Introduction

- Inflammation, a potential factor contributing to gut barrier dysfunction, is significant in colon carcinogenesis.
- On the other hand, a weakened gut barrier is more prone to the foreign antigens, causing endotoxemia and inflammation, which promotes colorectal cancer (CRC).
- Lipopolysaccharide (LPS)-binding protein (LBP): A biomarker for activation of innate immune responses to microbial products and a marker of LPS.
- Intestinal fatty-acid binding protein (IFABP): Elevated in conditions characterized by increased intestinal permeability.

Research Question

Does vitamin D and calcium supplementation affect the circulating biomarker of gut barrier function among individuals at high risk of CRC? If so, is there a difference in the treatment effect by BMI or pro-inflammatory cytokine level?

Method

Parent Study
- 11-center, randomized, placebo-controlled, partial 2x2 factorial chemoprevention clinical trial, the Vitamin D/Calcium Polyp Prevention Study (NCT00153816).
- Participants: ages 45-75 years with at least one colorectal adenoma removed within 120 days prior to enrollment and with scheduled 3-year or 5-year colonoscopic follow-up examinations (patients were from 2 centers: Georgia and South Carolina).
- Treatment Assignment: "4-arm study": elemental Ca 1.2 g/d, vitamin D3 1,000 IU/d, both, or placebo; “2-arm study”: women who declined to forego Ca supplementation were randomized to vitamin D or placebo.

Adjunct Study
- Participants: 118 participants
- Blood was drawn at the baseline and 1-year follow-up.
- LBP and IFABP level was analyzed through electrochemiluminescent Human LBP Assay Kit and ELISA.

Statistical Analysis
- $X^2$ Test for categorical variables and ANOVA or T-test to compare baseline characteristics of participants across treatment arms.
- Generalized linear model (PROC MIXED) to compare the difference in biomarker levels between treatment groups.
- Stratified analysis by median level of baseline serum 25-OH-vitamin D, total calcium intake, BMI and inflammatory biomarker (IL-6) concentration.
- All analysis was done on SAS version 9.4.

Result

- LBP decreased in vitamin D group relative to the no vitamin D group after 1 year of supplementation.
- LBP did not change in calcium group relative to the no calcium group and in the vitamin D and calcium group relative to the calcium group after 1 year of supplementation.
- IFABP decreased in vitamin D group relative to the no vitamin D group after 1 year of supplementation.
- IFABP also decreased in vitamin D and calcium group relative to the calcium group while there was no change in the calcium group and no calcium group after 1 year of supplementation.
- LBP decreased in vitamin D group relative to the no vitamin D group, in participants with greater than or equal to median BMI but not in participants with less than median BMI.
- IFABP decreased in vitamin D group relative to the no vitamin D group and calcium and in the vitamin D group relative to the calcium group, in participants with less than median IL-6 concentration but not in participants with greater than or equal to median IL-6 concentration.

Conclusion: Overall, our study findings indicate decrease in LBP and IFABP concentrations with administration of vitamin D over 1 year. This effect was stronger among individuals with higher BMI for LBP and among individuals with lower IL-6 concentrations for IFABP. Our results suggest that vitamin D could potentially be used as a protective agent against gut barrier dysfunction and inflammation, which is associated with CRC risk. Final analyses are being prepared to be submitted to the AACR conference or to be published.