Mechanisms of Chemoresistance in Pancreatic Cancer

Supported by the *Gail V. Coleman – Kenneth M. Bruntel Pancreatic Research Fund*
The Human Genome

Human Chromosome: 23 pairs

Chr: 12

1,430 genes

Chemoresistance

http://en.wikipedia.org/wiki/Chromosome
http://en.wikipedia.org/wiki/Homologous_chromosome
The Human Genome

> 30,000 genes in each human cell

http://en.wikipedia.org/wiki/Chromosome
The Human Genome

Chemoresistance

http://cnx.org/content/m46032/latest/?collection=col11496/latest
Mutations in Cancer

Original cancer cell

Mutant
Core Signaling Pathways in Human Pancreatic Cancers Revealed by Global Genomic Analyses

through this research, they hoped to unlock the mystery behind pancreatic cancer, and design new therapies against these genes.
Mutations in Pancreatic Cancer

~ 40 mutations per tumor
Mutations in Pancreatic Cancer

• ~40 different genes were mutated in more than 1 cancer
• No two tumors are alike
• The most common mutated genes were
  • KRAS
  • SMAD4
  • P16
  • P53
Limitations

1) **Which** mutations are most important?
2) **When** is each mutation important?
3) **Why** does each one occur?

What do we do with this information?
Mutations for Survival

Chemoresistance

1st carcinogenic alteration
Alteration conferring drug resistance
Metastatic alteration

Healthy tissue
Anti-cancer therapy

Time

(d) Invasion into distant organs
Targeted Cancer Therapy

Chemoresistance

Mutation

RESISTANCE

CELL

ON

OFF
Chemoresistance for Pancreatic Cancer

There are two top treatment regimens for advanced pancreatic cancer:
A. Gemcitabine & Abraxane
B. FOLFIRINOX

Goal: to determine the mutations that directly cause resistance to these treatments in patients
Chemoresistance

Trial

1) Sequence and compare
2) Identify unique mutations in resistant tumors"
Conclusions

Innovative trial in patients that will

1) Identify mutations that directly cause chemoresistance.

2) Lead to new therapies to enhance treatment efficacy.

3) This research is applicable to all cancers.
Thanks for your attention!