Researching Genetic Influences in Different Racial/Ethnic Populations and Cancer

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Off-Label Use Disclosure

I do not intend to discuss an off-label use of a product during this activity.
I have not had any relevant financial relations during the past 12 months to disclose.
### Ten Most Common Cancers, Hawai‘i, 2008-2012

<table>
<thead>
<tr>
<th></th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg. Cases/Yr. (%)</td>
<td>Avg. Cases/Yr. (%)</td>
</tr>
<tr>
<td>Prostate</td>
<td>785 (23.4%)</td>
<td>Breast</td>
</tr>
<tr>
<td></td>
<td>1,054 (32.3%)</td>
<td></td>
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<tr>
<td>Lung &amp; Bronchus</td>
<td>433 (12.9%)</td>
<td>Lung &amp; Bronchus</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>411 (12.2%)</td>
<td>Colon &amp; Rectum</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>204 (6.1%)</td>
<td>Corpus &amp; Uterus, NOS</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>171 (5.1%)</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>159 (4.7%)</td>
<td>Non-Hodgkin Lymphoma</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>135 (4.0%)</td>
<td>Melanoma of the Skin</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>130 (3.9%)</td>
<td>Pancreas</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>123 (3.7%)</td>
<td>Kidney &amp; Renal Pelvis</td>
</tr>
<tr>
<td>Pancreas</td>
<td>111 (3.3%)</td>
<td>Leukemia</td>
</tr>
</tbody>
</table>

Source: Hawai‘i Tumor Registry
## Ten Leading Causes of Cancer Deaths, Hawai‘i, 2008-2012

<table>
<thead>
<tr>
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<th>FEMALE</th>
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<tbody>
<tr>
<td></td>
<td>Avg. Cases/Yr. (%)</td>
<td>Avg. Cases/Yr. (%)</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td>317 (25.5%)</td>
<td>220 (21.7%)</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>123 (9.9%)</td>
<td>126 (12.5%)</td>
</tr>
<tr>
<td>Prostate</td>
<td>105 (8.4%)</td>
<td>95 (9.4%)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>95 (7.6%)</td>
<td>93 (9.2%)</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>83 (6.7%)</td>
<td>Ovary 46 (4.6%)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>52 (4.2%)</td>
<td>Non-Hodgkin Lymphoma 41 (4.0%)</td>
</tr>
<tr>
<td>Stomach</td>
<td>50 (4.0%)</td>
<td>Liver &amp; Intrahepatic Bile Duct 40 (4.0%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>49 (4.0%)</td>
<td>Corpus &amp; Uterus, NOS 38 (3.8%)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>42 (3.4%)</td>
<td>Leukemia 37 (3.7%)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>34 (2.7%)</td>
<td>Stomach 35 (3.5%)</td>
</tr>
</tbody>
</table>

Source: Hawai‘i Tumor Registry
According to SEER the national age-adjusted rates for lung and bronchus cancer for 2008-2012 was **70.1 for males** and **50.2 for females** per 100,000 individuals per year. (www.SEER.cancer.gov):
According to SEER the national age-adjusted rates for number of deaths due to lung cancer for 2008-2012 was **59.8 for males** and **37.8 for females** per 100,000 individuals per year.

Source: Hawai‘i Tumor Registry
Lung Cancer Research and the Multiethnic Cohort


- For moderate smokers (<10 cigarettes/day) the risk of developing lung cancer was significantly higher in Native Hawaiians and African Americans, and lower for Japanese smokers compared to White smokers.

- *Variation in the metabolism of nicotine* among different racial/ethnic populations may underlie differences in smoking behavior which can affect the uptake of carcinogens.

  - Le Marchand L. Smokers with the CHRNA lung cancer-associated variants are exposed to higher levels of nicotine equivalents and a carcinogenic tobacco-specific nitrosamine. Cancer Res. 2008 Nov 15;68(22):9137-40.


Breast Cancer Incidence and Mortality in Hawaii

- The national age-adjusted rates (per 100,000 women per year) for 2008-2012 (www.SEER.cancer.gov):
  - The number of new cases of breast cancer in the U.S. was 124.8. The number of deaths was 21.9.

![Graph showing breast cancer incidence and mortality trends in Hawaii.](image-url)
Breast Cancer by Stage at Diagnosis (2008-2012)

- **CHINESE**
  - In situ: 21%
  - Localized: 53%
  - Advanced: 26%
  - Unstaged: 25%
  - n=386

- **FILIPINO**
  - In situ: 23%
  - Localized: 48%
  - Advanced: 25%
  - Unstaged: 3%
  - n=951

- **NATIVE HAWAIIAN**
  - In situ: 2%
  - Localized: 30%
  - Advanced: 19%
  - Unstaged: 18%
  - n=1181

- **JAPANESE**
  - In situ: 2%
  - Localized: 56%
  - Advanced: 23%
  - Unstaged: 19%
  - n=1850

- **WHITE**
  - In situ: 3%
  - Localized: 53%
  - Advanced: 19%
  - Unstaged: 46%
  - n=1775

- **OTHER**
  - In situ: 3%
  - Localized: 33%
  - Advanced: 19%
  - Unstaged: 19%
  - n=478

Source: Hawaii Tumor Registry
Breast Cancer Disparities Research Focused on Hawaii’s Multiethnic Population

- Findings from the Multiethnic Cohort:
  - Light to moderate alcohol consumption increases postmenopausal breast cancer risk, and demonstrates this association in several ethnic groups besides whites. However, this association was not observed for Native Hawaiian women. (Park SY et al. *Int J Cancer*. 2014)
  - Circulating vitamin D (25(OH)D3 and 25(OH)D) was associated with a reduced risk of postmenopausal breast cancer among whites, but not for African American, Native Hawaiian, Japanese, and Latino women. (Kim Y et al. *BMC Cancer*. 2014)
  - BMI and adulthood weight gain were associated with a significantly higher risk of postmenopausal breast cancer and were found to vary across ethnic groups. Native Hawaiian and Japanese women with BMI≥30 had the higher risk than White women. (White KK et al. *Int J Cancer*. 2012)
  - The prevalence of hormone receptor positivity differed among the five racial/ethnic groups in the MEC. Native Hawaiian and Japanese women were more likely to be ER/PR(+) compared to White, African American, and Latina women. (Setiawan VW et al. *Amer J Epidemiology*. 2009)
Breast Cancer Subtype Classification based on Immunohistochemical Staining of Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal Growth Factor Receptor (HER2)

Luminal A
(ER+, PR+, HER2-)

Luminal B
(ER+, PR+, HER2+)

HER2-positive
(ER-, PR-, HER2+)

Basal-like
(ER-, PR-, HER2-)

Overall Survival by Subtype

Sandhu et al. LabMedicine 2010
Breast Cancer Subtype Distribution Across Different Racial Populations

Breast Cancer Subtype Distribution Across Different Racial/Ethnic Populations in Hawaii*

* single institution-based analysis of breast cancer cases at QMC (2000-2007) n=1,488; subtype designation based on immunohistochemical staining
Microarray Gene Expression Profiles Refine Breast Tumor Subtypes

534 genes

Survival trends differ across the breast cancer subtypes.

Estrogen Receptor

Sørlie T et al. PNAS 2003;100:8418-8423
Physical Activity Intervention for Breast Cancer Survivors (Pilot Study)

Investigators: Erin Bantum, Lenora Loo, Lynne Wilkens, Clayton Chong, Herbert Yu

Background: Physical activity after a cancer diagnosis can help reduce the risk of their cancer from returning and improve their overall survival. This has been demonstrated for individuals with breast, ovarian, colorectal, or prostate cancer.

Aim: To determine if hula could be a recommended form of culturally relevant physical activity for breast cancer survivors, leading to behavioral changes in physical activity and improve the quality of life for study participants.

Baseline
- consent and physician approval
- blood draw
- answer questionnaires

6 Month Intervention
- hula (60 min) 2 times per week at UH Cancer Center
- practice at home at least 3 times for 15 minutes each per week.

Month 6
- formal hula class ends
- blood draw
- answer questionnaires

Month 12
- blood draw
- answer questionnaires
Thyroid Cancer Incidence in the U.S. and Hawaii

SEER Stat Fact Sheets: Thyroid Cancer

Source: Hawaii Tumor Registry
Rates are per 100,000 and are age-adjusted to US 2000 Standard Population
Thyroid Cancer Incidence in Hawaii

According to SEER the national age-adjusted rates for thyroid cancer for 2008-2012 was **6.7 for males** and **20 for females** per 100,000 individuals per year.

(www.SEER.cancer.gov)

Source: Hawaii Tumor Registry
Thyroid Cancer Risk Factors

- **Established Risk Factors for Thyroid Cancer:**
  - Female sex
  - Asian race
  - Radiation exposure to head & neck (especially childhood)
  - Exposure to radioactive fallout
  - History of goiter
  - Family history of thyroid disease
  - Genetic conditions, e.g. multiple endocrine neoplasia

- **Possible Risk Factors:**
  - Iodine intake
  - Thyroid autoimmune conditions
  - Obesity
  - Poor pregnancy outcomes
Potential Role of Relaxin in Female Thyroid Cancer Disparities?

- Relaxin and Pregnancy
  - regulates uterine growth and remodelling in preparation for delivery
  - abnormal levels linked to miscarriage and preterm birth
  - common polymorphisms in the promoter region of relaxin (RLN2) associated with preterm birth

  - Filipino women had a higher rate of preterm births compared to Whites and other Asians and SNP genotypes associated with increased RLN2 expression

Prevalence of Preterm\(^1\) Birth, Hawaii, 2000-2013, by Ethnicity

Source: Hawaii State Department of Health, Office of Health Status Monitoring
\(^1\)Preterm births are those occurring before 37 weeks gestation
Thyroid Cancer Sex-Ethnic Disparities Research (pilot project)

- **Investigators:** Brenda Hernandez, Shane Morita, Gillian Bryant-Greenwood, Maarit Tiirikainen, Owen Chan

- **Aims:**
  - Examine the role of relaxin (RLN2), a hormone of the insulin-like super family, in thyroid cancer.
  - Evaluate RLN2 and its receptor protein expression patterns in papillary thyroid carcinoma tumor by sex and race/ethnicity.
  - Evaluate the prevalence of SNP genotypes in the promoter region of the RLN2 gene by sex and race/ethnicity.
Thank you

Questions?