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Predicting anthracycline treatment response in cancer patients

Researchers at Stanford University's Curtis Laboratory have used gene expression to categorize the sensitivity and resistance of anthracycline chemotherapy in breast cancer patients with utmost precision. This discovery can be used to develop a first in class predictive diagnostic assay to hone-in on individuals at risk of anthracycline's lethal complications (such as cardiotoxicity and increased tumor metastasis). Additionally, new therapeutic strategies may be developed by utilizing this critical software database.

Physicians base their treatment on observations like age, nymph node positive, ER, Her2 to administer anthracycline chemotherapy, but there is no way to predict which individuals are at risk of the toxic side effects or which ones would benefit from further treatment. Even with the potentially lethal risks, anthracyclines (such as doxorubicin and epirubicin) are still used in 30% of early stage breast cancer patients because it can also be highly effective when administered to the right patient.

The study was conducted in a cohort of more than 1,000 women with early-stage breast cancer and in human breast cancer cell lines. It is known that anthracyclines inhibit topoisomerase II (TOP2) on DNA. Building on this fact, researchers were able to identify certain chromatin regulatory genes that alter TOP2 to predict anthracycline response in cells whether it be negatively or positively.

By utilizing this data, researchers developed a robust signature and set of biomarkers that will allow providers to cater the most effective treatment to patients without the negative side effects – perhaps, revolutionizing cancer treatment. The extensive database (larger than any other available signatures) categorizes the specific biomarkers by testing and validating the gene expressions with those breast cancer patients that have been treated and not treated. This allows for a far superior predictive value than any other systems in the market. Moreover, this type of

specific and reverse engineering of biomarkers has not been done by any other lab and verifies that this discovery is clinically applicable – better patient outcomes, survival rates, therapy choices, and quality of life.

Stage of Development:

Inventors used in vitro (cell line) molecular and drug sensitivity data to identify genes associated with anthracycline treatment response and integrated this further with patient molecular data. Research is ongoing to refine and discover additional biomarkers.

Applications

- Genetic data can be used to develop a predictive diagnostic assay in response to anthracycline chemotherapy
- Broad scope of therapeutic use: applicable to other cancer tissues besides breast tissue

Advantages

- Superior to any other methodological methods on the market
    - More robust and better predictive value
- Only system to compare treated and non-treated samples to assess whether there is a significant difference in biomarker(s) expression
- Provides a platform for further insights
- Improves patient outcomes by minimizing toxicities
- Solves an unmet medical need – there is no test for choice of chemotherapy
- Guides treatment decisions for cancer
- Increased quality of life for the survivor post treatment

Publications

- Jose A. Seoane, Jacob G. Kirkland, Jennifer L. Caswell-Jin, Gerald R. Crabtree, Christina Curtis, Chromatin state as a mechanism of anthracycline response in breast cancer, American Association for Cancer Research (published July 2019).

Patents

- Published Application: WO2020205807
- Published Application: 20220233563

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