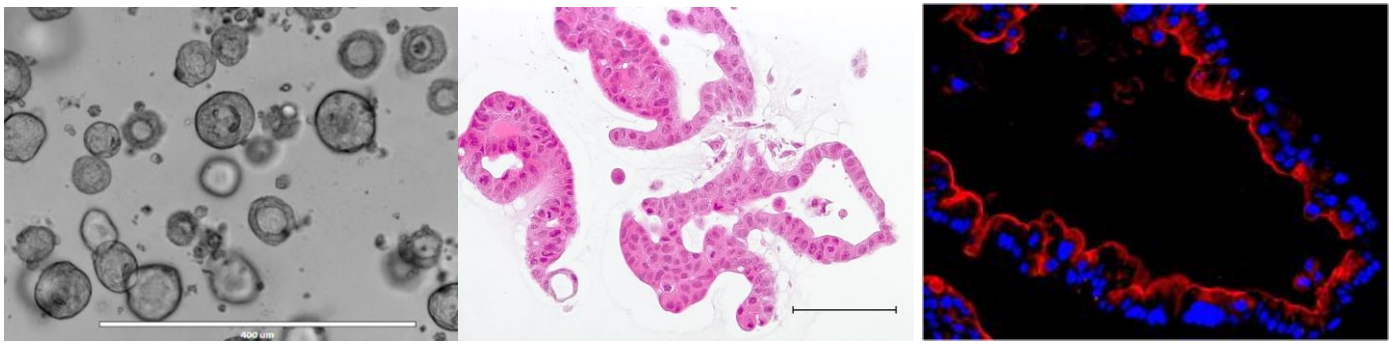
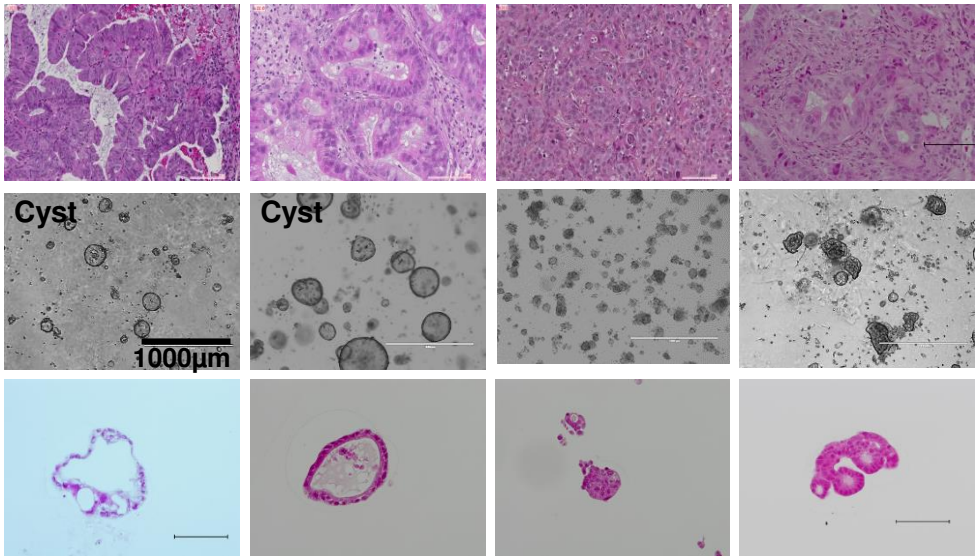
Inserm Institut national de la santé et de la recherche médicale
Aix*Marseille université
cnrs

Pancreatic Cancer Organoids

Organoids recent history





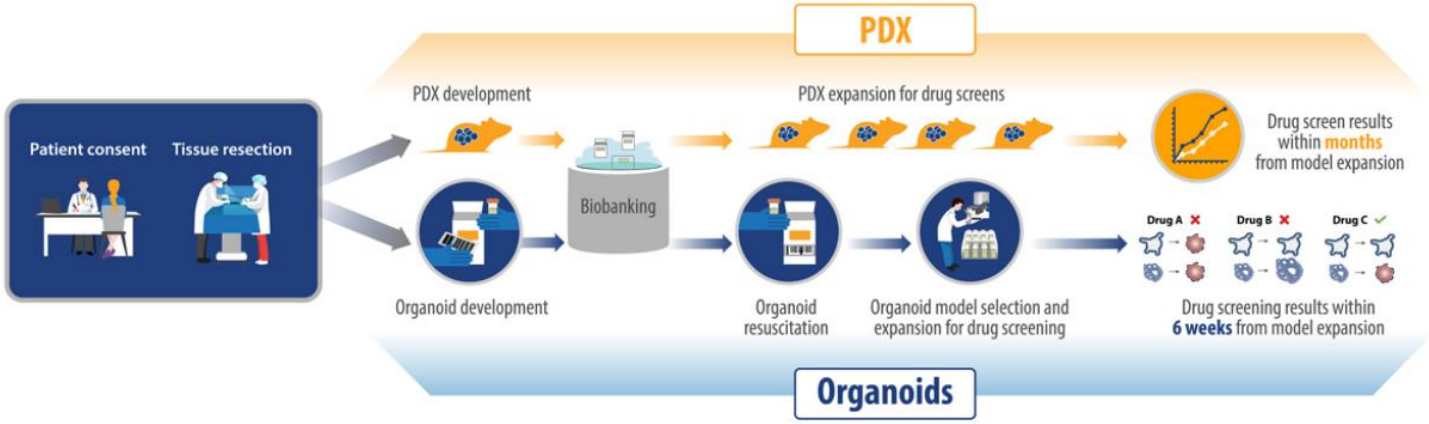
Differentiated

Undifferentiated

Focus on Pancreatic Cancer Organoids

Organoids in PDAC chemosensitivity prediction

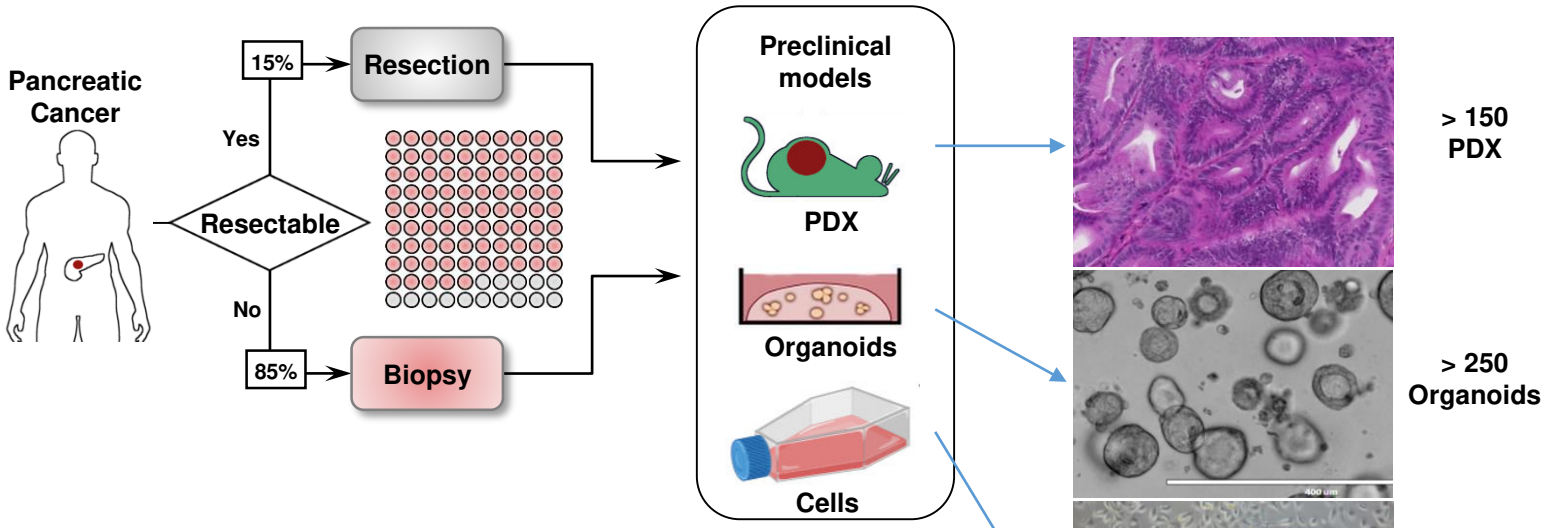
Organoids in clinical trials



Too much time for pancreatic cancer

Translational Research Projet

Systematic Generation of models and Multi-Omics Characterization



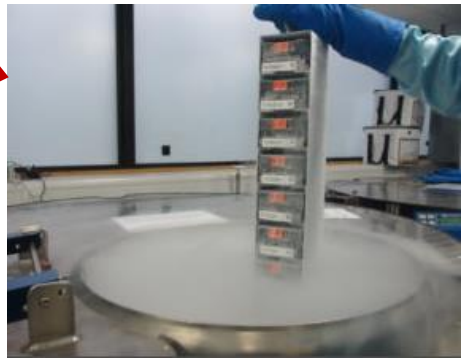
Patients from :

INSTITUT PAOLI-CALMETTES

Centre régional de lutte contre le cancer Provence-Alpes-Côte d'Azur

PaCaOmics Clinical Trial
NCT01692873

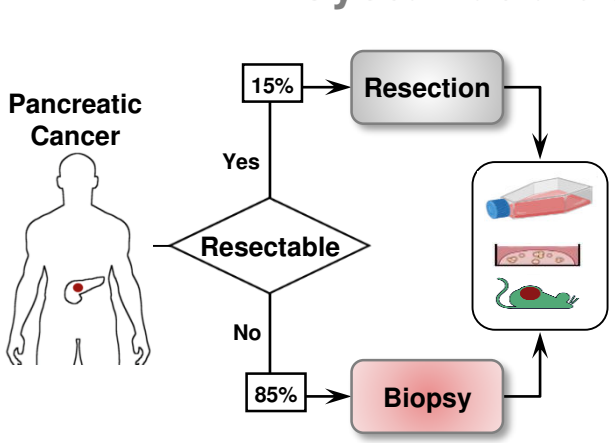
Serum
Plasma
Blood
Clinical data

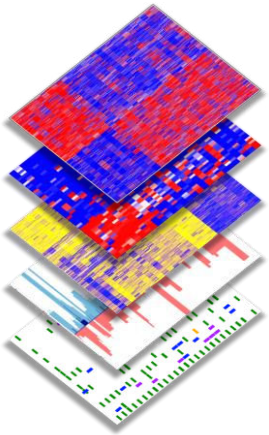


Pancreatic Cancer models Biobank

Translational Research Projet

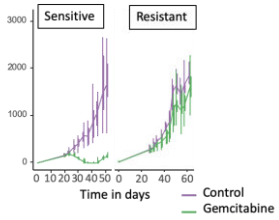
Systematic Generation of models and Multi-Omics Characterization





- Bioinformatic Analysis

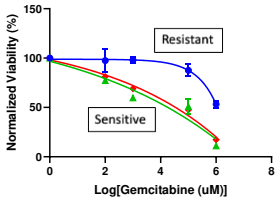
PDX



Drug Chemosensitivity analysis

Primary cultures

Organoids



- Biomarkers, targets and signatures identification

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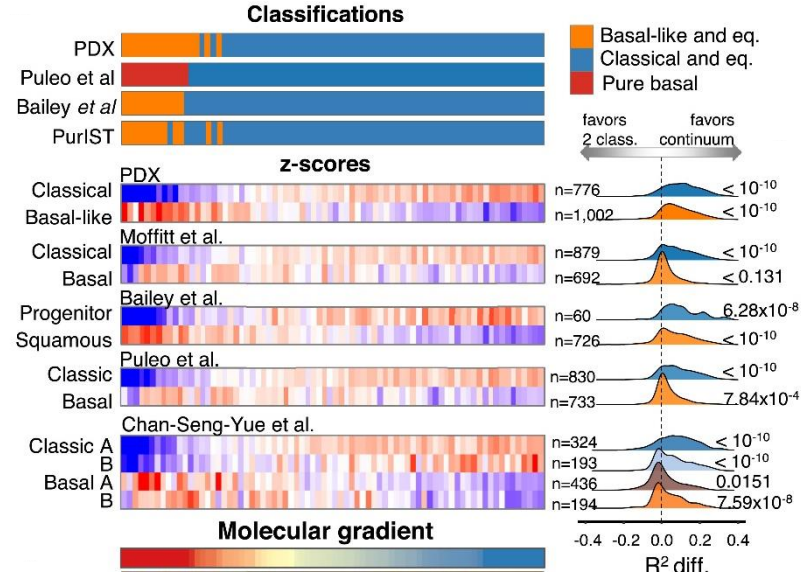
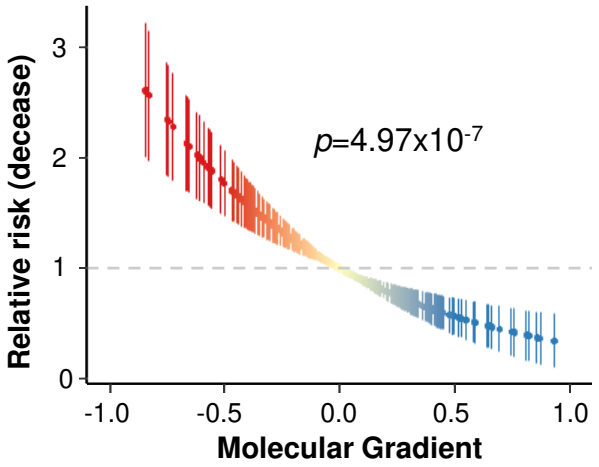
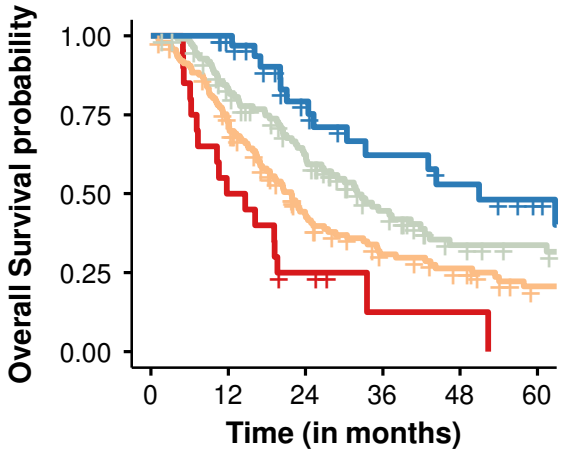
Molecular Gradient System for PDAC



Stratification of 76 PDX from PaCaOmics cohort





EBioMedicine. 2020 Jul;57:102858

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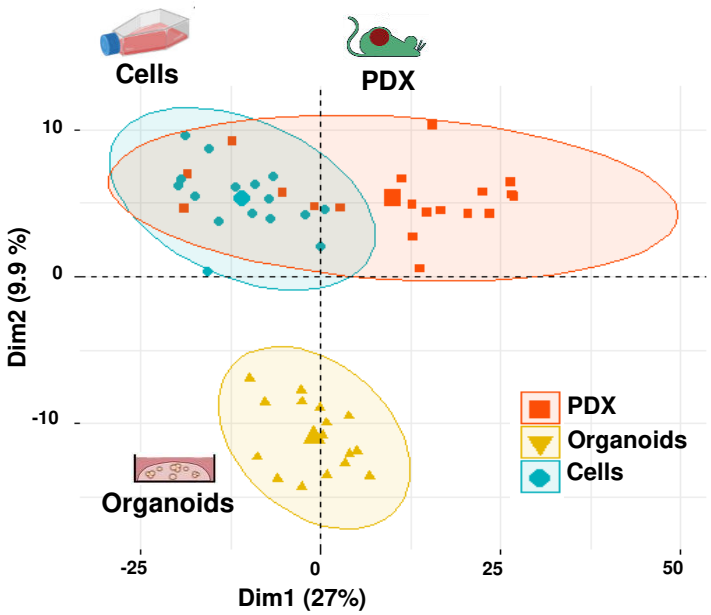
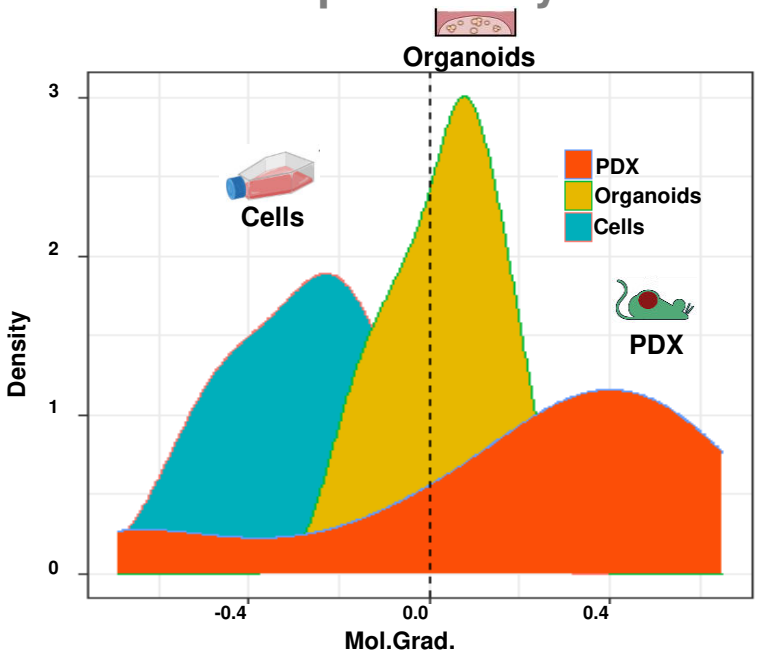
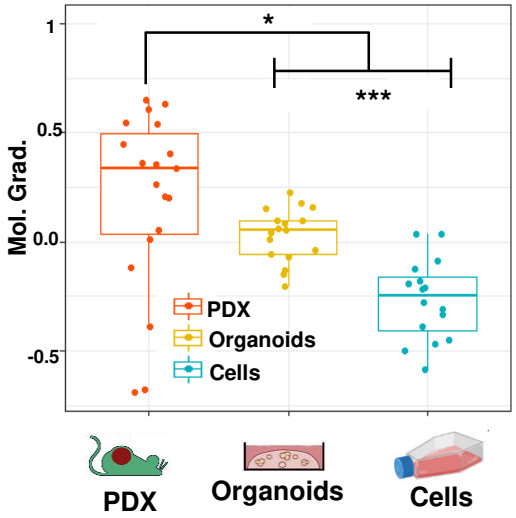
Model comparison by transcritome

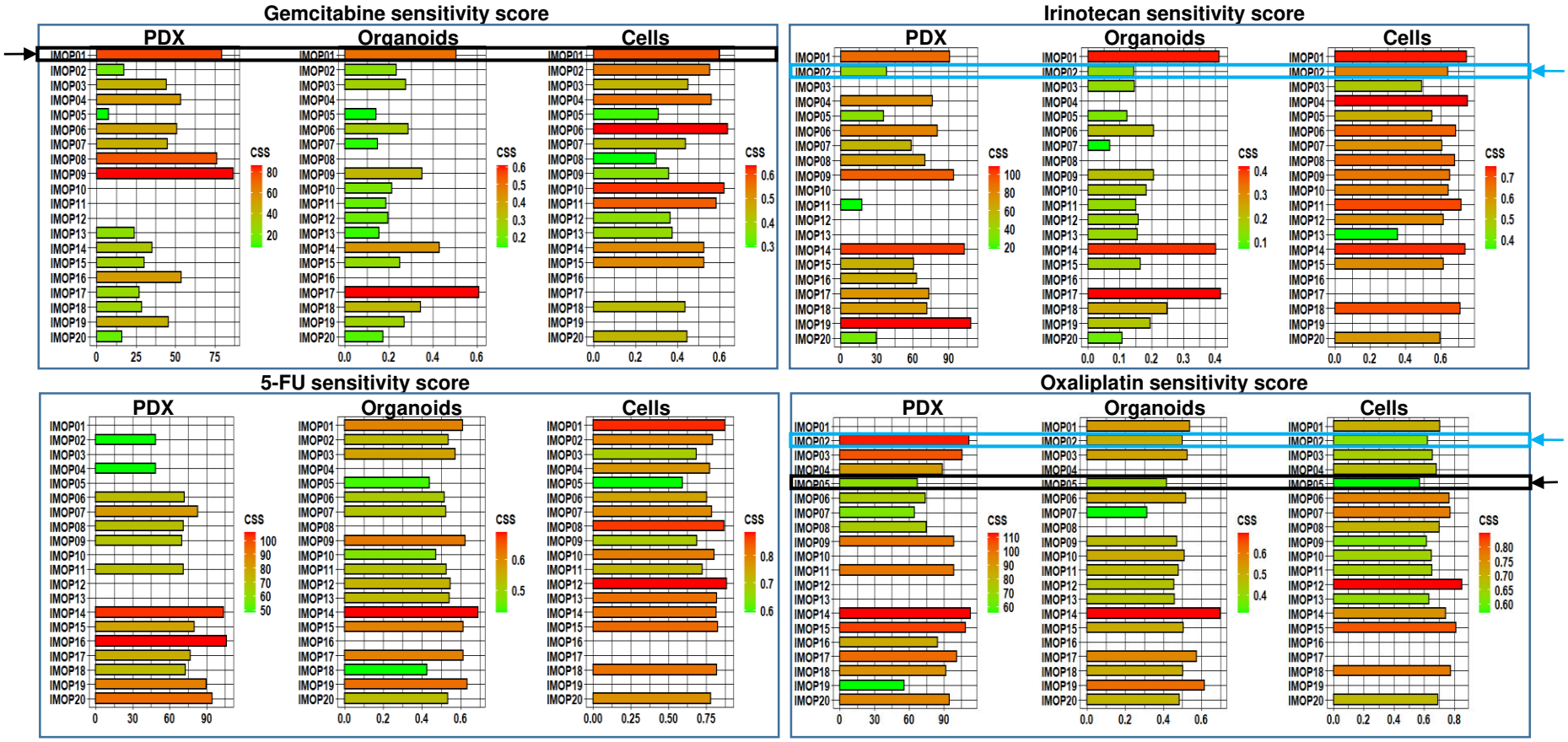






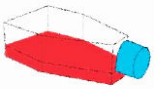
Translational Research Projet

Chemogram scoring in the different type of models

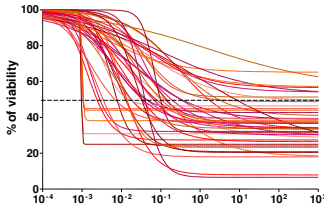


Translational Research Projet

Predicting chemoteraphy sensitivity

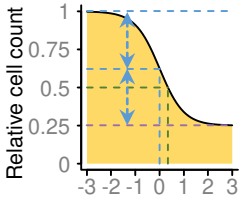


Patient derived primary cell cultures



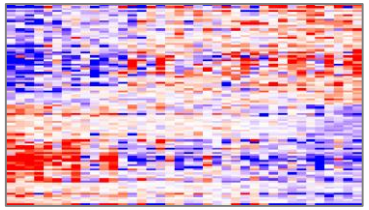
Gemcitabine response

Gemcitabine response



Duplication rate

RNA expression in cell cultures



Independent Component Analysis (ICA)

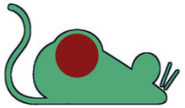
Component 1
Component 2
…
Component k

Select systems with distinct proliferation and response components

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

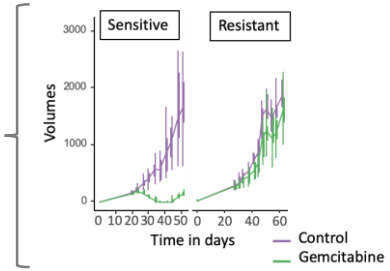
GemPred algorithm

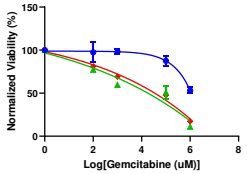
Integration of PDAC models



Patient derived xenografts

Organoids





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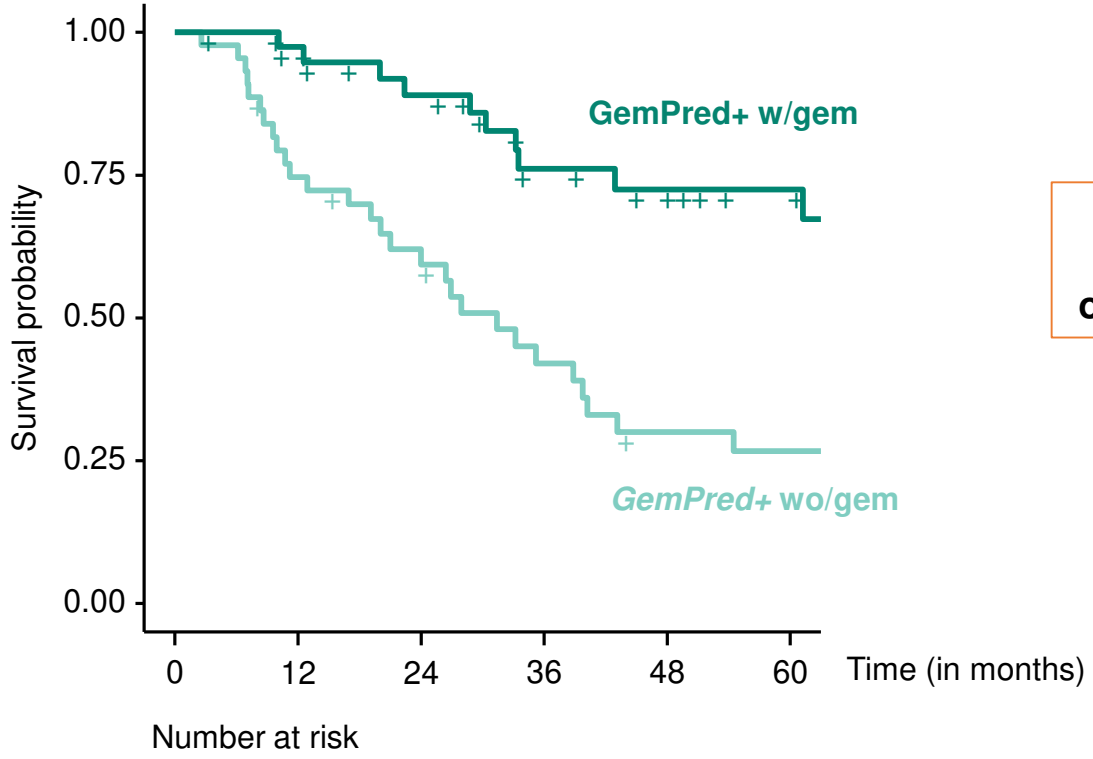
GemPred signature validation

Stratified by adjuvant Gemcitabine & *GemPred*



Number at risk

GemPred+ wo/gem	44	32	23	14	9	8
GemPred+ w/gem	41	37	31	22	19	15

Validation in a cohort of 435 operated patients

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Translational Research Projet

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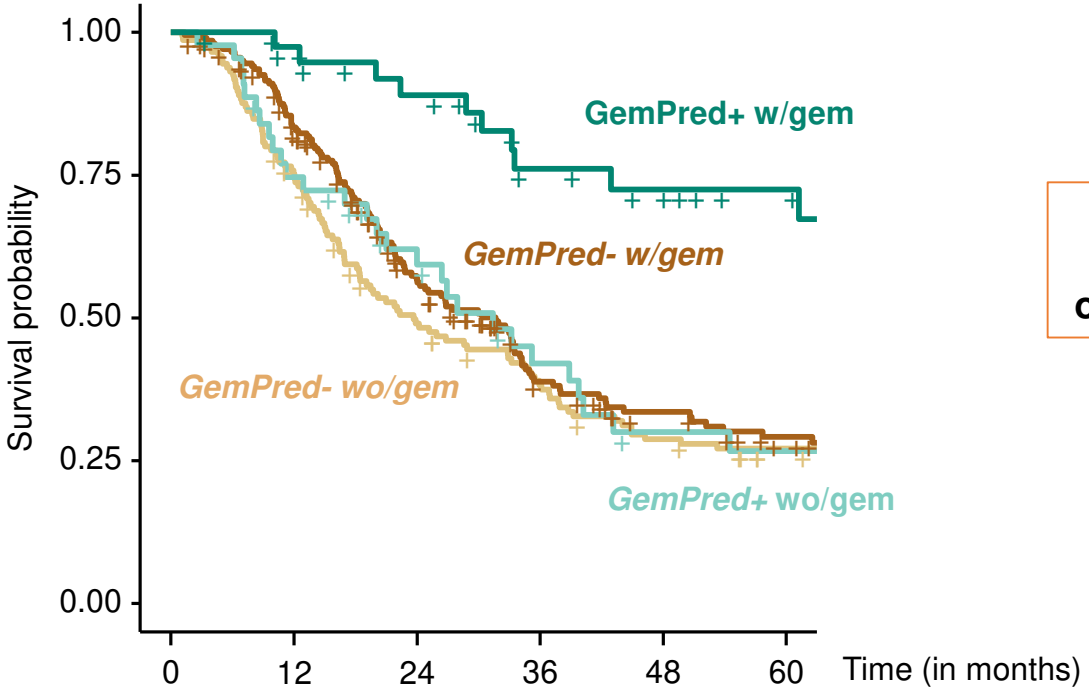

Number at risk

GemPred- wo/gem	145	107	66	49	36	29
GemPred- w/gem	205	161	96	54	40	30
GemPred+ wo/gem	44	32	23	14	9	8
GemPred+ w/gem	41	37	31	22	19	15

Validation in a cohort of 435 operated patients

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Translational Research Projet

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