Why do Men of African Descent Have Unfavorable Prostate Cancer Outcomes?

A Transdisciplinary, Translational Approach

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## Disparities in Cancer Mortality (Men)

<table>
<thead>
<tr>
<th>Site</th>
<th>African American</th>
<th>European American</th>
<th>Ratio of African:European American</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>62.3</td>
<td>25.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Larynx</td>
<td>5.0</td>
<td>2.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Stomach</td>
<td>11.9</td>
<td>5.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Myeloma</td>
<td>8.5</td>
<td>4.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Oral cavity and pharynx</td>
<td>6.8</td>
<td>3.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.7</td>
<td>0.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Liver</td>
<td>10.0</td>
<td>6.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>32.7</td>
<td>22.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Esophagus</td>
<td>10.2</td>
<td>7.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>95.8</td>
<td>72.6</td>
<td>1.3</td>
</tr>
<tr>
<td>Pancreas</td>
<td>15.5</td>
<td>12.0</td>
<td>1.3</td>
</tr>
</tbody>
</table>

*Per 100,000, age-adjusted to the 2000 US standard population.
**CPHHD1 Research Framework**

1. **Genetic Susceptibility** → **Biomarkers** → **Early Lesions** → **CaP, Severity, Outcomes**

2. **Preclinical and Clinical Studies:**
   - Screening, Treatment

3. **Impact on Patient and Community:**
   - Dissemination of Research, Quality of Life, Access to Care, Policy
1. Molecular Events in Prostate Cancer

- **RNASEL** constitutively expressed latent endonuclease that mediates the antiviral activities of the interferon-inducible 2-5 A system
- **MSR1** Member of an extended family of scavenger receptors

1. Genotype, Neighborhood Context and PSA Failure

<table>
<thead>
<tr>
<th>Neighborhood Dysregulation</th>
<th>Effect of RNASEL ivs7 indelTTA</th>
<th>Effect of MSR1 R462Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest Tertile</td>
<td>0.72 (0.15-3.36)</td>
<td>No Failures</td>
</tr>
<tr>
<td>Middle Tertile</td>
<td>1.07 (0.17-6.81)</td>
<td>No Failures</td>
</tr>
<tr>
<td>Highest Tertile</td>
<td>9.40 (1.18-74.89)</td>
<td>3.27 (0.85-12.61)</td>
</tr>
</tbody>
</table>

**Lessons Learned:**
Genotype Effects on Prostate Cancer Outcomes Depend on Context
### 2. Treatment and Mortality in Prostate Cancer
(Wong et al. JAMA 2006)

<table>
<thead>
<tr>
<th></th>
<th>Untreated</th>
<th>Treated</th>
<th>Relative Risk of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men &gt;65</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European American</td>
<td>12,468 (25%)</td>
<td>36,907 (75%)</td>
<td>1.24</td>
</tr>
<tr>
<td>African American</td>
<td>1,071 (39%)</td>
<td>1,657 (61%)</td>
<td>1.37</td>
</tr>
</tbody>
</table>

**Lessons Learned:** Unequal Application of Treatment by Race Leads to Mortality Differences
2. Prostate Cancer Mortality and Residential Segregation

Lessons Learned: Residential Segregation Affects EA and AA Men Differently
3. Racial Differences in Quality of Life
(Hughes-Halbert 2007)

Lessons Learned:
Quality of Life May Affect Response
to Prostate Cancer Diagnosis
3. Cultural Differences by Race
(Hughes-Halbert 2008)

Lessons Learned:
Survivorship Programs Require Incorporation of Cultural Values
Community Engagement

1. Genetic Susceptibility → Biomarkers → Early Lesions → Individual Exposures

2. Preclinical and Clinical Studies: Screening, Treatment

3. Impact on Patient and Community: Dissemination of Research, Quality of Life, Access to Care, Policy

CPHHD2 Translation & Intervention

Context-Specific Biomarker Prediction

Context-Specific Screening & Treatment

AA-Specific Survivorship Program
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Cells to Society: Overcoming Health Disparities
How Are the CPHHDs Changing the Face of Health Disparities?

- Emergence of Common Research Synergies and themes
  - Genetic susceptibility and regulation of gene expression
  - Cumulative physiological dysregulation
  - Biological effects of a threatening social environment
  - Contextual effects of individual- and area-level factors

- New Transdisciplinary Paradigm
  - New research methods & tools
  - Comparative effectiveness research integrating biology, behavior, neighborhood, environment, and health care
  - Training, dissemination, and community engagement
Challenges and Opportunities for Eliminating Health Disparities

- Novel transdisciplinary research
  - Enhanced integration of disciplines
  - Maturation of emerging scientific themes

- Develop and test comparative effectiveness interventions
  - Exploit synergies of population health, biology, and personalized medicine
  - Targeted screening/prevention strategies
  - Novel therapies and applications of existing therapies
  - Optimize health care use
  - Policy impact
Questions for the NCAB

• How can the next phase of the CPHHD best be leveraged to more broadly engage the cancer and chronic disease communities to address health inequities?

• How can NCI best ensure that the state of the science concerning disparities informs policy making?

• Given that NHLBI is joining NCI on the CPHHD, what other opportunities might there be to synergize these areas of science (cancer and other chronic diseases including cardiovascular diseases) to address these problems.