

Research in IBD at University of Colorado Denver

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Mucosal Inflammation Program

Epidemiology of PSC-IBD

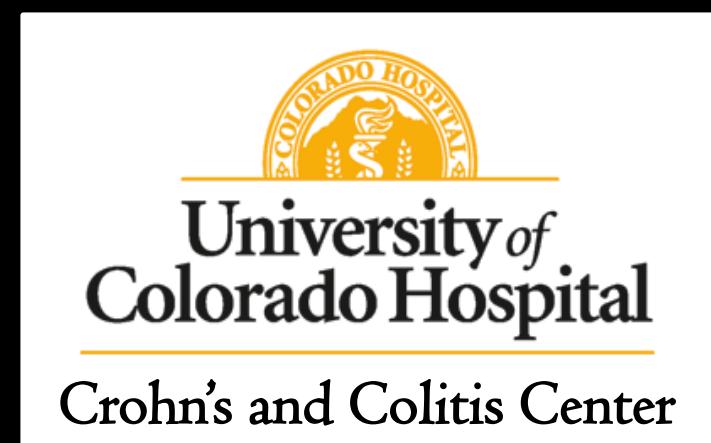
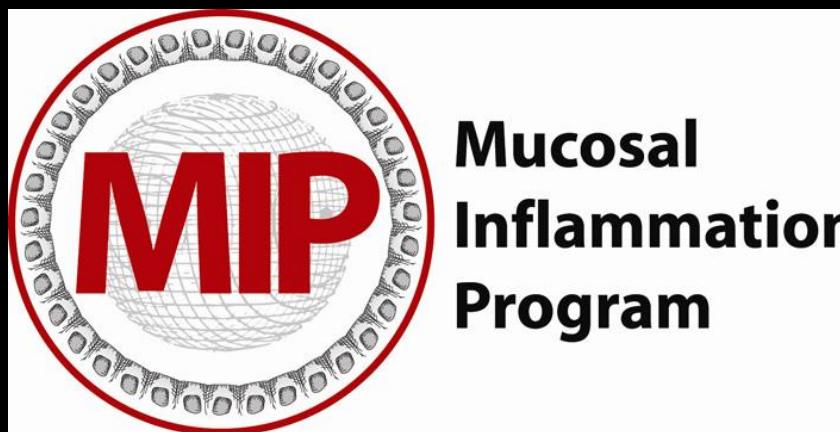
- ~1.4 million with IBD in the US
 - ~5% of UC with PSC
 - Up to 90% of PSC with UC
- >50,000 with IBD in the Mountain West
- >12,000 along the front range

Major Regional IBD Centers



IBD Research Model at UCH

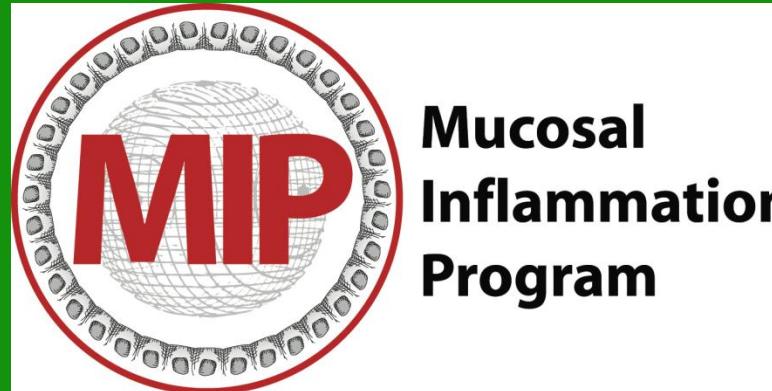
- Three highly collaborative clinical and basic science research arms



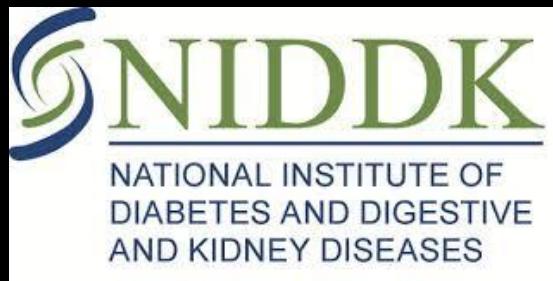
4 P's Physical Proximity Promotes Partnership



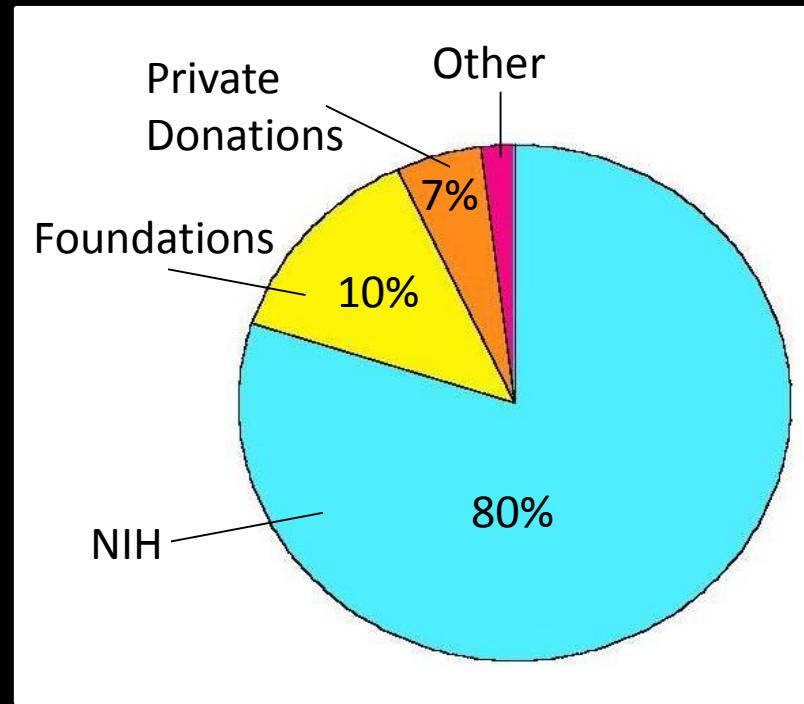
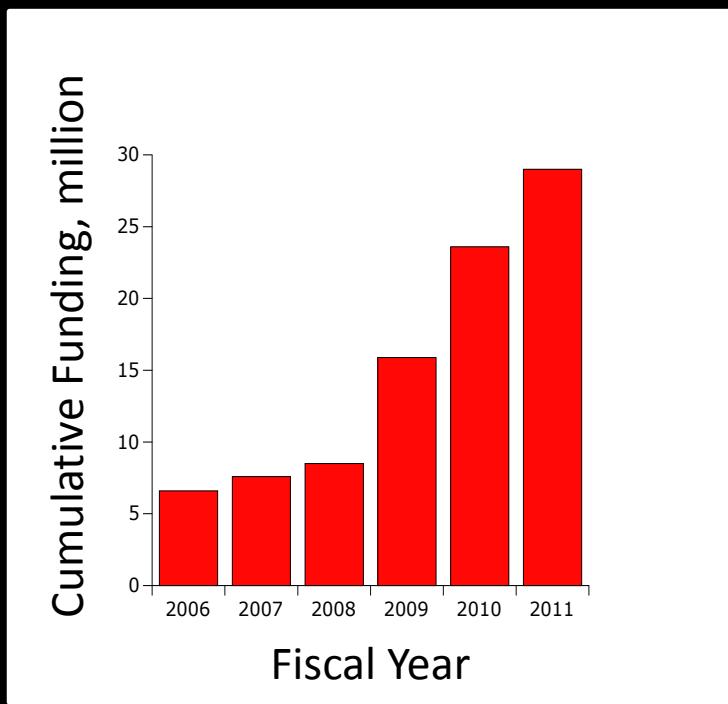
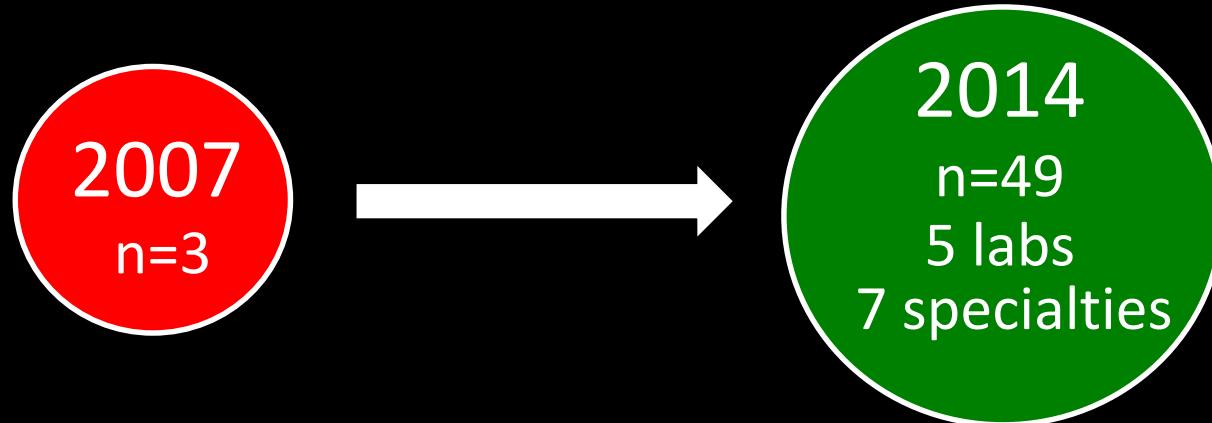
Anschutz Medical Campus
Aurora, Colorado



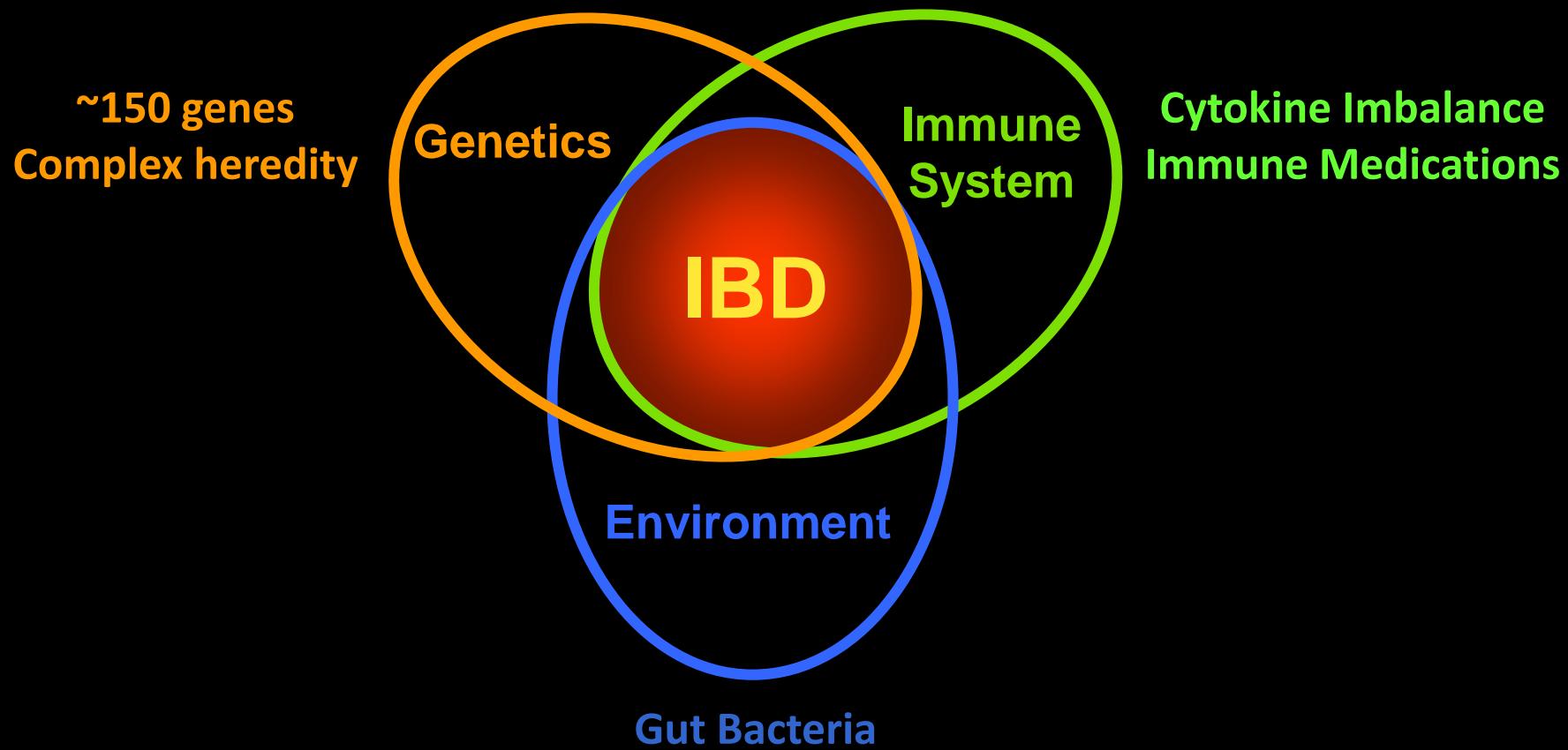
A multi-disciplinary center of excellence committed to the identification of *novel targets* for diagnosis and directed therapy of mucosal disease.



Mucosal Inflammation Program



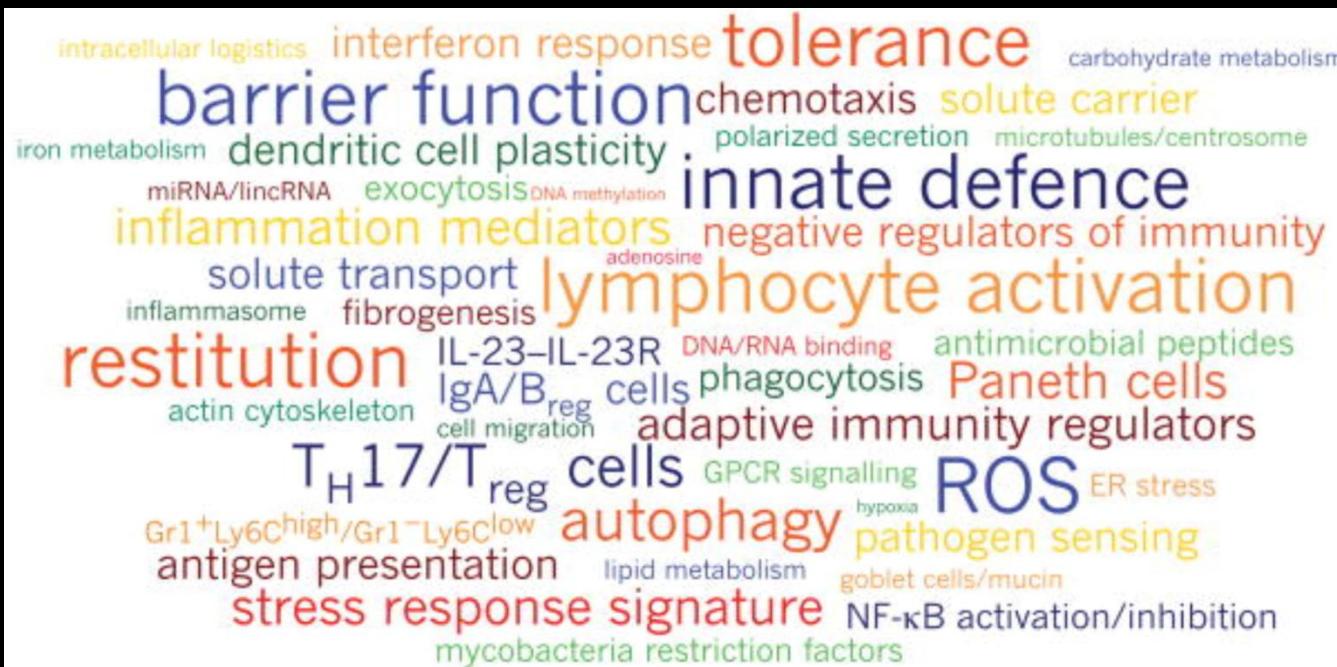
Inflammatory Bowel Disease Pathogenesis



Immunity of IBD

- Meta-analysis of GWAS (CD 2010, UC 2011)
 - ~150 SNP's
 - 99 total disease loci
 - 28 shared loci

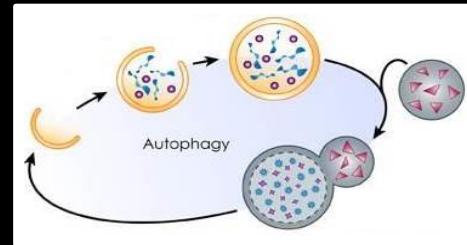
>85% of IBD genes relate
to Innate Immunity



Ongoing Work in Innate Immunity



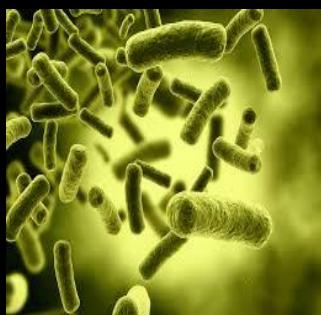
Neutrophil Trafficking



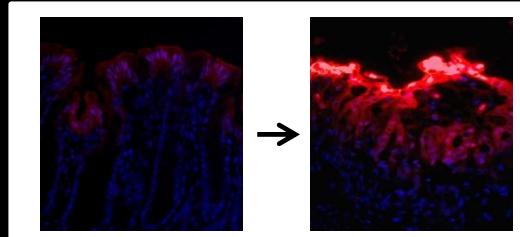
Autophagy



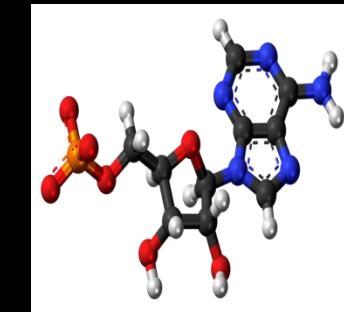
Angiogenesis



Shifts in the Microbiome

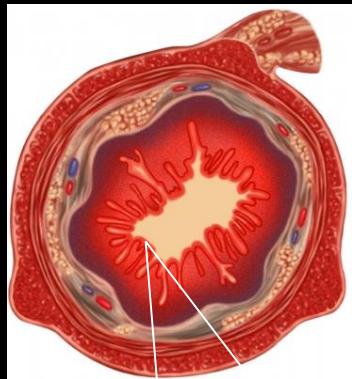


Oxygen Metabolism



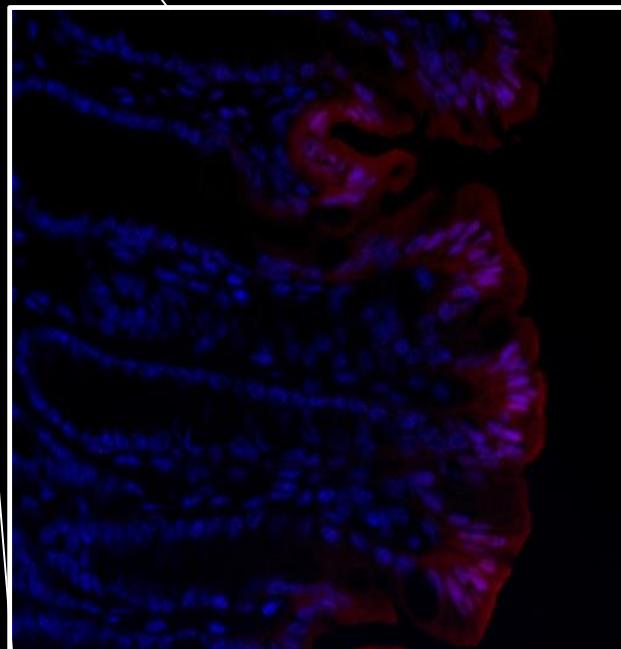
Nucleotide Metabolism

Hypoxia in IBD

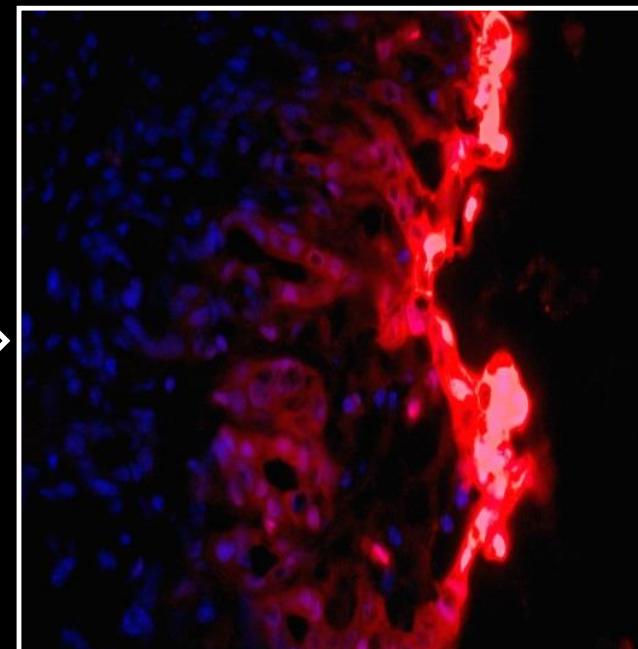


Hypoxia = Low Oxygen

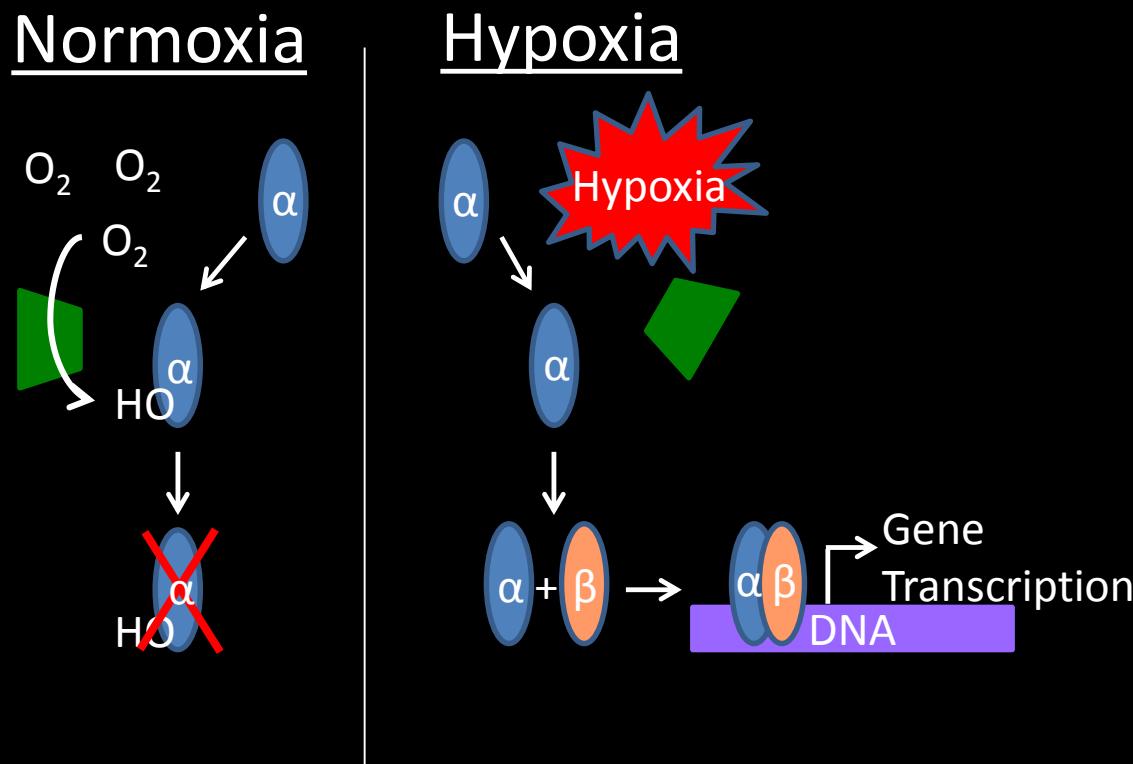
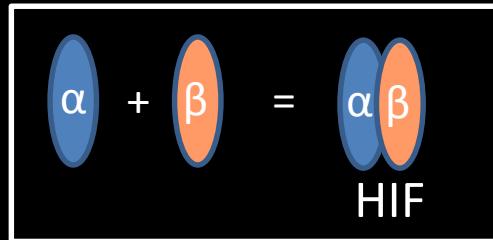
Normal



Colitis

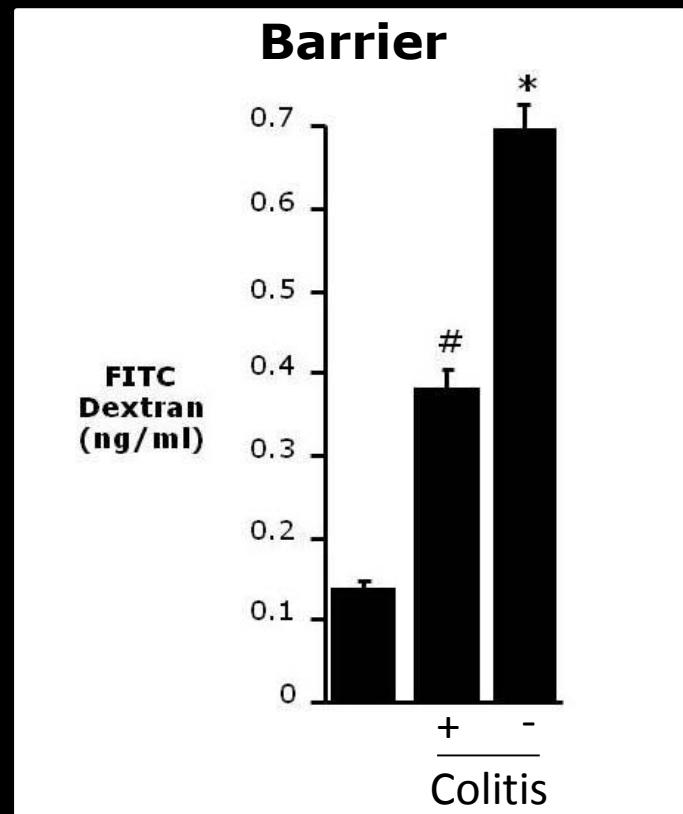
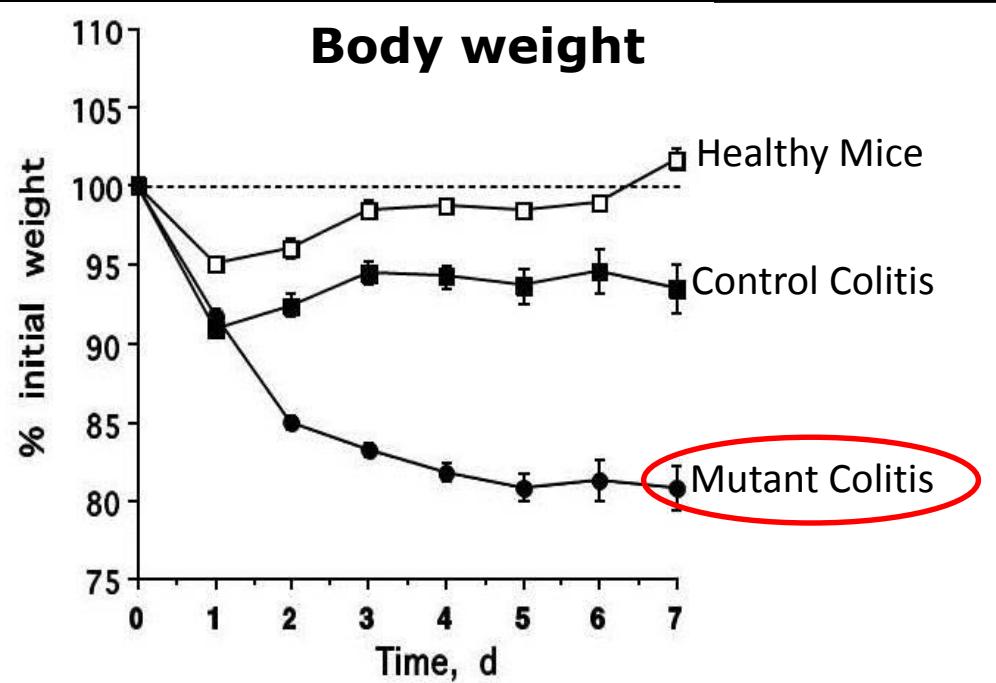


Hypoxia Inducible Factor - HIF



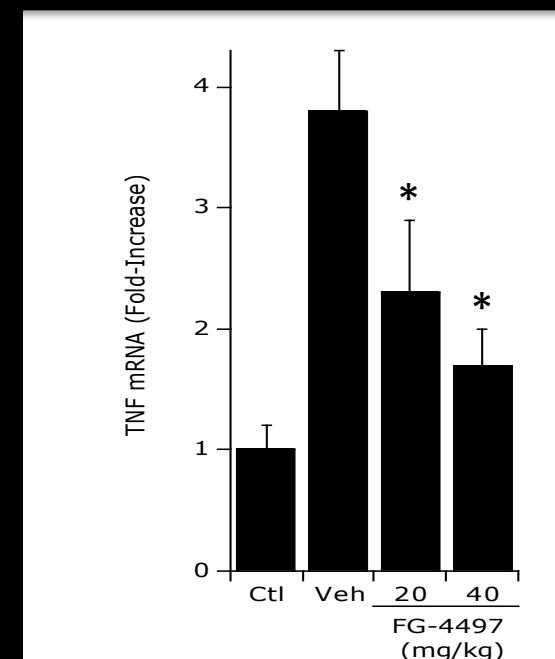
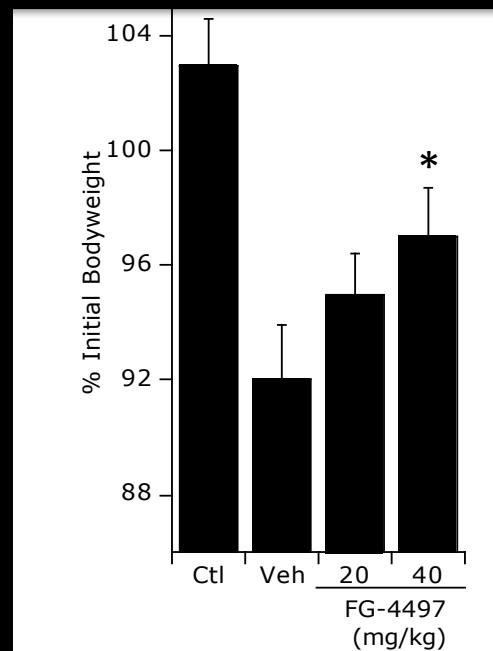
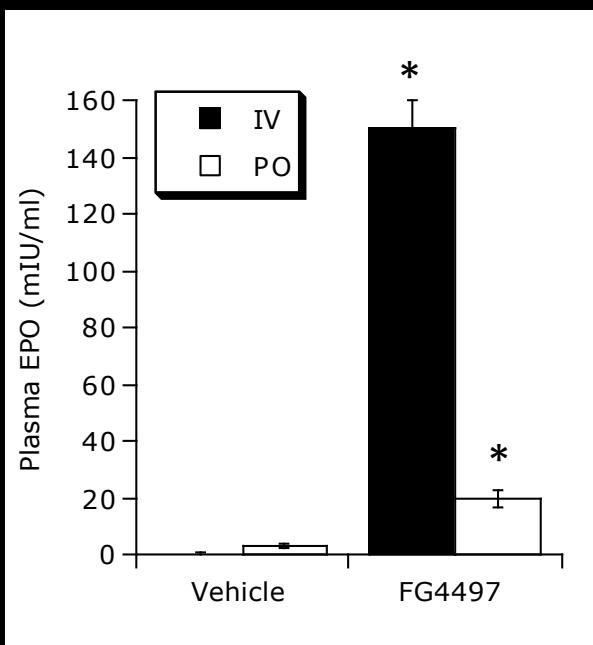
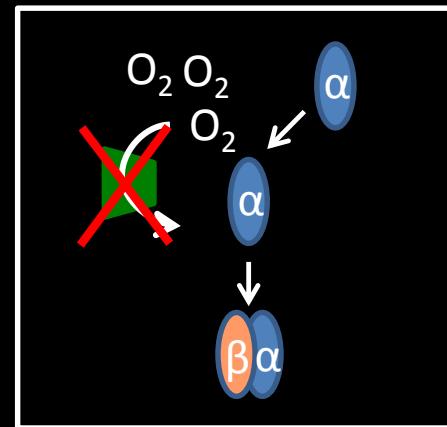
HIF in Mouse Models of Colitis

HIF Knockout Mice – DSS Colitis



HIF in Mouse Models of Colitis

- FG4497 Treatment
- HIF Stabilizer (\uparrow HIF levels)
- Oral delivery benefit
- Decreases tissue TNF



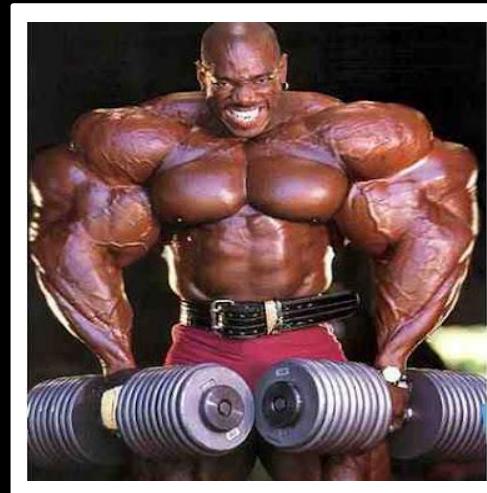
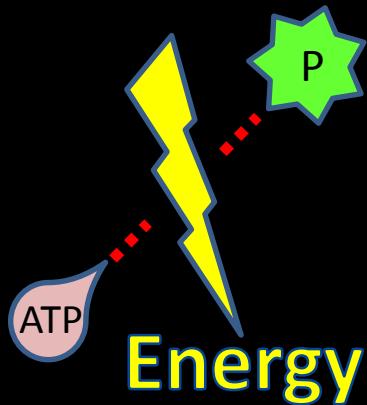
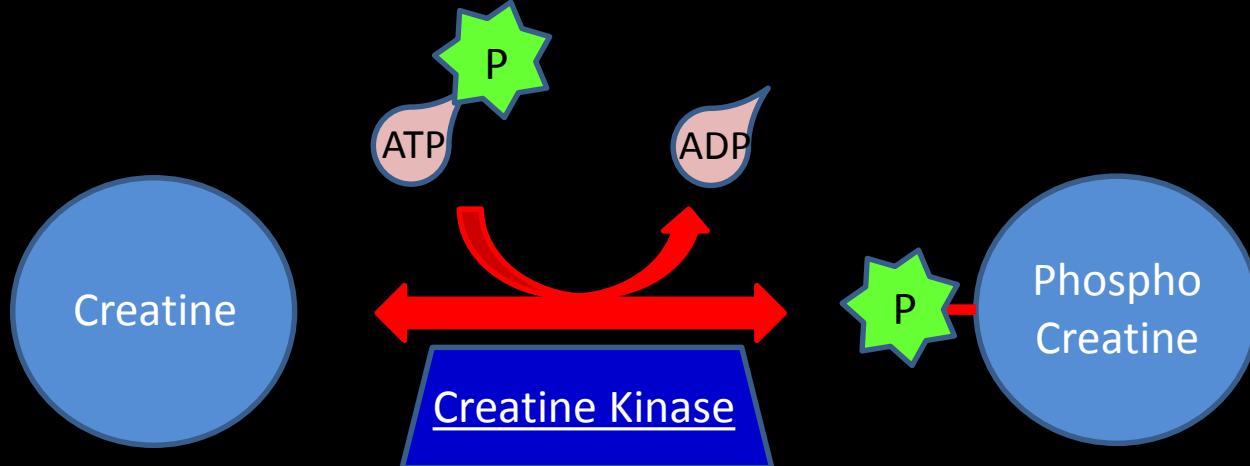
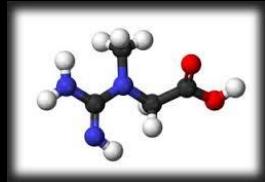
HIF in Mouse Models of Colitis



Gastroenterology 134: 145-155, 2008

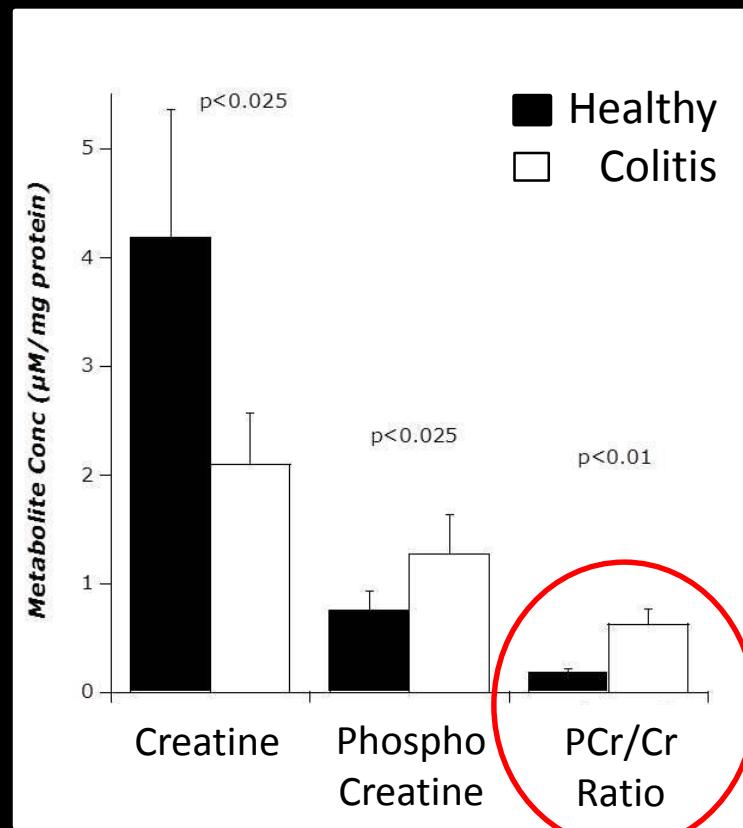
- HIF is protective at many levels in colitis
- FG4497 (HIF mimetic) is a strong therapeutic option for oral delivery
 - FG4592 in Phase III Clinical Trials for Anemia

Creatine Metabolism



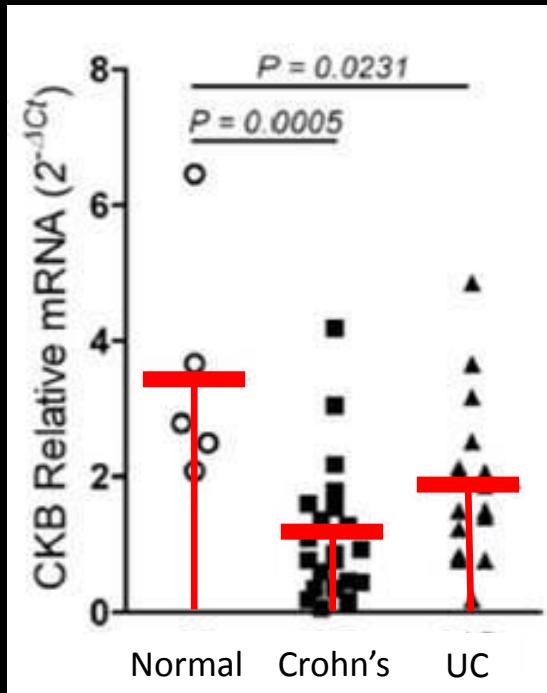
Creatine as a Biomarker in Colitis

Creatine Concentration – TNBS

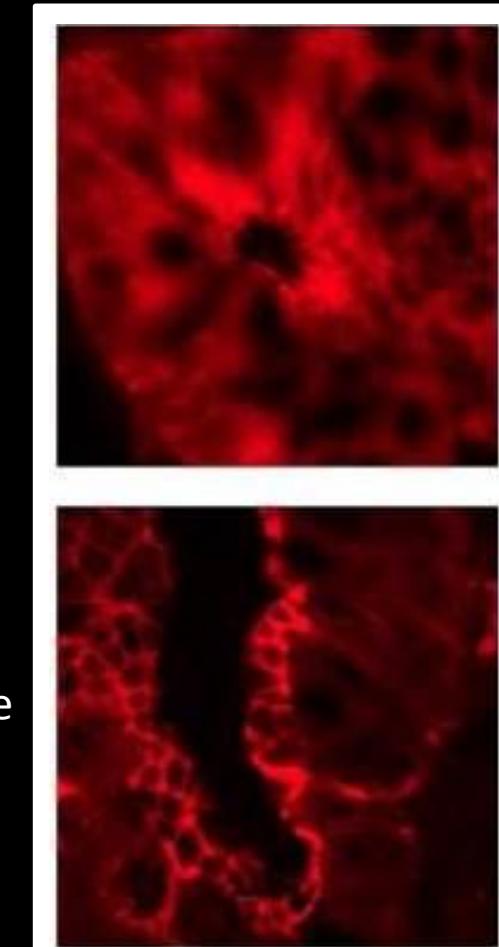


Decreased Levels of CK in Human IBD

Creatine Kinase Levels in IBD

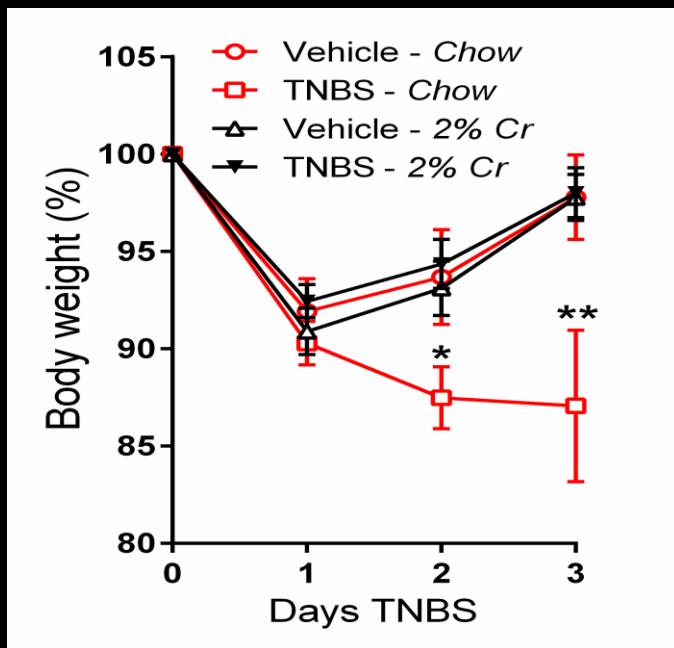


CK Staining in IBD

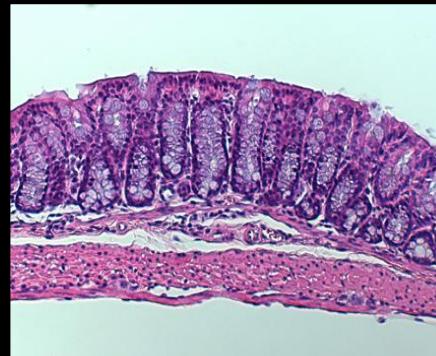


Abnormal Creatine/Phospho-Creatine Pathway in IBD

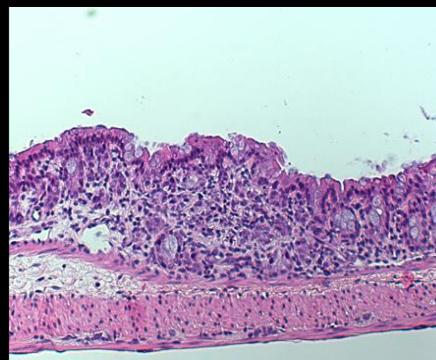
Creatine Supplements in Colitis



Healthy



Colitis



Colitis + 2% Cr

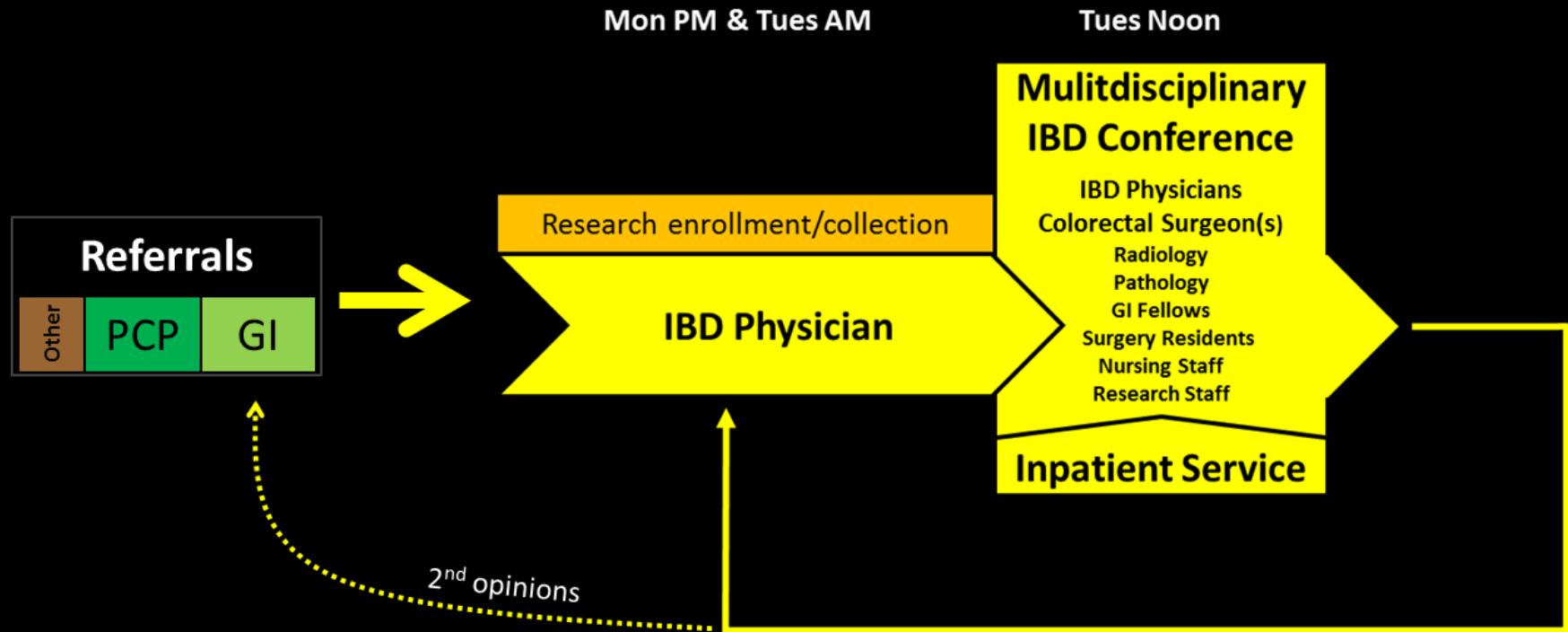


- Creatine supplementation improved colitis severity in a mouse model

UCH Crohn's and Colitis Center



UCH Crohn's and Colitis Center



Clinical Research in IBD at UCH

RESEARCH

- IBD Database
 - Umbrella protocol
 - Disease Phenotype
 - Disease Activity Measures
- Biorepository: > 500 patients
 - Serum
 - Tissue
- Clinical Trials:
 - CCFA Clinical Research Alliance
 - **MERIT-UC**
 - **PUCCINI**
 - Industry-Sponsored studies
 - **Placental Stem Cell infusions**
 - Investigator-Initiated studies
 - **Creatine supplementation**



POPULATION MGMT

- Evidence-Based Care
- QI Initiatives
- Performance Measurement
 - PQRS: AGA BTE Program

IBD Clinic



Clinical Research Trials

- **MERIT-UC**
 - NIH funded study using Methotrexate in UC
- **PUCCINI**
 - Study to clarify the risks associated with the use of IBD medications at the time of surgery
- **Placental Stem Cell Infusion**
 - Study of placental stem cell infusions as adjunct therapy in severe/refractory Crohn's disease
- **Creatine Supplementation in UC**
 - Study of Creatine supplementation in treatment of mild-moderate UC

IBD Research at UCH

- Exciting ongoing research through the MIP and UCH Crohn's and Colitis Center
 - Basic science
 - Translational research
 - Clinical trials in new IBD therapies
 - Quality improvement initiatives in patient care
- Multidisciplinary approach to clinical IBD care

Thank You