# CU Research Forum 2024 Abstract

**Title:** ASCENDING AND DESCENDING COLON TISSUE METABOLITE DIFFERENCES OF HEALTHY ADULTS ACROSS BMI CLASSES

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Obesity is an established risk factor for development of colorectal cancer (CRC) via metabolic reprogramming of normal colonic metabolism and inflammation. Few studies have examined the colon tissue metabolism of healthy adults and metabolic profile distinctions between ascending and descending colon with changes to body mass index (BMI). In this study, we employed non-targeted metabolomics as a sensitive technique to explore the variation in metabolite profiles across a suite of chemical classes. Metabolite distinctions in respective ascending and descending colon tissue among normal weight (NW), overweight (OW), and obese (OB) adults merits attention to reduce CRC risk.

An ascending and descending colon tissue sample was taken from 24 healthy adult volunteers during a screening colonoscopy in Fort Collins, CO: NW (n=9), OW (n=9), OB (n=6). Adults provided written informed consent, and all samples were de-identified prior to extraction for non-targeted metabolomics analysis using ultrahigh-performance liquid chromatography-tandem mass spectroscopy (UHPLC-MS/MS). Raw data were imputed and rescaled with median set to 1. Relative abundances underwent secondary analysis by fold change (FC) analysis, partial least square discriminant analysis (PLS-DA), variable importance in projection (VIP) scores, and two-sample t-tests. Statistical significance was determined using $p<0.05$. Protocols were approved by the Colorado State University IRB No. 15-6051, and University of Colorado Health IRB No. 0010144.

PLS-DA revealed distinct separation in metabolite profiles in ascending and descending tissues among different BMI groups. A total of 61 metabolites were significantly different in OW and OB compared to NW (OB=13, OW=48). In the descending colon, 57 metabolites were significantly different in NW compared to OB and OW (OB=7, OW=50). Histamine was in the

top 5 VIP scores of the NW vs OB comparison with elevation in the OB population (FC=3.16 ascending, FC=3.72, descending). This increase was significant in the descending colon ($p<0.05$) and near significance in the ascending colon ($0.05<p<0.10$), compared to NW. Multiple monoacylglycerols had significant increases in only the ascending colon of OW compared to NW.

Metabolite profile distinctions between the ascending colon tissue of NW, OW and OB adults as well as for descending colon revealed increased chronic-low grade inflammation in obese individuals. Monoacylglycerols may play a role in driving fat storage metabolism and endocannabinoid signaling that influence physiological processes such as pain, appetite, and immunity dysregulations in overweight individuals. Datasets of healthy adult colon metabolite signatures could become biomarkers of metabolic reprogramming during weight management and for reduced inflammation in control and prevention of CRC. Future studies with a diet-controlled intervention prior to colonoscopy may inform left and right colon tissue metabolites that reduced CRC risk.