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BME 100 LAB 1
HER2 4HER: A Breast Cancer Diagnostic

Existing Healthcare Issue:

Breast cancer is one of the most common types of cancer in the United States. In 2018, an estimated 266,120 new cases of invasive breast cancer and 63,960 new cases of non-invasive breast cancer are expected to be diagnosed. Approximately 85% of breast cancers occur in women who have no family history of it. As such, many women don't know they need to get an evaluation until the later stages, at which point it is often too late to successfully treat (U.S. Breast). This is an incredibly important issue, since breast cancer is treatable and manageable if caught early. But, because these women are currently not getting tested when they need to, women are dying from preventable deaths.

Before proceeding, it is important to consider the pathology of breast cancer. Most breast cancers are carcinomas, which means that they begin in the epithelial cells. More specifically, most breast cancers are adenocarcinomas, which means that they start in the glandular tissue. If the excessively growing cells are contained within the lobules or breast ducts, the cancer is considered to be in-situ carcinoma. If the cells have broken out of the lobules or ducts, it is considered to be invasive or infiltrating carcinoma (Understanding).

There are a myriad of different proteins, antigens, and biomarkers associated with an increased risk of breast cancer. One of these, is the protein HER2, which is a growth-promoting protein on the outside of all breast cells. Breast cells with higher than normal levels of this protein are associated with women being at higher risk for breast cancer. The types of cancers associated with HER2 tend to grow and spread faster. However, these types of cancers are also more treatable if caught early. It is thus important for women to know their HER2 levels. Currently, HER2 is tested through a biopsy or surgery sample that is later tested using immunohistochemical stains (IHC) and fluorescent in situ hybridization (FISH), which are often used for the same sample. Although these tests are accurate, they are expensive, invasive, and take a long time to process the results (Breast Cancer).

Different types of diagnostics for breact cancer, including screening, and the aforementioned tests are often expensive and inaccessible since they require going into a doctor and some types of insurance do not cover these tests. In addition, these tests are often invasive, uncomfortable, and painful, which deters women from getting evaluated. When women finally do get evaluated, it is often in the later stages of the cancer, which has a low efficacy prognosis. HER2 diagnosis has a high success rate for individualized prognosis and treatment for women, however, the previously mentioned issues with diagnostics prevent women from being diagnosed and successfuly treated. The issues taken with currently available diagnostics for breast cancer and HER2 levels will be the healthcare issue evaluated in this lab.

Our Device:

We seek to make a point-of-care diagnostic for breast cancer in a pill form such as to make it more accessible and attractive to use. This pill would work by detecting the protein HER2. If a woman has increased levels of HER2, the device would change the color of urine of the woman, signaling her to go to a doctor for further evaluation so she can receive prognosis and treatment.

Current Solutions:

General Breast Cancer Diagnostics

	Mammogram	Biopsy
Advantages	-Low radiation doses -Reduce breast pressure -Steady detection rates (Cancer Treatment centers of America)	-Definitive diagnosis -Even if the result is benign, it can diagnose the likelihood of risk for harmful breast cancer -Woman can begin taking preventative measures if she finds out she is at risk (Imaginis)
Disadvantages	-Overdiagnosis and risk of false alarm -Misses lesions that form earlier on -Limited use in premenopausal women due to the oncogenic potential of the x-ray procedure (NCBI)	-Stressful and painful procedure -The more invasive, the greater the degree of risk -Percutaneous breast biopsies carry a risk of bruising, infection, and hematoma -Open surgery breast biopsies require sutures (Imaginis)
Unmet Needs	This device needs to decrease the amount of false positives, and needs to be more accurate in identifying lesions earlier on.	This needs to be less invasive and eliminate the need of surgery since not all patients are comfortable with this test and decline testing.

Diagnostics Specifically for HER2 Levels

	Immunohistochemical Stain (IHC)	Fluorescent in situ Hybridization (FISH)
Advantages	-Easy Multiplexing: More colors and narrower emission spectra than chromogenic dyes for analysis -Better Target Co-localization**:** Fluorescent dyes allow separate identification of co-localized targets -Higher Dynamic Range**:** Easier to visualize rare and high abundant targets on the same slide -Fewer Steps: No step for substrate addition (Novus Bio)	**-**FISH can be used to target not only ribosomal genes, but also functional genes (via mRNA) relevant in bioremediation -FISH is routinely used in medical fields such as genetic counselling, disease identification, and microorganism species identification due to its accuracy (ITRC)
Disadvantages	-Susceptible to Photobleaching: Exposure to light may diminish fluorescent signal over time -Processing time can take weeks (Novus Bio)	-Cost -Time -The detection limit of FISH is high -Standard protocols for sample collection and storage prior to FISH analysis have not yet been developed -The FISH method is not widely commercially available (ITRC)
Unmet Needs	This product needs to be less sensitive to photobleaching, such that the sample can be preserved over time, and needs to take less time to process. It also needs to be more cost effective.	This device needs to be more user friendly and accessible. It also needs to be less time consuming and more cost effective.

Given the above information, it is clear our device is more marketable. All of these diagnostic devices have stilting issues, whether they be time, cost, accessibility, or level of invasiveness. Furthermore, 85% of women who have breast cancer do not have a family history of it, and therefore for don't get tested because they don't think they are at risk. These two facts deter many women from getting tested early, and when they finally do get tested, it is often

already in the later stages, at which point it is often too late for testing. Our device would help fix these issues, as it is a cheaper, quicker, less invasive, easy to obtain alternative.

Customer Validation:
-Provista Diagnostics
https://www.provistadx.com/

-Agendia
http://www.agendia.com/

-Myriad Genetics
https://myriad.com/

-Biotheranistics
http://www.biotheranostics.com/

-US Diagnostics
http://www.usdiagnostics.com/

-Genomic Health, Inc
http://www.genomichealth.com/

-BCR Diagnostics
http://www.bcrbiotech.com/

-Caris Life Sciences
https://www.carislifesciences.com/platforms/

-Avant Diagnostics
https://www.avantdiagnostics.com/

-Breast Cancer Research Foundation
https://www.bcrf.org/?gclid=Cj0KCQiA-qDTBRD-ARIsAJ_10yL_MB7FxzBPI3xlZHiQ-9p37I3i5-1aFc26CE2tfFj4aTaM5ssyt3oaAkQ1EALw_wcB

-American Cancer Society
https://www.cancer.org/?&gclid=Cj0KCQiA-qDTBRD-ARIsAJ_10yKdoF0ZQ_B8DsMJeCv94MHggQX1_xJBwy52fAgpUorNgiVfR6BbOQUaAnUwEALw_wcB

-Arizona Oncology
https://arizonaoncology.com/locations-physicians/locations/detail-phoenix-biltmore/

-Mayo Clinic Cancer Center
https://www.mayoclinic.org/diseases-conditions/cancer?mc_id=us&utm_source=yext&utm_medium=l&utm_content=departmentcancer&utm_campaign=mayoclinic&geo=national&placementsite=enterprise&invsrc=cancer&cauid=10514

-Ironwood Cancer & Research Centers
http://ironwoodcrc.com/

-Accelerate Diagnostics
http://acceleratediagnostics.com/

-Alveo Technologies
https://alveotechnologies.com/

-21st Century Oncology
https://www.21co.com/

-Banner-University Medicine Women's Institute
https://www.bannerhealth.com/locations/phoenix/banner-university-medical-center-women-s-center

-True Diagnostics
http://truediag.com/

-Integrative Women's Health Institute
http://integrativewomenshealthinstitute.com/

All of the above companies are likely to be open to trying our product because they are all seeking to increase the efficacy of breast cancer diagnostics and treatment. This is a commonality among all of these organizations. Many of them are currently partnered with ongoing research for breast cancer diagnosis and treatment, which leads us to believe they would be open to trying new products, such that they had the scientific backing to warrant them.

IP Position:

1) Breast Cancer Diagnostic Blood Test (Feller)

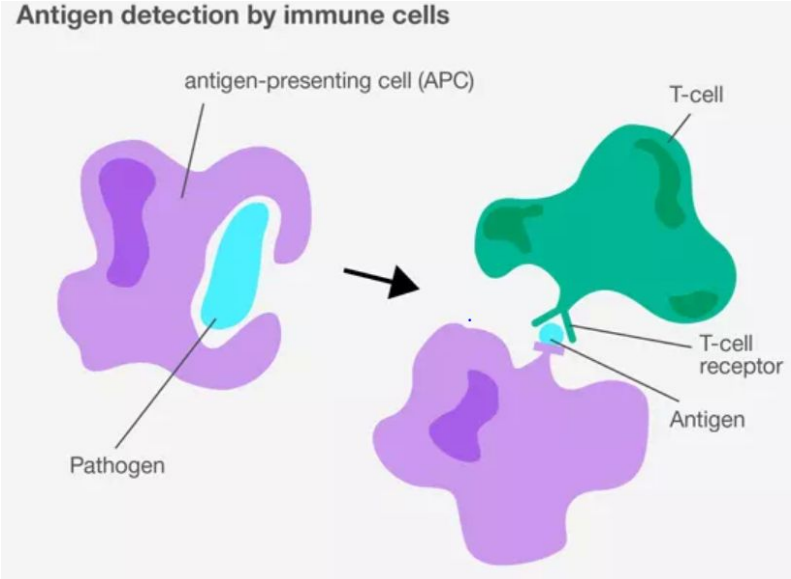
-Assignee: Georgetown University

-File Date: January 3, 1984

-Summary: This product works by detecting an antigen in a plasma or serum sample. This requires conditioning the sample by separating the antigen being detected, and then using an immunological assay to screen for a specific antigen. This assay is then used to evaluate if the patient is at high risk for breast cancer. The traditional diagnostic technique of palpation is often not as effective at diagnosing lesions that form earlier on, so by the time women are properly diagnosed, the cancer has already metastasized. This is why using blood serum and detecting antigens associated with breast cancer has more efficiency and efficacy. This specific patent primarily focused on detecting glycosyl transferases, casein, which is found in breast tissue, and human mammary epithelial antigens, which are all associated with an increased risk of breast cancer.

-Relevant Images:

Figure 1: This shows the process of antigen detection (Breast Cancer Now Explains)



This patent helped establish the precedent for using blood tests and serums to diagnose antigens and biomarkers associated with breast cancer, which is relevant to our product since we are aiming to diagnose HER2 protein levels in the blood.

2) Cutoff Point Delta Ct. Method for HER2 PCR Testing in Breast Cancer (Yu)

-Assignee: Genetics Development Corporation

-File Date: February 13, 2013

-Summary: This HER2 test utilizes the polymerase chain reaction (PCR) in order to provide standardization for the test. It works by measuring HER2 mRNA expression level using

quantitative real-time PCR technique, and then using a simplified scoring system to evaluate the levels and determine if the patient is at high risk for breast cancer. The process of the PCR technique entail preparing a sample that is in line with American Clinical Pathology (ACP) and American Society of of Clinical Oncology (ASCO) standards, extracting the RNA and measuring its concentration, running reversa transcription and PCR with built in quality control for each step, and then performing data analysis. Following the data analysis, it is determined if the patient has increased HER2 levels, and subsequently a high risk of breast cancer.

-Relevant Images:

Figure 1: This figure shows the normal breast cancer cells compared to the cells with raised HER2 levels (HER2)

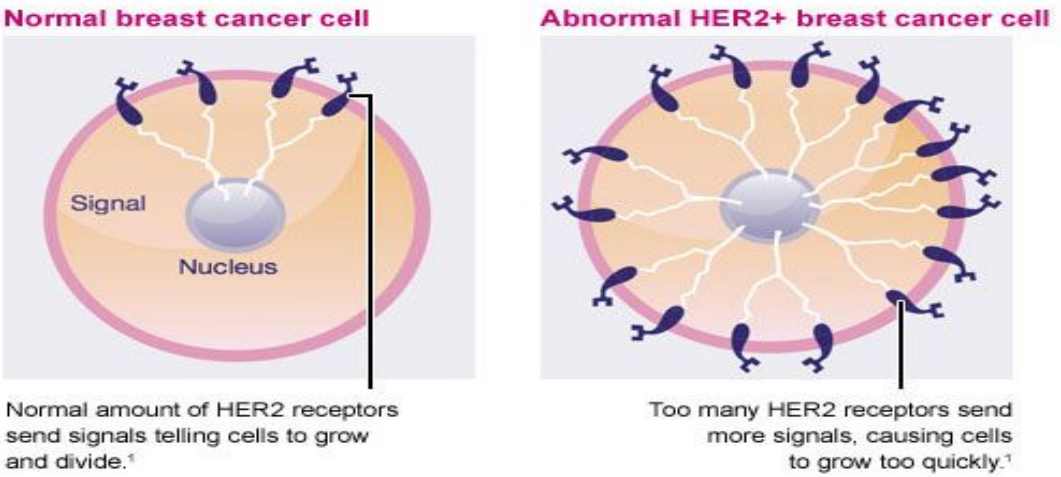
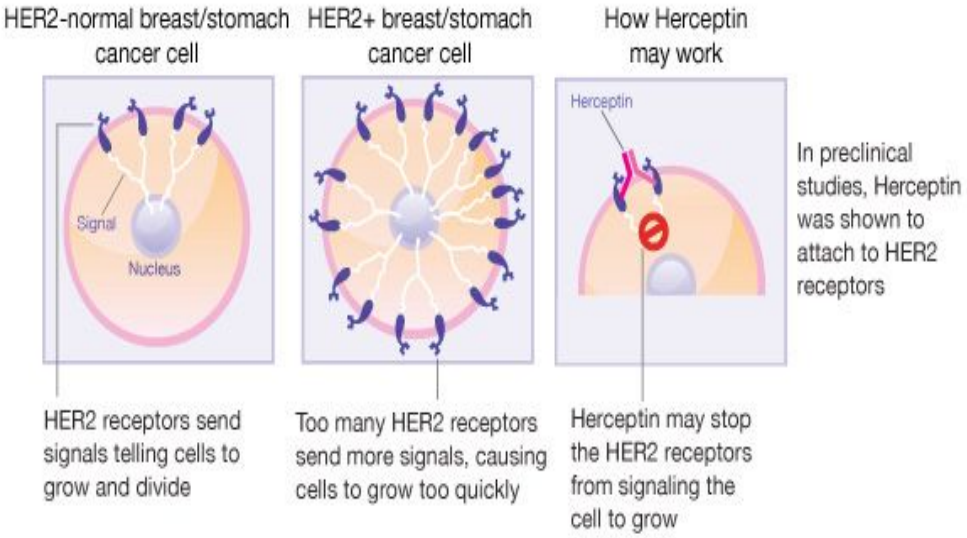


Figure 2: This figure further shows the difference between normal cells and cells with increased levels of HER2, in addition to how a possible treatment, Herceptin, works (Smart)



This patent helps provide precedent for using HER2 levels to assess the risk of breast cancer. This is useful to our product since that is exactly what our diagnostic is testing.

3) Tissue Analysis and Kits

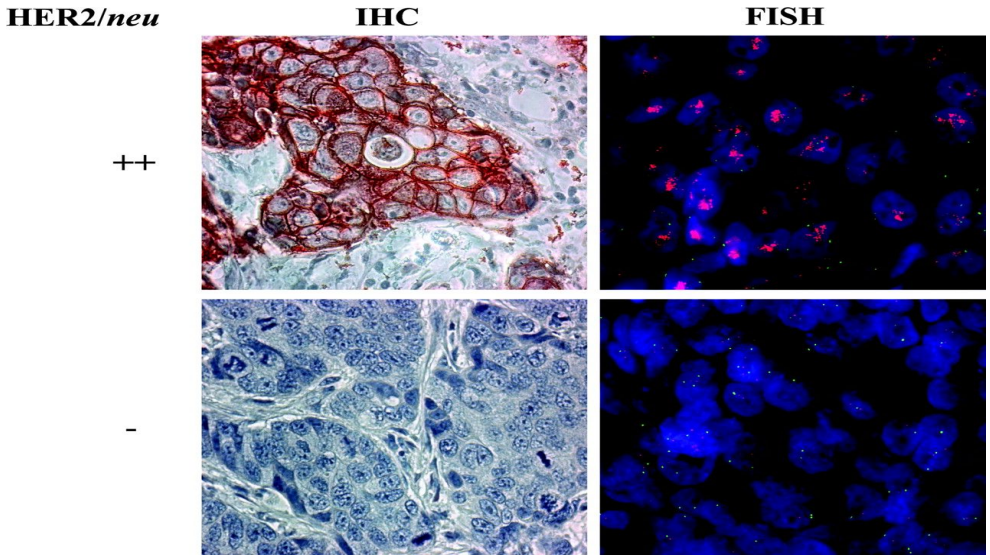
- Assignee: Cytometry Associates

- File date: October 1, 1999

- Summary: The purpose of this diagnostic is multifaceted. First, the purpose of this is to develop screening technology for substances that are linked to a higher risk of breast cancer. Second, is to develop molecular-targeted drugs for breast cancer with higher efficacy and lower risk of adverse reactions in order to improve clinical managements. These purposes utilize tissue analysis through morphological staining and immunohistochemistry (IHC) with fluorescence in situ hybridization (FISH). This allows for accurate and simplified prognostic, diagnostic, and research applications on a subject's tissue sample. The HER2 levels are evaluated, and subsequent analysis for breast cancer risk is conducted, as well as which drugs best target treating this cancer.

- Relevant Images:

Figure 1: This figure shows the IHC and FISh tests, which are often performed together (Xia)



These tests are the most popular tests available for detecting HER2 levels in breast cells. This patent provides precedent to our method for our diagnostic.

Fundability Worksheet Score:

Customer Validation: 1

Competition: 2

IP Position: 1

We arrived at this score based on multiple reasons. For Customer Validation, we scored a 1 because there is not enough data and products similar to these to predict the success of this

product. We are also not currently in contact with possible customers, so we do not actually know if customers are open to trying our product. In competition we scored a 2, because there are only two existing products similar to ours, (IHP) and (FISH), but they still have many unmet needs. For IP Position we received a 1 because there are no current patents on our specific product.

Works Cited

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