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UMassD Cranberry Health Research Update
January 2019

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UMass Dartmouth
Director, UMass CHRC
UMass CHRC Research Objectives: Colon Health Initiative

• Dietary cranberry and inflammatory colon cancer
  • *Mouse model study published* – Xiao and Neto

• Content and distribution of “bioactive” cranberry compounds in fruit and products
  • *Ongoing studies by Neto research group*

• New Colon Health Initiatives funded by Albert Charitable Trust & MA
  • *Cranberry, gut microbes and immune system* - Vanni Bucci
  • *Nanoscale targeted delivery of cranberry compounds* – Milana Vasudev
Effect of cranberry on colon cancer and inflammation in a mouse model

Hang Xiao (UMass Amherst, Food Science)
Cathy Neto (UMass Dartmouth)
Study Objectives

• Earlier studies showed that several cranberry compounds decrease tumor cell growth

• Here, we evaluated effect of cranberry-supplemented diets in a mouse model of colitis-associated colon cancer

• Measure tumors and inflammation in mouse colon in response to treatments
Experimental design of mouse feeding study

Control Diet (AIN-93G)

Cranberry Powder (1.5%)

Polar extract (0.1%)

Non Polar extract (0.05%)

Mice age (weeks)

<table>
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<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
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</thead>
</table>

After 20 weeks on diet, mice are sacrificed.

Number and volume of colon tumors was assessed.

Tissues analyzed for changes in markers of inflammation and carcinogenesis.

n = 20
Whole cranberry powder reduced tumors, inflammation in mice by up to 50%

- Article published in Molecular Nutrition & Food Research, Dec. 2018

- AOM/DSS-treated mice mimic colitis, a colon cancer risk factor
- 20 weeks on CB diet (1.5% w/w WCP in AIN93G chow), n = 20
  - Equivalent to 3/4 cup or 75 g/day fresh fruit for a person weighing 150 lbs
- Outcomes measured:
  - Tumor size and number
  - Inflammatory gene and protein expression in colon tissue
  - Markers of cell proliferation, apoptosis, angiogenesis, metastasis
- Effects are likely due to multiple compounds in cranberry fruit
  - PACs (6%), Anthocyanins (2%), Ursolic & Oleanolic Acids (1%)
Whole cranberry powder significantly reduced multiple cancer markers

<table>
<thead>
<tr>
<th>Group</th>
<th>Control</th>
<th>Colitis model</th>
<th>Colitis + cranberry</th>
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<tbody>
<tr>
<td>Colon length (mm)</td>
<td>96.6 ± 2.4</td>
<td>87.8 ± 2.9</td>
<td>92.7 ± 3.0</td>
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<tr>
<td>Tumor incidence</td>
<td>0</td>
<td>80%</td>
<td>50%</td>
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<tr>
<td>Tumors/mouse</td>
<td>0</td>
<td>5.91 ± 1.0</td>
<td>2.77 ± 0.88</td>
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<td>Tumor burden (vol/mouse mm³)</td>
<td>0</td>
<td>17.7 ± 2.5</td>
<td>4.64 ± 1.26</td>
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<tr>
<td>Tumor volume</td>
<td>0</td>
<td>18.8 ± 1.9</td>
<td>10.3 ± 1.3</td>
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<tr>
<td>COX-2 expression (fold change)</td>
<td>0</td>
<td>1</td>
<td>0.3</td>
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<tr>
<td>Cyclins/kinases</td>
<td>0</td>
<td>1</td>
<td>0.25-0.75</td>
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<td>Metastasis markers (MMPs)</td>
<td>0</td>
<td>1</td>
<td>0.05-0.60</td>
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</table>

Anti-cancer mechanisms observed *in vivo* are consistent with those observed in cranberry-treated prostate cancer cells (Hurta & Neto)
All three cranberry preparations significantly reduced tumors

Average tumor number per mouse

Control  WCP  Polar  Nonpolar

Number of tumors in colon

Average total tumor volume in colon

Control  WCP  Polar  Nonpolar

Tumor volume (mm$^3$)

Results indicate that a combination of different “bioactives” may support gut health. We need to better understand interactions with bacteria, immune system & tissues.
Cranberries and products as a source of gut-healthy “bioactives”

- PACs
- Anthocyanins
- Ursolic and Oleanolic Acid
- Quercetin
- Complex carbohydrates from fiber

- 10 cultivars of cranberry fruit harvested in MA & OR (Liang Xue)
  - Stevens, Mullica Queen, Crimson Queen, Demoranville, Early Black, Pilgrim, Welker, Scarlet Knight, GH1

- 10 commercial cranberry “supplements” from various suppliers (John Turbitt)
Cranberry supplements vary in composition and quality (J. Turbitt)

“Cranberry” or not so much?
Chemometric analysis of ten commercial products by NMR

- Less than half of products tested were comparable to whole cranberry powder model (WCP)
- Most supplements were far lower in bioactives content than WCP
  - Ursolic and oleanolic acid
  - Total PACs
  - Quercetin, anthocyanins
Content of bioactives in cranberry fruit from MA cultivars (L. Xue)

**Total PACs content**

- Mullica Queen
- Early Black
- Pilgrim
- were tops!

**Ursolic and Oleanolic acid**

- Similar data in 2016
- No clear cultivar trends, but higher in 2016

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<th>PACs</th>
<th>Concentration (mg/g Dry weight)</th>
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<td>CQ MA</td>
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<td>ST MA</td>
<td>53.20</td>
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<tr>
<td>DEM MA</td>
<td>49.32</td>
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<tr>
<td>MQ MA</td>
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<td>EB MA</td>
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Average Cranberry Bioactives Content, Regional Comparison (2016-2017)

n = 45

MA ≈ OR

MA ≈ OR

OR >> MA

MA >> OR

OR > MA

Total PACs (DMAC)

Conc. (mg/g DW)

MA | OR

Anthocyanin content (T_{acy})

Conc. (mg/g DW)

MA | OR

*** p<0.001

Antioxidant activity (DPPH)

% Inhibition

MA | OR

*** p<0.001

Ursolic and Oleanolic Acid content

Conc. (mg/g DW)

MA | OR

*** p<0.001

Average Cranberry Bioactives Content, Regional Comparison (2016-2017)
Bioengineering to optimize cranberry targets in colon and gut

Targeted delivery of cranberry bioactives

- Encapsulation of cranberry compounds with micellar, liposome or peptide-based carriers
- May enhance bioavailability of these compounds
- Goal: target tumors \textit{in vivo}

Interactions of cranberry with gut microbiome

- Using a computational approach to analyze changes in \textit{gut microbial community} & tissues in response to cranberry
- Cranberry as “prebiotic” could boost population of probiotic or “good” bacteria in the gut
Next steps: Modeling the gut and its response to delivery of cranberry “bioactives”

- Mouse model of gut microbiome
- Team plans to study interactions between microbes, colon tissues when treated with cranberry
- Our aim is to provide data for proposals to NIH, others
- Challenge: state funding has a strict FY deadline and 6 month “window” for expenditures
Many thanks to:

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Milana Vasudev

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Rep. Strauss
CCCGA
UMass Cranberry Station
OSU Cranberry Station