The holistic approach to targeting breast cancer

Part I: Understanding Breast Cancer

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Main topics

- What is breast cancer?
- Cancer incidence and related deaths across the world.
- Factors known to cause breast cancer or increase risk.
- Introduction to breast cancer: Cellular perspective.
- Role of neighboring cells and structures in inhibiting or promoting cancer.
- Current treatments available: drawbacks.
- Need for holistic approaches.
What is Breast Cancer?
Cyclical changes in breast during normal lifecycle

Female hormones

Estrogen

Progesterone
Breast Cancer

Normal Breast

Development of cancer

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Cells disseminate into capillaries and lymph nodes.
Breast Cancer metastasis

Stage IV Cancer

Tumor can be of any size

Multiple lymph node metastasis

Metastases
- Brain

Lung

Liver

Bone
Worldwide Cancer Incidence and Death
Corpus uteri: 23733 (3.0%)
Leukemia: 24285 (3.1%)
Cervix uteri: 24385 (3.1%)
Ovary: 42737 (5.5%)
Stomach: 43673 (5.6%)
Other: 236487 (30.4%)

Europe: Cancer Incidence and death in women

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World Cancer Report 2014
North America: Cancer Incidence and death in women

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Comparison of breast cancer incidence and mortality in Europe and North America to East and Central Asia
Age standardized (World) cancer incidence rates per 100000 - all cancers combined - in women

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence Rate</th>
</tr>
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<tbody>
<tr>
<td>USA: White*</td>
<td>296.9</td>
</tr>
<tr>
<td>Denmark</td>
<td>292.7</td>
</tr>
<tr>
<td>USA: Black*</td>
<td>281.5</td>
</tr>
<tr>
<td>Australia</td>
<td>274.2</td>
</tr>
<tr>
<td>Slovakia</td>
<td>222.8</td>
</tr>
<tr>
<td>Uganda*</td>
<td>212.2</td>
</tr>
<tr>
<td>Spain*</td>
<td>202.6</td>
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<tr>
<td>Colombia*</td>
<td>201.3</td>
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<tr>
<td>China*</td>
<td>180.0</td>
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<tr>
<td>Japan*</td>
<td>171.2</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>161.8</td>
</tr>
<tr>
<td>India*</td>
<td>109.3</td>
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</tbody>
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What’s the reason behind so much difference in cancer incidence?
From a global perspective, the cancer burden for each country and the most common tumor types are associated with the value of the Human Development Index (HDI) = industrialization.

Increase in industrial development results in higher burden of cancer overall, and of specific types.
Why does cancer incidence increase with industrialization?
Factors that increase the risk of breast cancer

1. **Food:**
   
i) Pesticides (eg. Atrazine) in fresh foods.
   
ii) Bisphenol (BPA) in processed and canned food and plastics.
   
iii) Hormonal additives in dairy and meats.
   
iv) Food preparation in non-stick cookware containing PFCs.

2. **Exposure to radiation:**
   
i) Repeated X-Rays, diagnostic and therapeutic CT/PET/MRI scans.
   
ii) Therapeutic radiation exposure and mammograms.
   
iii) Workplace exposure
3. Water and Air

Organic Solvents
Toluene, methylene chloride, trichloroethylene and formaldehyde. Sources: air pollution, waste incineration, cleaning products and some cosmetics. They are also used in the manufacture of computer parts.

1,3-butadiene
Internal combustion engines and petroleum refineries. It is also found in tobacco smoke. Main route: Inhalation.

Aromatic Amines
Found in the plastic and chemical industries, in environmental pollution such as diesel exhaust and tobacco smoke. Have a direct effect on cell division.

Vinyl Chloride
PVC synthesis. Found in the air near hazardous waste sites and landfills and in tobacco smoke. It has also been linked to increased mortality from breast cancer among workers involved in its manufacture.

Polycyclic Aromatic Hydrocarbons (PAHs)
Byproducts of combustion. Sources: Coal burners, diesel engines, grilled meats and cigarettes. Exposure is primarily through inhalation. They have been shown to increase risk for breast cancer.

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4. Cosmetics

Phthalates: Nail polish and synthetic fragrance

Triclosan: Antibacterial soaps, deodorants and toothpastes.

Parabens: Preservative in creams, lotions, ointments and underarm deodorants.

Polycyclic Aromatic Hydrocarbons (PAHs) Naphthalene. Some cosmetics and shampoos are made with coal tar - contain PAHs.

Lead: Contaminant in over 650 cosmetic products, including sunscreens, foundation, nail colors, lipsticks and whitening toothpaste.

Sunscreen: Many sunscreens contain chemicals with significant estrogenic activity,

Hormonal disruption
Early or late puberty
Loss of fertility in men and women
Increased risk of Breast cancer

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Risk factors for breast cancer

Genetic Predisposition/ Family history:

A. Get our genes from mum and dad.
B. Inherited mutations in genes.
C. 5-30 fold increased risk in women with mutation.

Carrier of mutation

Exposure to carcinogens

Full Blown mutation

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Lifestyle - Imbalance of *hormones*:

**Child Birth:** None/Late

**Obesity/Overweight**

**Diet and nutrition:**
- i) Vegetables, Fruits and nuts.
- ii) Excess carbohydrates, Processed foods, refined sugar – most common and cheapest.
- iii) Unhealthy fats.
- iv) Exercise!!

**Stress**

**Estrogen** containing drugs – HRT.

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What is breast cancer?

A cellular perspective
Why does cancer occur and how?

Precipitating factors:
- Environment
- Diet
- Viruses
- Lifestyle
- Tobacco use
- Genetic predisposition

Cells of one’s own body: Gone haywire

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Types of breast cancer

Ductal Carcinoma in situ or invasive

Lobular Carcinoma in situ or invasive

Normal duct  Intraductal carcinoma in situ  Invasive ductal cancer
Subtypes of invasive breast cancer include:

**Hormone-sensitive breast cancer** – Estrogen and progesterone.

**HER2 positive breast cancer** - overabundance of the Her2 receptor.

**Triple negative breast cancer** – Neither. Non-responsive to treatment.

[Diagrams showing estrogen and HER2 receptors]
Time taken by cancer to develop

- Majority of malignancies – not palpable for several years or decades.

- Pace of growth: *doubling time*.

- 1 mm tumor: Smallest size detectable. Takes ~ 6 yrs.

- Mass of 4-5cm. is a journey of many years.
Why the delay in cancer development?
Tumor Microenvironment
The Tumor and its surroundings: Love thy neighbour!

Soldiers of the body
The Tumor Environment: Cancer spread and metastasis


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The Tumor Microenvironment: Love thy neighbour!

1) Cancer cells recruit and manipulate normal cells such as fibroblasts, immune cells and endothelial cells by secreting chemo-attractants and hormones.

2) Initially the cells try to suppress the tumor utilizing their wound healing functions.

3) Under continuous signaling from the cancer cells, however, normal cells undergo modification to support cancer growth, proliferation and invasion and even resistance to therapy.
Current Therapies for breast cancer

**Surgery:** Surgical removal of breast tumor tissue and a part of surrounding tissue.
  - Cancer cells may not be completely removed.
  - Remaining cells can proliferate which can induce malignancy from a non-malignant tumor.

**Radiation:** Targeted beam of high intensity radiation used to incinerate the tumor tissue.
  - Damaging to normal tissue.
  - Not recommended for carriers of BRCA mutations – might induce non-cancerous cells to become cancerous.

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Chemotherapy - Chemical onslaught
Chemotherapy:

- Chemotherapy uses powerful chemicals that are injected directly to the bloodstream.
- Systemic therapy - *kills rapidly dividing cells* !! Not just cancer cells.
  - Bone marrow.
  - Intestines
  - Hair
  - Immune cells
- Detrimental side effects including hair loss, diarrhea, nausea and vomiting, weakness, fatigue, impaired immunity and organ damage.
Drugs used as chemotherapy (severely cytotoxic)

1. **Alkylating agents**: Act by irreversibly damaging DNA. Eg. Cyclophosphamide, Carmustine.
   
   i) **Causes long-term damage to bone marrow; increases risk of leukemia.**

2. **Taxanes**: Disruption of microtubule function. Docetaxel, Paclitaxel.

3. **Antimetabolites**: Interfere with RNA and DNA synthesis. Eg. 5-fluorouracil, 6-mercaptopurine, Methotrexate.


5. **Platinum drugs**: Direct damage to DNA. Cisplatin, Carboplatin.
Targeted therapy/ adjuvant therapy for breast cancer

1. **Trastuzumab/ Herceptin**: Monoclonal antibody against HER2 receptor.

2. **Ado-trastuzumab emtansine**

3. **Lapatinib (Tykerb)**: Lapatinib is another drug that targets the HER2 protein.

4. **Bevacizumab (Avastin®)**: A monoclonal antibody against vascular endothelial growth factor (VEGF).
Hormone blocking drugs are used to block ER/PR.

1. **Tamoxifen**: Given after surgery to prevent recurrence and relapse in metastatic breast cancer. Serious side effects ensue after long-term treatments including uterine cancers, deep vein thrombosis, pulmonary embolism and heart attacks.

2. **Aromatase inhibitors**: Inhibit enzyme aromatase. Preventing production of estrogen. Eg. letrozole. Speed up osteoporosis, increase muscle and joint pains, hot flashes.
Limitations of chemotherapy

1. Extremely cytotoxic to all dividing cells!


3. Severely debilitating: Breaks down body’s support systems.

4. Long term side-effects: Cardiac problems, peripheral neuropathy, damage to many organs.

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Need for holistic approaches!

• Approaches that not only target and kill cancer cells, but enhance and support body’s support systems and cellular health.

• Multi-pronged attack
  - Apoptosis
  - Inhibition of MMPs
  - Support to immune system

• In such approaches, because of multifaceted approach, resistance is difficult to develop.
This can be achieved with micronutrient mixtures which allow us to do this:
Take home message

- Respect your body! Make healthier choices for yourself.
- Go natural!
- Don’t be a cancer cell!
Thank You