Pharmacogenetic markers for anticancer treatment outcome

TEDCO/NIH/NCI Technology Showcase

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Pharmacogenetics

Therapeutic Window (toxicity vs. efficacy)

Toxicity -

Anticancer drugs have high toxicity

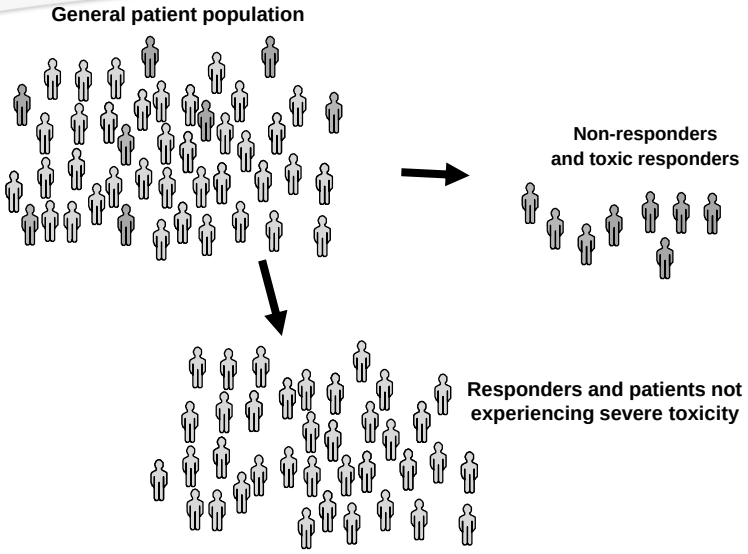
High doses => Dose-limiting toxicity

Efficacy

Drugs need to have a biological effect

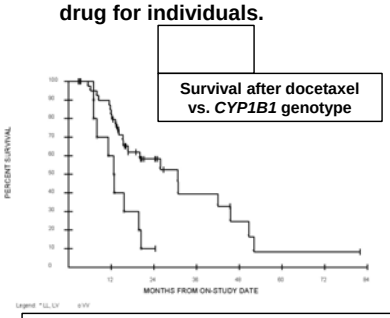
Low doses => Low efficacy

Pharmacogenetics



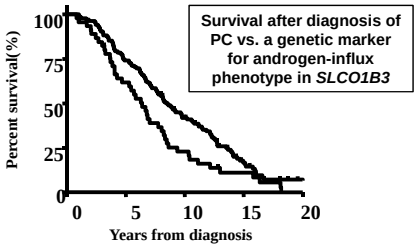
Pharmacogenetics Applications

1. Determine the best drug for individuals.



Example: Taxotere, ixabepilone, or satriplatin to treat AIPC in patients carrying variant alleles?

2. Define optimal treatment schedules for patients receiving a given drug.

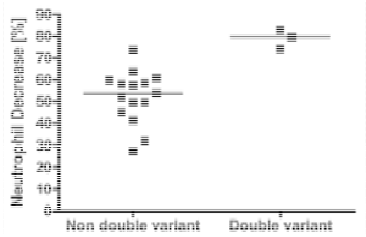


Example: Escalated antiandrogen dose for individuals at risk of early onset AIPC?

Pharmacogenetics Applications

3. Inform clinical decisions regarding pretreatment for toxicity.

Neutrophil % Decrease after paclitaxel vs *ABCB1* genetic variants



Example: Growth factor pretreatment in double variant population?

Commercial Applications

- **Gene chip technology allows for the combination of multiple genotype assays in a single genetic test kit.**
  - Validated assays are easy to perform with minimal invasiveness (i.e. germline DNA is obtained via a simple blood sample).
  - Low cost genotyping strategies are available.
  - Multiple genetic markers can be genotyped on a single chip to provide a multigenic approach to diagnostics.
  - Minimizing adverse events during therapy can reduce overall costs to clinics and the pharmaceutical industry, and potentially reduce the time to FDA approval during drug development.

Collaboration Opportunities

- ***ABCB1* genotyping to predict taxane-mediated toxicity**
- **ABCB1 genotyping to predict romidepsin cardiotoxicity**
- **OATP1B3 genotyping to predict survival after diagnosis of prostate cancer (time to androgen independence).**
- **Use of CYP1B1*3 Genotyping to Predict Survival to Docetaxel Treatment in Androgen-Independent Prostate Cancer**
  - Retrospective validation in larger patients cohorts from different cancer types.
  - *In vitro* and *in vivo* models
  - Preclinical testing
  - Determination of most effective therapeutic strategies for individuals with a specific genetic background.
  - Determine genetic modifiers
  - Prospective clinical trials

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