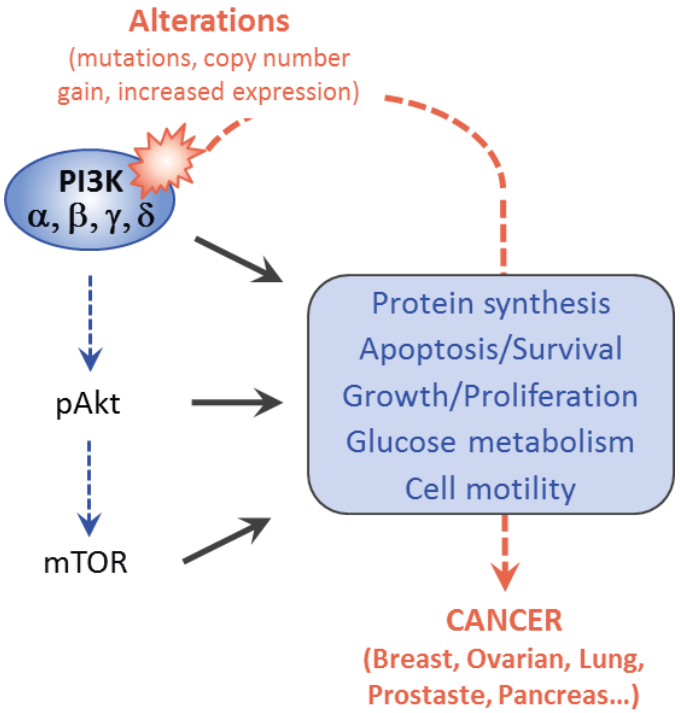
ComPep

A biomarker to predict patients response to PI3K inhibitors

March 2018

Targeting PI3K signaling in Cancer

- Hyperactivation of PI3K signaling is frequent in numerous cancers → **PI3K isoforms are attractive targets**
- Modest clinical effects have been observed with inhibitors targeting all PI3K isoforms, due to high toxicity and difficulties to predict the targeted patient populations → **need to stratify patients for clinical trials**
- **Mutational patterns of PI3K pathway or its level of expression are not sufficient to predict sensitivity to PI3K-targeting drugs**
- PI3K isoforms play divergent roles in cellular signaling and cancer → **isoform selective inhibitors are emerging with promising success**

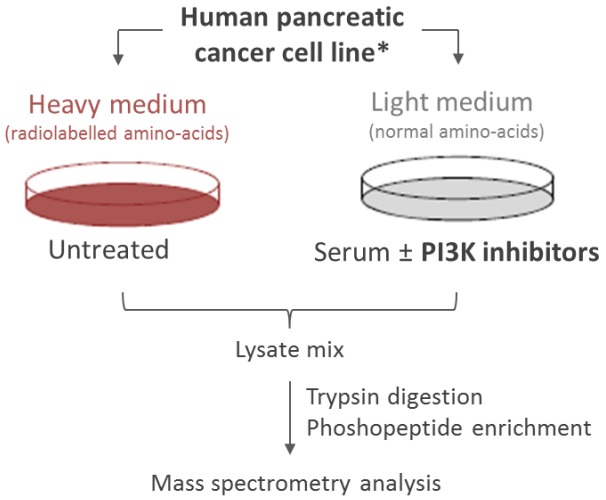


PI3K pathway and Cancer

→ NEED FOR BIOMARKERS OF PI3K ISOFORM SELECTIVE INHIBITORS SENSITIVITY

phosphoPALK, a new biomarker for PI3K selective inhibition

- A screening approach for biomarkers

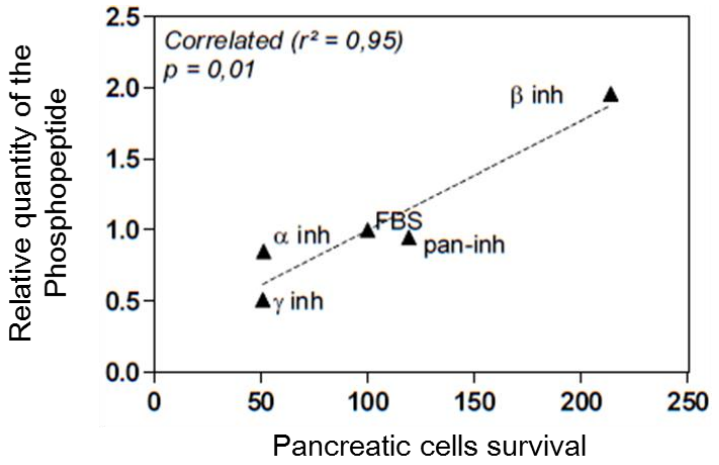


SILAC-based experiment

Comparative study of phosphoproteome in pancreatic cancer cells treated or not with PI3K isoform selective or non-selective inhibitors

➔ **IDENTIFICATION OF phoshoPALK PHOSPHOPEPTIDE**

➔ **EXPRESSION OF phosphoPALK STRONGLY CORRELATES WITH PANCREATIC CELL SENSITIVITY TO PI3Kα AND γ INHIBITION.**



FBS	pan-inh	α-inh	β-inh	γ-inh
1	0,95	0,85	1,96	0,51

PhosphoPALK relative expression

(Pan-inh: non isoform selective inhibitor)

** Representative of common genetic alterations found in Pancreas Ductal Adenocarcinoma.*

phosphoPALK, a new biomarker for PI3K selective inhibition

phosphoPALK BIOMARKER BENEFITS

- Selective for PI3Kα and γ isoforms
- Enable patients stratification for pancreatic cancer PI3K based-therapy
- Potential extension to other solid cancers : colon

ONGOING WORK FOR phosphoPALK BIOMARKER VALIDATION

- Correlation between phosphoPALK expression level and sensitivity to PI3K isoform selective inhibition *in vitro* on cancer cell lines
- Correlation between phosphoPALK expression /sensitivity to PI3K isoform selective inhibition/patients survival in ex-vivo experiments (tissue sections, ascites)

- **Patent EP17306625 (November 2017)** registered by Inserm and Toulouse Paul Sabatier University on behalf of the Cancer Research Center of Toulouse

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