MOLECULAR BASIS OF PROGRESSION IN PANCREATIC CANCER

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Background

Pancreatic ductal adenocarcinoma (PDAC) is the fifth most common cause of death by cancer in the western world. Because of the anatomic localization of the pancreas and the delay of clinical symptoms, PDAC is detected in 85% of patients at advanced stage.
PDAC Progression

Early Alterations
- K-Ras
- P16 Loss
- EGFR amplification

Late Alterations
- P53 mutation/loss
- Smad4 mutation/loss
- BRCA2/LKB1

Normal duct

PanIN 1

PanIN 2

PanIN 3

IPMNs

MCNs

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PDAC Progression

Normal duct

PanIN 1

ACINAR DUCTAL METAPLASIA (ADM)

PanIN 2

PanIN 3

IPMNs

MCNs

PDAC

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Background

Epithelial cells (PDAC)

Stromal Cells

However, because PDAC usually exhibits an intense desmoplastic reaction, the molecular study of the entire tumor may not reflect the real levels of some gene expressions.
Background

Several studies showed that the inflammatory and fibroblast cells in the stromal tissue, which represents the body's normal attempt to fight transformed cells, were characterized by different levels of gene expression pattern with respect to tumor cells.
Primary Cell Cultures
Primary Cell Cultures
Laser Microdissection
CYB5A AND CHROMOSOME 18

Gene expression (AU)

- **FBX015**
  - Deletion
  - $P = 0.29$

- **c18orf51**
  - Deletion
  - $P = 0.01$

- **CYB5A**
  - Deletion
  - $P = 0.01$

- **CPGL**
  - Deletion
  - $P = 0.21$

- **CPGLB**
  - Deletion
  - $P = 0.37$
CYB5A AND CHROMOSOME 18
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CYB5A AND CHROMOSOME 18

Autophagy Modulators

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MICRORONA (miR-21)

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c-Met Oncogene

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Our ITT Project

IPMNs and PDACs Lesions

Quantification of MUCs and some mRNAs inhibiting their expression

Mutation Analyses of 20 most important genes involved in cancer progression

Statistical Analyses
Best Biological Markers

New Chip tailored for IPMN (Best Significant Markers)

Best Supportive Care

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