Health, Wellness and Cancer Prevention

Orlando E. Silva, M.D.
Dedication

To The Fallen and The Standing Patients
Along the way.
Here’s to the Wives,
And the Mothers,
The Sisters and the Daughters
Who made a difference
And guided the way.

Thank You.
We are still trying.
How can the organ that nurtures us with life, become the executioner of so many ???
Breast Cancer Risk Factors

- Gender
- Age
- Hormonal Factors
  - Early menses
  - Late menopause
  - No pregnancy
  - Late pregnancy
  - No lactation
  - Other Estrogens
- Mammographic Breast Density
- Family history
- Inherited Susceptibility Genes
- Diet/ETOH consumption
- Radiation
- Benign Breast Disease
- Ethnicity
Endocrine Disrupting Environmental Toxins

- Organochlorines
- Biphenyl A (coated receipts)
- PBBs (flame retardants Polybrominated Biphenyls)

- 95% of all U.S adults have BPA in their urine.
- Higher levels of BPA related to Met Syndrome
- Independent risk factor besides lifestyle
## Reversible Biomarkers and Relative Risk

<table>
<thead>
<tr>
<th>Serum Hormone Levels</th>
<th>2-4X</th>
</tr>
</thead>
<tbody>
<tr>
<td>(upper quartile vs lower)</td>
<td></td>
</tr>
</tbody>
</table>

| Serum IGF-1, IGF-1/IGFBP-3 | 2X |
| (pre-menopausal) | (upper quartile vs lower) |

| Mammographic breast density | 5X |
| (>75% vs <5%) |

| Breast IEN | Hyperplasia | 2X |
| (Dx Bx) | (Dx Bx) | 4-5X |
| ADH | In situ cancer | 10-20X |

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Mammographic Density
“And Now What???”
It is all in the Genes right?

It’s all genetic?

Nigerian Paradox!
Alzheimer’s - Incurable but PREVENTABLE!

- The Nigerian Paradox

- Nigeria should be the country with the highest rate of Alzheimer’s due to genetics but, it is actually the lowest in the world.

- Nutrition can trump genetics!
Breast Cancer Risk Factors

• Inflammation!!!
Fighting Cancer through Nutrition/Activity

Decreases Inflammation and Increases Immunity

Metabolic Syndrome
- Increased BP
- Increased Lipids
- Central Obesity
- Insulin Resistance
- Skin Tags
- Darkening of Axillary folds

Inflammation
\( \downarrow \) (IL-6)
1 disease
\( \downarrow \)
different expressions

- Diabetes Mellitus II
- Cancer
- Alzheimer’s (Apo E-e4)
- Depression
ANTI-Inflammation!!!

- Inflammation
  - Leading culprit in developing:
    - Metabolic Syndrome/Insulin Resistance
    - Diabetes/Obesity
    - CAD
    - Alzheimer’s
    - Depression
    - Cancer
Metabolic Syndrome

- Centripetal Obesity - belly fat
- Insulin Resistance - High circulating Insulin levels
- High Blood Pressure
- High Lipids
- Acanthosis Nigricans - darkening of the folds around neck and axillas
- Skin Tags around neck and axillas
- High levels of pro-inflammatory cytokines
Hypertension

• ↑BP can cause LV hypertrophy and can lead to CHF even if EF is normal.

• Women with chronic heart failure, even if asymptomatic have a ↓ mortality by 65%.

• Standard of care is to start dual therapy early even if asymptomatic if EF < 50 (ACE/ARB and BB as 1st line therapy) for anthracycline and TKI associated cardiomyopathy.

• B-Blockers - ↑OS in TNBC, in retrospective studies, by ↓ norepi, ↓ angiogenesis and cell migration and may boost immunity.
Cardiac consultation

- Diltiazem – Interferes with lots of chemo drugs.
- Ondansetron can cause QTc prolongation – Keep K+, and Mag on the high side.
34% of the country

**Atherogenic:**
- Insulin resistance +/- glucose intolerance
- Dyslipidemia
- ↑ inflammatory markers (CRP)

**Prothrombotic:**
- ↑ homocysteine
- ↑ fibrinogen / ↑ PAI-1
- ↓ Mag
Obesity at diagnosis is linked to prognosis in breast cancer

*Meta-analysis of 82 studies looking at obesity and survival in breast cancer*

<table>
<thead>
<tr>
<th></th>
<th>Breast Cancer-Specific</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR [95% CI]</td>
<td>HR [95% CI]</td>
</tr>
<tr>
<td>All patients</td>
<td>1.35 [1.24-1.47]</td>
<td>1.41 [1.29-1.53]</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>1.75 [1.26-2.41]</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>1.34 [1.18-1.53]</td>
<td></td>
</tr>
</tbody>
</table>

RR, relative risk.
Interaction of Estrogen and Insulin Pathways in Setting of Obesity

Adipose Tissue

↑ Estrogen
↓ SHBG

↑ Insulin
↓ IGFBP

↑ IGF-1

ER/PgR
IRαβ
IGF-1R

Proliferation
Anchorage Independent Growth
Reduced Apoptosis

Pathways:
PI3, ras-raf, map kinase
Obesity in the United States

- In 1999-2002, 34% of adults were overweight and 30% were obese

% Overweight Over Time

<table>
<thead>
<tr>
<th>Years</th>
<th>’76-78</th>
<th>’88-94</th>
<th>’98-02</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-74</td>
<td>42.0%</td>
<td>51.2%</td>
<td>61.7%</td>
</tr>
<tr>
<td>55-64</td>
<td>53.7%</td>
<td>66.3%</td>
<td>72.2%</td>
</tr>
</tbody>
</table>

www.cdc.gov/nchs/fastats/overwt.htm
Potential Mechanisms Underlying Relationship Between Fat Intake or Weight and Breast Cancer Outcome

- High intake of dietary fat
- Excess weight at dx or weight gain after diagnosis

Mechanisms:
- Estrogens
- Sex Hormone Binding Globulin
- Insulin
- Insulin Growth Factor 1 (IGF-1)
- Insulin Growth Factor Binding Protein (IGFBP)
Low-Fat Dietary Pattern and Risk of Invasive Breast Cancer: The Women's Health Initiative Randomized Controlled Dietary Modification Trial

R. L. Prentice, B. Caan, R. T. Chlebowski, and Colleagues
WHI DM Trial

373,092 completed the eligibility screening form

56,139 eligible

316,953 excluded (refused, low fat intake, info not avail)

7,304 excluded (staff/participant reevaluation, history of breast cancer, other)

48,835 randomized

Intervention 19,541

Status 3/31/05
17,674 alive & retained
1,867 lost, deceased, or withdrew

19,541 included in analysis

Comparison 29,294

Status 3/31/05
26,677 alive & retained
2,667 lost, deceased, or withdrew

29,294 included in analysis

Interpretation

• Intensive intervention resulted in significant and sustained dietary fat reduction and vegetable and fruit increase.

• Observed 9% lower breast cancer rate (15% among “adherent women”) but the difference was not large enough to be statistically significant.
Impact of Weight on Prognosis in Women Diagnosed with Breast Cancer

- Multiple studies have examined impact of weight and/or BMI on breast cancer prognosis.
- In review by Chlebowski et al:
  - 26 studies (n=29,460) demonstrated a statistically significant association between increased weight and poor outcome (recurrence or death).
  - 8 studies (n=3,727) revealed no significant relationship.

Chlebowski et al. JCO 20:1128-43, 2002
Meta-analysis Evaluating Measures of Adiposity at Dx and Prognosis

<table>
<thead>
<tr>
<th></th>
<th>Recurrence at 5 yrs</th>
<th>Death at 10 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR [95% CI]</td>
<td>HR [95% CI]</td>
</tr>
<tr>
<td>Body Weight</td>
<td>1.78[1.50-2.11]</td>
<td>1.36[1.19-1.55]</td>
</tr>
<tr>
<td>BMI</td>
<td>1.91[1.52-2.40]</td>
<td>1.60[1.38-1.76]</td>
</tr>
</tbody>
</table>

Nurses’ Health Study Analysis of Weight Gain and Breast Cancer Survival

- 5204 Nurses’ Health Study participants diagnosed with breast cancer
- Change in BMI calculated from pre-breast cancer dx to first reported BMI > 12 months later
- Adjusted for smoking, menopausal status, and relevant breast cancer variables

Kroenke et al: JCO 23:1370-78, 2005
# Weight Gain After Diagnosis in Never-Smoking Women

<table>
<thead>
<tr>
<th></th>
<th>MAINTAIN</th>
<th>GAIN 0.5 to &lt; 2.0 kg/m²</th>
<th>GAIN ≥2.0 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrences*</td>
<td>1.00</td>
<td>1.40</td>
<td>1.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[1.02-1.92]</td>
<td>[1.04-2.24]</td>
</tr>
<tr>
<td>Breast CA Deaths*</td>
<td>1.00</td>
<td>1.35</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.93-1.95]</td>
<td>[1.07-2.51]</td>
</tr>
<tr>
<td>All Cause Mortality*</td>
<td>1.00</td>
<td>1.35</td>
<td>1.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[1.00-1.82]</td>
<td>[1.12-2.27]</td>
</tr>
</tbody>
</table>

*multivariate RR
95% CI

\[ p = .01 \]
\[ p = .03 \]
\[ p = .04 \]

Kroenke et al
Obesity

Adipokines – 7 Hormones (Resistin)

- Insulin Resistance - $\uparrow$ levels of Insulin
- Fat $\uparrow$ Estrogen
- $\uparrow$ Inflammation
Diet

• Veggies
  - Spinach/carrots (carotenoids / flavonoids)
    - rich in magnesium & alpha lipoic acid
    - antioxidant
  - Asparagus, beets, broccoli, brussels sprouts, garlic, onions, leeks, kale, cabbage, scallions

• Dark Chocolate
  - at least 99%;
    - Cuna Indians from San Blas islands (off the Coast of Panama)
      - lowers BP and rich in oleic acid

• Fruits
  - Berries
    - antioxidants/anti-angiogenesis
### Dietary Sources of Naturally-Occurring Antiangiogenic Substances

<table>
<thead>
<tr>
<th>Green tea</th>
<th>Red grapes</th>
<th>Lavender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strawberries</td>
<td>Red wine</td>
<td>Pumpkin</td>
</tr>
<tr>
<td>Blackberries</td>
<td>Bok choy</td>
<td>Sea Cucumber</td>
</tr>
<tr>
<td>Raspberries</td>
<td>Kale</td>
<td>Tuna</td>
</tr>
<tr>
<td>Blueberries</td>
<td>Soy beans</td>
<td>Parsley</td>
</tr>
<tr>
<td>Oranges</td>
<td>Ginseng</td>
<td>Garlic</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>Maitake mushroom</td>
<td>Tomato</td>
</tr>
<tr>
<td>Lemons</td>
<td>Licorice</td>
<td>Olive oil</td>
</tr>
<tr>
<td>Apples</td>
<td>Turmeric</td>
<td>Grape seed oil</td>
</tr>
<tr>
<td>Pineapple</td>
<td>Nutmeg</td>
<td>Dark chocolate</td>
</tr>
<tr>
<td>Cherries</td>
<td>Artichokes</td>
<td>Others</td>
</tr>
</tbody>
</table>

Source: Angiogenesis Foundation (www.angio.org)
Diet

• Fibers & Grains
  - Walnuts - 14 halves a day, also rich in magnesium
  - 50 grams/day

• Milk – Horizon/Organic Valley Milk (0% Fat)
  - UNSWEET!
  - ALMOND MILK!!!

• Turmeric – inhibits nFKB
Homemade Almond Milk

1. Soak 1 cup almonds up to 2 days
2. Drain & rinse almonds
3. Blend almonds with 2 cups water
4. Line a glass measuring cup with cheesecloth or nut bag
5. Pour blended almonds in
6. Squeeze & press to extract about 2 cups of milk
7. Refrigerate & use within 2 days
Diet

- Fish – Salmon, mahi mahi, cod, halibut
  - rich in Omega-3 fatty acids

- Extra virgin olive oil (Oleic acid)

- **Fat intake**
  - eat mono & polyunsaturated fats
  - extra virgin olive oil (Oleic acid)

- **Sugar intake (no sweeteners)-Agave/Stevia**

- Limit red meat (avoid processed meat)-Grass fed beef

- Limit salt intake
Oster Steamer

Throw out your microwaves!!!
Insulin Levels

- Centripetal obesity leads to insulin resistance and higher levels of insulin

- BC expresses receptors for insulin

- Premenopausal women 2x with high circulating levels
↑ Sensitivity to insulin (↓ insulin resistance)

- Physical activity - Salsa/Rueda - Casino/Tennis
- Ping- pong/ Water aerobics
- Calorie restriction
- Cinnamon ½ teaspoon / day
- Ginseng berries
- Grapefruit
- Dark Chocolate (100%)
- Leafy Green tea - Folic Acid replacement
- Coffee (no sugar, no milk)
- Fiber- 50 grams / day
- Metformin!!!
Biologic pathways linking obesity and breast cancer not clear, but likely involve metabolic and inflammatory mediators

Insulin and Breast Cancer Prognosis

- Cohort study of 512 women without known diabetes, T1-3 N0-1 disease

  HR [95% ci]

  Highest vs Lowest Insulin Quartile

  Recurrence 2.0 [1.2-3.3]
  Death 3.1 [1.7-5.7]

- In multivariate model adjusting for BMI, tumor, and treatment factors, prognostic significance of insulin levels was maintained

Goodwin et al JCO 20:42-51, 2002
# Prognostic Effects of Insulin in Breast Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>Factor Measured</th>
<th>Recurrence</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwin</td>
<td>2002</td>
<td>512</td>
<td>Fasting Insulin</td>
<td>HR=2.0</td>
<td>HR=3.1</td>
</tr>
<tr>
<td>Pasanisi</td>
<td>2006</td>
<td>110</td>
<td>Fasting Insulin, IRS</td>
<td>HR=2.42, HR=3.0</td>
<td></td>
</tr>
<tr>
<td>Pritchard</td>
<td>2011</td>
<td>667</td>
<td>Non-fasting C-peptide</td>
<td>p &lt; 0.05*</td>
<td></td>
</tr>
<tr>
<td>Irwin (HEAL)</td>
<td>2010</td>
<td>689</td>
<td>Fasting C-peptide</td>
<td></td>
<td>HR=3 (significant)</td>
</tr>
<tr>
<td>Duggan (HEAL)</td>
<td>2010</td>
<td>527</td>
<td>HOMA</td>
<td>HR=4.3 (BC death), HR=1.6 (overall mortality)</td>
<td></td>
</tr>
<tr>
<td>Emaus</td>
<td>2010</td>
<td>1364</td>
<td>IRS Components: BMI, cholesterol, BP, exercise</td>
<td>HR 1.3-3.0 (significant)</td>
<td></td>
</tr>
</tbody>
</table>

Studies also show links between other metabolic and inflammatory mediators and cancer recurrence

**Adiponectin and breast cancer mortality**

- Hazard Ratio for each tertile:
  - Tertile 1
  - Tertile 2
  - Tertile 3

- Significance: \( P = 0.04 \)

**C-reactive protein and breast cancer mortality**

- Hazard Ratio for each C-reactive protein level:
  - <1.2 mg/L
  - 1.3-3.8 mg/L
  - >3.8 mg/L

- Significance: \( P = 0.002 \)

References:

Duggan C, et al. JCO 2011

Pierce, et al. JCO, 2009
Can we improve prognosis in (obese? inactive?) breast cancer patients by targeting metabolic and/or inflammatory pathways?
Targeting metabolic pathways: Metformin

Circulating insulin levels → Gluconeogenesis → AMPK → Metformin → PI3K/PTEN/Akt → Ras/Raf/Erk → TSC2 → mTOR → Protein translation, cell growth, proliferation

Liver
Metformin use associated with better response to neo-adjuvant chemotherapy

- 2529 patients receiving neoadjuvant chemotherapy for early-stage breast cancer at MD Anderson:
  - 2374 women without diabetes
  - 68 diabetics taking metformin
  - 87 diabetics not taking metformin

Jiralerspong S. JCO 2009; 27:3297-3302
Pathological complete response rates by diabetes status and metformin usage

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion with pCR (%)</th>
<th>95% CI</th>
<th>( P(v \text{ metformin}) )</th>
<th>( P(v \text{ non-metformin}) )</th>
<th>Overall ( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>24</td>
<td>13 to 34</td>
<td>—</td>
<td>.007</td>
<td>.07</td>
</tr>
<tr>
<td>Non-metformin</td>
<td>8</td>
<td>2.3 to 14</td>
<td>.007</td>
<td>—</td>
<td>.02</td>
</tr>
<tr>
<td>Nondiabetic</td>
<td>16</td>
<td>15 to 18</td>
<td>.10</td>
<td>.04</td>
<td></td>
</tr>
</tbody>
</table>

Jiralerspong S. JCO 2009; 27:3297-3302
NCIC MA-32
PI: Pamela Goodwin

N: 3582 breast cancer patients
- Completed with primary therapy
- Within 12 months of diagnosis

Randomize

Metformin: 850mg/BID for 5 years
Placebo

Primary Outcome: Invasive Disease Free Survival

Secondary: fasting insulin, weight, QOL, breast cancer free interval, OS, distant DFS, hospitalization for CV disease, diabetes, AE's

NCT01101438
Targeting inflammation

- Evaluation of anti-inflammatory drugs in breast cancer prevention and treatment in early stages

- Observational studies suggest that regular use of aspirin and NSAIDS linked to lower breast cancer risk and better outcomes

### Risk of breast cancer death by use of pain relieving drugs in NHS

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>1 Day/Wk (95% CI)</th>
<th>2-5 Days/Wk (95% CI)</th>
<th>6-7 Days/Wk (95% CI)</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>1.0</td>
<td>1.07 (0.70-1.63)</td>
<td>0.29 (0.16-0.52)</td>
<td>0.36 (0.24-0.54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>1.0</td>
<td>1.03 (0.43-2.43)</td>
<td>1.17 (0.61-2.24)</td>
<td>0.52 (0.30-0.88)</td>
<td>0.04</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>1.0</td>
<td>2.40 (1.22-4.71)</td>
<td>1.28 (0.72-2.27)</td>
<td>1.44 (0.81-2.57)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Aspirin for Breast Cancer (ABC) -A011502

Eligibility
- Node positive
- (any ER status) or
- High risk node neg
- (ER neg and > 2cm)
- HER2 negative
- Within 1 year of dx
- Age < 70

Randomize

Aspirin 300 mg daily x 5 yrs

Stratification factors:
- ER pos vs neg
- BMI (< vs ≥ 30)

Placebo daily x 5 yrs

Primary endpoint: invasive disease free survival

Accrual goal: 2963 women over 2 years
80% power for HR of 0.75 (assume 5 year iDFS survival 77%)
Inflammation and metabolism are interconnected:
Can we target both simultaneously?

Gucalp et al. Disease of the Breast 5th Edition
Lifestyle interventions affect metabolic and inflammatory pathways

*Nutrition and Exercise Study for Women (NEW Trial)*

- Designed to evaluate the impact of dietary weight loss and exercise upon biomarkers linked to breast cancer risk
- Enrolled 439 sedentary, overweight or obese, postmenopausal women
- Participants randomized to 1 of 4 groups:
  - Dietary weight loss
  - Exercise
  - Dietary weight loss + exercise
  - Control
- Endpoints:
  - Primary: change in sex steroids
  - Secondary: change in insulin, metabolic and inflammatory hormones

Weight loss led to significant reductions in metabolic and inflammatory biomarkers

* P<0.001

Weight Change:

- Diet: -10.8%
- Diet + Exercise: -11.9%
- Exercise: -3.3%
- Control: -0.6%

Physical Activity

- 25,624 Norwegian Women followed over 13.7 years
  - 37% ↓ risk breast cancer among women who exercised regularly
  - Greatest benefit seen in women less than 45 y/o who exercise regularly over 3-5 yrs

Thune, NEJM 1997
Physical Activity

- 2,296 Women from Nurse’s Health Study with Stages I, II, III BC

  - Death from BC was at every level of physical activity vs. sedentary
  - 5 hrs/ wk the risk of BC by 50%

Holmes, AACR 2004
Limited data also suggest that energy balance interventions could impact tissue biomarkers

* Protocol amended to allow use of diagnostic biopsy

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**PreHAB**
Pre-Operative Health and Body Study

NCT01516190
Exercise upregulated immune markers in breast tumors

Significantly* Up Regulated Pathways

- Cytokine-cytokine receptor interaction
- NF-κB signaling pathway
- Complement and coagulation cascade
  - Osteoclast differentiation
  - Cell adhesion molecules (CAMs)
  - Taste transduction
  - Neuroactive ligand-receptor interaction
  - Hematopoietic cell lineage
  - Toll-like receptor signaling pathway
  - Olfactory transduction
  - TNF signaling pathway
  - Chemokine signaling pathway
  - Intestinal immune network for IgA production

- Natural killer cell mediated cytotoxicity
  - Jak-STAT signaling pathway
  - ABC transporters

- Antigen processing and presentation

- T cell receptor signaling pathway

*adjusted p value < 0.1 (q-value)

NCT01516190
What is a PET Scan?
Inflammation & Prognosis

• **Adenocarcinoma of Pancreas after surgery**
  - CRP < 10= median survival 21.5 months; > 10= 8.4 months (p=0.015)

• **Prostate cancer survival 10 yrs after intital dx & trx**
  - CRP predicted overall survival & prostate cancer specific survival (HR 1.80 [1.01-3.52] p < 0.05)

• **Gastro-esophageal cancer survival after surgery**
  - CRP < 10= median survival 79 months; > 10= 19 months (HR:3.53 [1.88-36.64]; p<0.001)

• **Breast cancer survival in HEAL study**
  - CRP increased overall survival HR 2.27 [1.27-4.08; p=.002] & trend towards decreased disease free survival (p=.07)

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Decrease Inflammation

- Flossing
- Fiber
- Alcohol
- Physical activity
- Vitamin – D3
- Abdominal Fat
Scientific Corner

Fiber - 75-100 grams/Day

↓ Heart Disease
↓ Stroke
↓ Obesity
↓ DM

For Every 20 grams of Fiber consumed
↓ Risk of B.C. by 15%
TURMERIC

• Turmeric – inhibits NFkB
• Most Powerful Anti-inflammatory agent known
• Crosses The Blood Brain Barrier
• Curcumin is the active ingredient
• 1 tablespoon/person/day
• Must take with black pepper/Ginger
• 1/2 teaspoon per day mixed with the turmeric
Boost Immune System

• Prayer/Meditation/Laughter/Dream
• Family & Friends
• Sleep 6-7 hrs/day
  – Melatonin

• Deep nasal breathing 10x AM & 10x PM
  – 5 secs in & 7 secs out

• Flossing 1-2X’s/ Day
• Baby aspirin/ Vit D/ probiotic
• Exercise and Stretching
CDK 4/6 Inh.- ↑ Immunity

- A) ↑ CD8 Tcell proliferation in Tumor
  (↑Antigen presenting cell, IFN mechanism)

- B) ↓ Immune suppression cells (↓Treg)
Conclusions

- Obesity at diagnosis is a poor prognostic factor in early breast cancer

- Emerging evidence suggests that interrelated metabolic and inflammatory pathways may underlie connection between obesity and breast cancer

- Observational and early clinical data suggest that metformin may have potential as a therapeutic agent in breast cancer; MA-32 will evaluate its role in the adjuvant setting

- Early trials are evaluating the role of anti-inflammatory agents in breast cancer

- Energy balance interventions can also impact metabolic and inflammatory pathways
Books and Websites

- “Anti-Cancer, A New way of Life”
  by David Servan-Schreiber MD, Ph.D

- “A Prescription for Wellness”
  by Carolyn I. Sartor, MD.

- “How Not to Die” by Michael Greger, MD

- nutritionfacts.org by Michael Greger, MD

- “The Blue Zones” by Dan Beuttner
Thank You

Patients

Professor J.A. van Dongen
Dr. Jennifer A. Ligibel
Dr. Hyman Muss
Dr. Stephen Richman

Amanda Martin

Firenze
Culprits of Derangements

- High Glycemic index (refined sugars)
- Fructose/High fructose corn syrup
- Advanced glycosylation end products
  - caramelized sugars
  - meats cooked high temps (microwaves)
- Transfats and long-chain saturated fats
- ETOH
Vitamin D

- U.S. 2nd lowest in the world
- 25 OH levels (hydroxy) – measures steady state
- Normal levels 30-100, shoot for 75 (Carlson)
- Replace with Vitamin D, D3 once a day with food
- Toxic to breast and prostate cancer cells
- Breast and prostate cancer express Vitamin D receptors
- Salmon is the richest fish in Vitamin D and lowest in mercury
- 20 mins in the sun gives 15,000 units of Vitamin D
- Calcium Citrate D is very low in Vitamin D
  - Take Calcium and Magnesium
    - with NO other meds (They are Resins)
Antioxidants

- Are substances that help neutralize free radicals
  - Free radicals damage cells, DNA and cause cell death
  - Free radicals contribute to aging, cancer and heart disease
  - Bind free radicals so they are excreted in the urine
Beverages

• **Coffee (Black)** 2-4 cups per day
  - ↓ Bad Cholesterol (LDL)
  - ↑ Protection of the Liver
  - Helps clear Hepatitis C Virus
  - Rich in Antioxidants

• **Lemon** - Mix with warm water
  - 2 glasses/day – (1) Before Lunch/ (1) Before Dinner

• **Green Tea** 2 cups per day (may be decaf) -must be supplemented with folic acid 1mg/day in women of childbearing age
  - Avoid from Japan (radiation risk)

• **Ginger Root Tea** 1-2 cups per day
  - Helps ↓ prostate size
  - Ginger Root Tea 1-2 cups per day - plain, nothing added
Leafy Green Tea
(Camellia Sinesis Plant)

• Highest concentration of polyphenol - potent antioxidant
  – 1/3 caffeine of black tea and more polyphenol
• EGCG 1/6 catechins

• 2-3 cups per day (no milk with tea)
  Stroke/ Heart Disease/BC/Prostate Cancer/Colon Cancer/Cholesterol (HDL)

• Folic acid supplementation is needed !!!

• Do not take while getting chemotherapy/pregnant/breast feeding/MAOI (hypertensive crisis)/Coumadin/ or if have bleeding disease
Alcohol

- Smashed
- 2 drinks per day risk 1.4-1.7x’s
- Dietary folate may help counteract the risk
- Recommend:
  - 2oz Red wine/day (Resveratrol)
  - Folic Acid 800 mcg/day, which also ↓ Homocysteine levels.
  - ↑ HDL
General Health tips

- **Flossing**
  - Gums, areas in body of highest inflammation in the body
  - Floss 2x’s per day
  - followed by waterpik
  - Dental cleaning every 6 months
  - Healthy gums heart attacks and strokes

- **No Smoking/No Chewing Tobacco**
  - 20 million Americans have died since 1964 because of smoking
  - Lung cancer
  - head and neck cancer
  - bladder cancer
  - heart disease
General Health Tips (Cont.)

Sleep Hygiene
- Recommended 7 hours/night
- If sleep aid is needed - Melatonin
  - will **only** work if lights are out
  - boosts immunity
  - does not hurt memory
- If not resting - see pulmonologist to test for sleep apnea.

Filter Drinking Water
- Filter it twice, with an external filtering device, such as PUR or Zero Water, etc.
- Heavy metals, such as Arsenic
Your Allies - Spices

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Effect</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turmeric/Curcumin</td>
<td>inhibits Nfkb</td>
<td>1 TBS/person/day</td>
</tr>
<tr>
<td>Black pepper</td>
<td>↑ absorption of Turmeric</td>
<td></td>
</tr>
<tr>
<td>Ginger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saffron</td>
<td>Best to prevent Alzheimer’s</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olive Oil</td>
<td>1 teaspoon (5cc) = 100 cal</td>
<td></td>
</tr>
<tr>
<td>Basil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oregano</td>
<td>Rich in anti-oxidants</td>
<td></td>
</tr>
<tr>
<td>Parsley</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardamom</td>
<td>Boosts activity of NK cells</td>
<td></td>
</tr>
<tr>
<td>Cumin</td>
<td>Rich in Salicylic acid</td>
<td></td>
</tr>
</tbody>
</table>
Exercise

- Inflammation (Decreases CRP levels)
- Immunity
- IGA Levels- cuts colds in half
- Circulating Insulin Levels
- Glucose Levels
- Lipids
- Risk of breast cancer
- Risk of prostate cancer
- Heart Attacks and strokes

Walking briskly 60 mins a day [6 days a week]
- At a pace that you cannot use or speak on your cell phone
- Hot flashes of menopause
- Strengthens bones
Your Weapons

- Whole Food, Plant Based, Gluten Free, Dairy Free, Salt Free Diet:
- Fruits 5 servings per day - sweetest in the AM
- Veggies 5 servings per day
- Gluten Free - UDi’s Bread (in Freezer section)
- Pasta - Spinach/Quinoa/Brown Rice
- Fiber 50-75 grams per day
  - colon cancer, Breast Cancer
  - Rice/Black Brown
  - Quinoa
  - Metamucil sugar free (2 tablespoons + 2 glasses of water)
    or Psyllium Husk Powder (2 tablespoons + 2 glasses of water)

- Greens - Rich in antioxidants
  - Broccoli lightly steamed (Better Crunchy!)
  - Asparagus
  - Avocados
### Your weapons

<table>
<thead>
<tr>
<th>Red onions (Quercetin)</th>
<th>Red Grapes (Quercetin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ LDL Cholesterol</td>
<td>✓</td>
</tr>
<tr>
<td>✓ Immunity</td>
<td>✓</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Kale</th>
<th>Blueberries</th>
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<table>
<thead>
<tr>
<th>Cabbage</th>
<th>Oranges</th>
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<table>
<thead>
<tr>
<th>Spinach</th>
<th>Strawberries</th>
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<tbody>
<tr>
<td></td>
<td>Fight Barrett's Esophagus, the precursor to Esophageal Cancer</td>
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<table>
<thead>
<tr>
<th>Leeks</th>
<th>Pears</th>
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<table>
<thead>
<tr>
<th>Watercress</th>
<th>Almond Milk</th>
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<table>
<thead>
<tr>
<th>Arugula</th>
<th>Berries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rich in antioxidants</td>
</tr>
<tr>
<td></td>
<td>✓ Immunity by ✓ NK cells</td>
</tr>
<tr>
<td></td>
<td>✓ Anti-inflammation</td>
</tr>
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<table>
<thead>
<tr>
<th>Collard Greens</th>
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</table>

<table>
<thead>
<tr>
<th>Broccoli</th>
<th>✓ Immunity</th>
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</table>
Your Weapons

Mushrooms (cooked are best)
- White mushrooms fight Breast cancer
- Anti-inflammation/Allergies
- Immunity
- IGA by 50%

Beans (Every day)
- Red/Black/Fava
- Lentils
- Black Eyed Peas
- Split Peas
- Chick peas - Hummus

Tomato Sauce/Pasta
- Lycopene – anti-inflammatory
- Especially for prostate cancer
- 1 tablespoon in AM and PM

Legumes
- (beans, split peas chic peas, and lentils)

Organic Ground Flaxseed
- 1 tablespoon per day
- Add to smoothie or gluten free cereal
- Bob’s Red Mill Organic
  100% whole ground Golden Flaxseed Meal
Snacks

- 10:00 AM 10 almonds & 1 pear
- 4:00 PM 10 almonds & 1 red apple
- Broccoli Chips - with Garlic
- Kale Chips - with Garlic
- Mary’s Gone crackers
  - Gluten free super seed crackers
- Glutino - Gluten free crackers
- NO SUGAR
- Healthy sugar substitutes:
  - Agave (1 drop) or Stevia
Breakfast

• Smoothies
  – Blender Brands - Nutribullet/Ninja Blender/Vitamix…
  – Add protein “LEAN” vanilla veggie protein
  – Almond Milk – plain, unsweetened (Almond Breeze 30 calories or Slik)
  – Fruits/Veggies
  – Organic ground flaxseed – 1 teaspoon
  – No juicing (fiber must be included) (Skin of fruit/vegetable must remain inside the smoothie)
BEST BREAKFAST EVER

• Oatmeal (Steel cut), WATER/ALMOND MILK, CINNAMON (antioxidant), BERRIES, CHOCOLATE (100%), QI’A

• ORGANIC GROUND FLAXSEED (1 Teaspoon)

• Gluten Free Toast

• Hummus
Lowers Blood Pressure

Legumes (beans, split peas, chic peas, and lentils)

Watermelon

Hibiscus Tea (5 teabags in 2-3 cups/day)

Nitrate rich diet (↑ Nitric Oxide level)
- causes arterial walls to relax
[arugula (#1), cilantro, basil, beets (remolacha)]

0 Salt! NOT in the cooking pan and NOT on the plate!

Did you know?
Yanomamo Indians deep in the Amazon have a whole plant, 0 salt diet and never develop high blood pressure even in the very

100% Dark Chocolate
(Lindt 99% or Scharfenberger 100%)
pure cocoa causes arterial walls to relax

Did you know?
Kuna Indians, off the coast of Panama have a diet that is rich in pure cocoa and they do not develop high blood pressure.

Garlic

Organic ground flaxseed (2 teaspoons/day)
Scientific Corner

Fiber - 75 - 100 grams/Day
↓ Heart Disease
↓ Stroke
↓ Obesity
↓ DM

For Every 20 grams of Fiber consumed
↓ Risk of B.C. by 15%
Your Enemies

Animal Protein —

Fish and shrimps (wild caught) once/week (salmon, Sea Bass, Halibut, etc.)

Beef (Grassfed is best! once a month, and make it count
Ex: Argentinian Parrillada or juicy burger w/ egg on top)

Dairy/Yogurt
Cheese (↑ salt)

Chicken (On Chicken Day, every other year
Ex. Peruvian Aji de Gallina)
(↑ Salt, ↑ Cancer Risk,
Salmonella and campylobacter)

Eggs/Eggwhites

Turkey (On Thanksgiving)
Pork (On Christmas/“Nochebuena”)
Lamb (On Easter/Passover)
Processed Meat (the worst)
Scientific Corner

Animal Protein stimulates IGF1 (growth factor for cancer)

Plant based diets
IGF1 Binding Protein - which binds to IGF 1

Consumption of Beef
↑ Risk of dying from cancer and heart disease

Red Meat - ↑ heme Iron - ↑ free radicals
(pro-oxidant)
Conclusion

• Insulin resistance and chronic low-grade inflammation are associated with obesity and inactivity and both have been associated with increased breast cancer risk, as well as recurrence and death among women diagnosed with breast cancer.

• Chronic Inflammation can contribute to insulin resistance in the metabolic syndrome through increased levels of pro-inflammatory cytokines such as TNF-α, which can impair glucose uptake and metabolism by altering insulin signal transduction and IL-6 which can increase glucose production by the liver.

• These inflammatory cytokines, growth factors and activated stromal proteins can promote breast cancer pathogenesis.
Weight loss and exercise interventions have been shown to impact insulin and other serum biomarkers linked to breast cancer risk and prognosis in healthy women and in breast cancer survivors.

Animal models also suggest that lifestyle interventions can reduce malignant transformation of breast cells and impede tumor growth, potentially through immune mechanisms.

Women with newly diagnosed breast cancer with exercise interventions may upregulate immune and inflammatory pathways within human breast tumors.