EFFECTS OF AOM INJECTION AND RESISTANT STARCH CONSUMPTION ON THE INHIBITION OF COLORECTAL CARCINOGENESIS IN AN A/J MOUSE MODEL

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OUTLINE

• Background
• Purpose
• Hypothesis
• Methods
• Results
• Discussion
COLORECTAL CANCER

- Third most prevalent cancer among both males and females
  - 108,000 new diagnoses each year
- Effect of diet on Colorectal Cancer
  - Fiber can inhibit carcinogenesis
- Risk factors: obesity, inactivity, red meat consumption, smoking
AZOXYMETHANE (AOM)

- Carcinogen used to induce colonic tumors
- Correct dosage of 7.5 mg/kg body weight was validated in previous study
- Mice receive injections prior to experimental diets
  - Prevents diet interference with AOM metabolism
RESISTANT STARCH (RS)

- Type of fiber that escapes normal digestion in the small intestine
  - Available for fermentation in the colon that is hypothesized to decrease carcinogenesis through tumor inhibition
- Types of Resistant Starch
  - RS1 – Grains
  - RS2 – Bananas
  - RS3 – Potatoes and Rice
  - RS4 – Chemically modified
  - RS5 – SA-complexed
PURPOSE

• To study the effects of two resistant starch diets (HA7 and RS5) in an A/J mouse model injected with Azoxymethane (AOM) compared to a saline control (corn starch) on the inhibition of carcinogenesis within the colon and rectum
HYPOTHESIS

• We hypothesize that a positive correlation will exist between the resistant content of the starch and the inhibition of carcinogenesis.
• Rationale: A higher resistant content allows for more fermentation in the large intestine $\rightarrow$ protective effect against colorectal cancer
**Study Timeline**

- **0 Weeks**
  - Diet Begins (3 days post-injection)
- **2 Weeks**
- **6 Weeks**
- **16 Weeks**
- **36 Weeks**
  - Sacrifice
- **Acclimation**
- **4 Weekly Injections of AOM**

**Control Diet**

**Experimental Diets**
**METHODS- VARIOUS Diets**

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<tr>
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**Diet Groups**

- Control
  - Commercially available corn starch (negligible)
- HA7
  - High-amylose type 7 corn starch (25.9%)
- RS5
  - Resistant starch type 5, aka SA-HA7 (59.1%)
FOOD DISAPPEARANCE DATA

Weeks

Weight (grams)

CS Saline
CS-AOM
HA7-saline
HA7-AOM
RS5-Saline
RS5-AOM

0 5 10 15 20 25 30 35

0.00 5.00 10.00 15.00 20.00 25.00 30.00
FOOD DISAPPEARANCE DISCUSSION

1.) The initial climb in food disappearance peaks at INJ week 3 where it then declines through INJ week 4
   - likely cause: stress

2.) Post INJ week 4: increase in food disappearance
   - assumption: stress from injections is short-lived

3.) Branching: HA7 and RS5 diet groups show the greatest degree of food disappearance
   - due to diet consistency

4.) No significant differences observed between Saline and AOM treated groups
Body Weight Discussion

1.) No major observable differences between diet or treatment groups

2.) AOM impacts body weight during injections: greater stress → less consumption → lower BW
   - Mice are able to rebound after: short-term stressor

3) Body weights began to plateau at week 20 of the study

4) Body weights are predicted to decrease with progressions of carcinogenesis
HEALTH SUMMARY

Mice appear to have declining health consistent with stress and aging
- Excessive barbering has led to a scruffy appearance

2 Control AOM and 1 RS5 Saline were euthanized due to gross observation
DISCUSSION END POINTS

• HA7 and RS5 are sustainable for life and appear to be palatable
• Body weight is predicted to decrease once tumors have begun to form
• Food disappearance still gradually declining
What’s Left in this Study?

- Study will conclude in 5 weeks
- Mice will be sacrificed
- Colons and rectums will be extracted for analysis
- Tumors and preneoplasia by histopathology
- Completion of study will support or refute our hypothesis
ACKNOWLEDGEMENTS

Dr. Diane Birt

Dr. Elizabeth Whitley

Nicole Cray

Bridget Nelson

Nidhi Shah