

Targeting Glycolysis Reduces Inflammation in a Murine Model of Rheumatoid Arthritis and Crohn's Disease

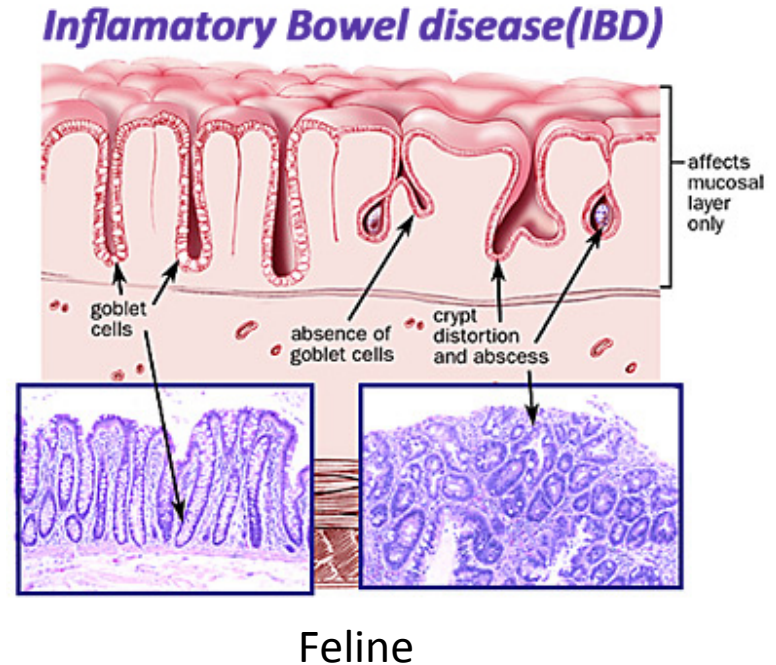
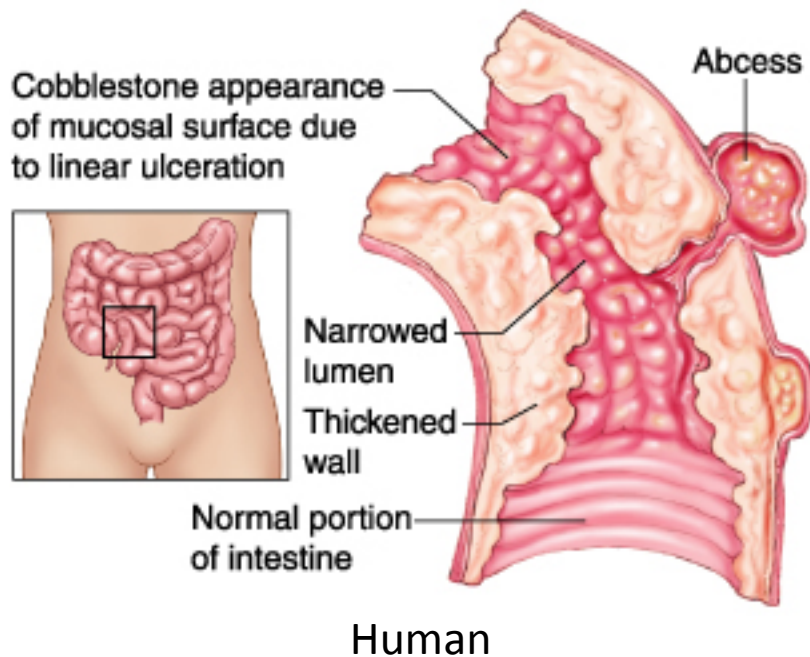
Katrijn Whisenant¹, Peter B. Ernst^{1,2}, Monica Guma²

1. UC Davis School of Veterinary Medicine, Davis, CA
2. Departments of Pathology and Medicine, UC San Diego, La Jolla, CA

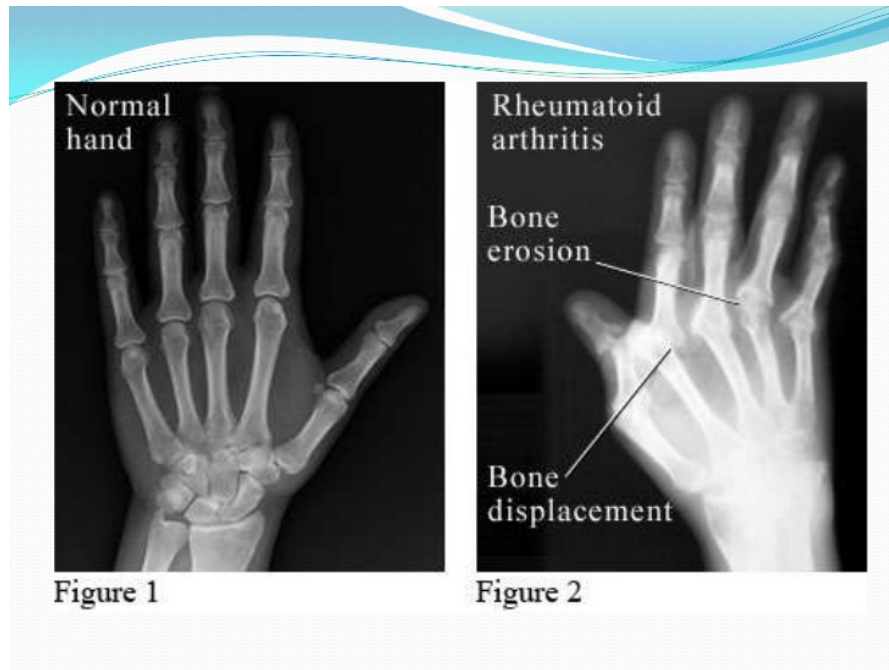


Immune-Mediated Diseases

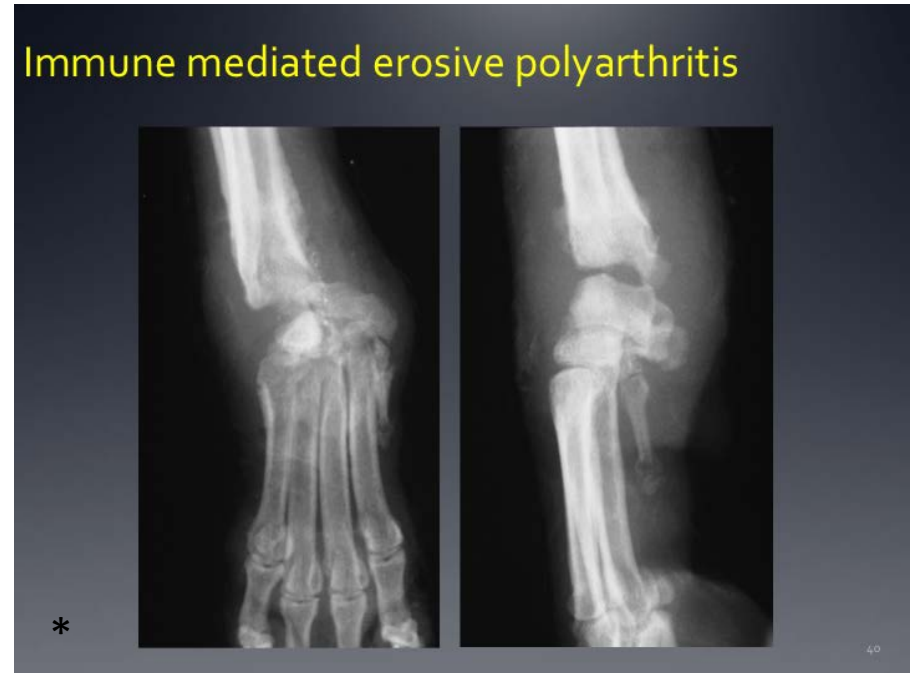
- Crohn's Disease – symptoms of abdominal pain, diarrhea and weight loss



- Rheumatoid Arthritis– symptoms of painful joint swelling and deformity



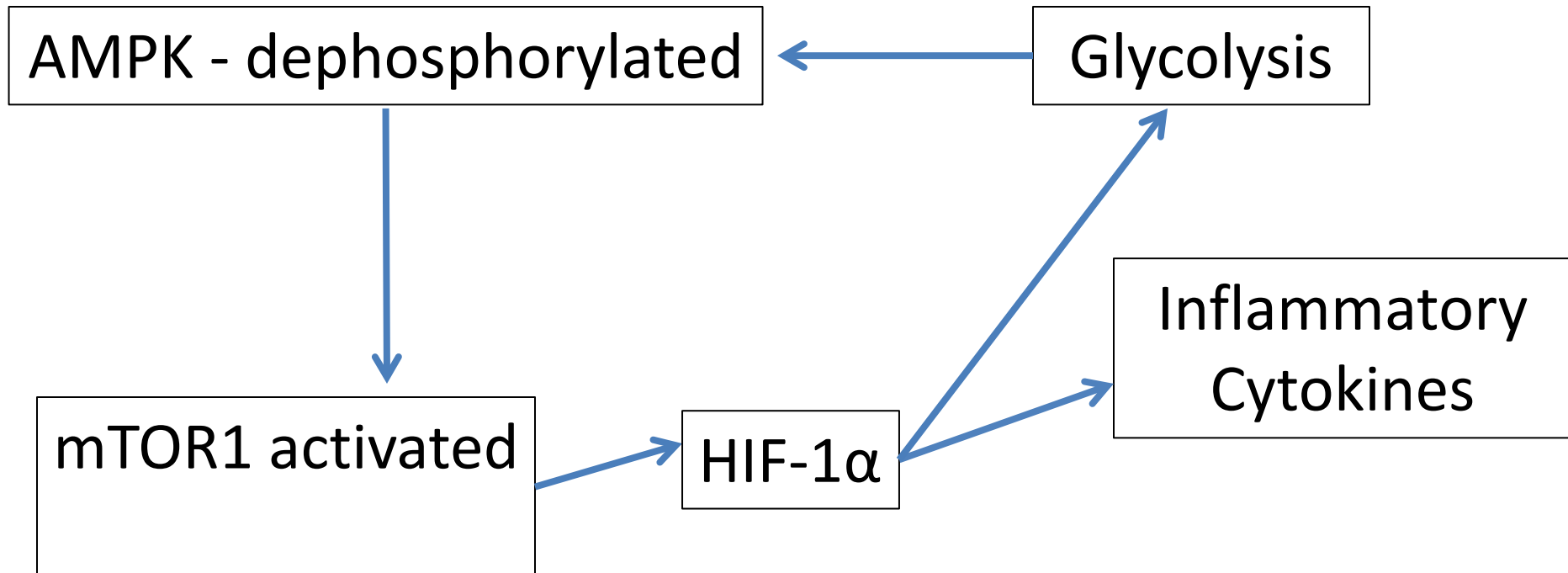
Human



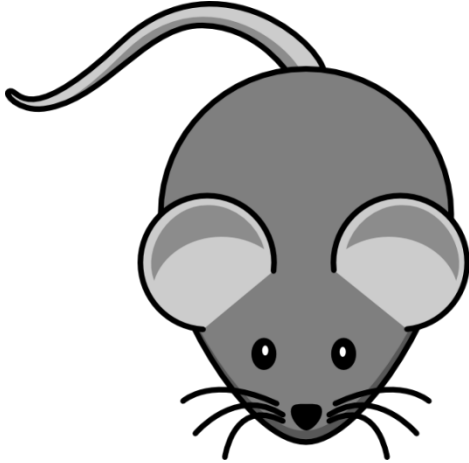
Canine

Warburg Effect

- Metabolic switch: Ox. Phos. → Glycolysis
- Glycolytic metabolism: possible targets within the pathway to reduce inflammation



Methods



TNF Δ ARE

Rx with 3-
bromopyruvate



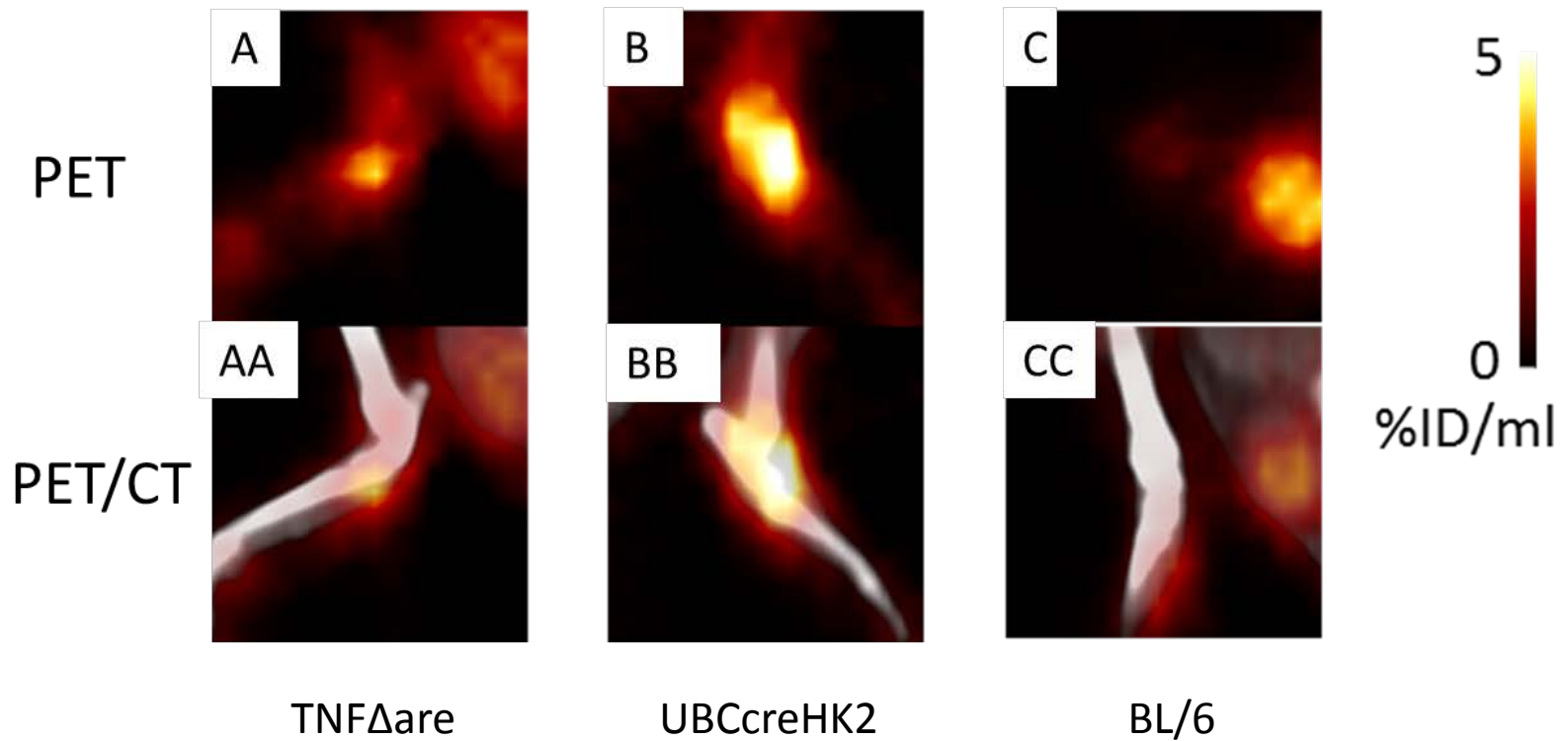
UBCcreHK2^{F/F}

Rx with tamoxifen

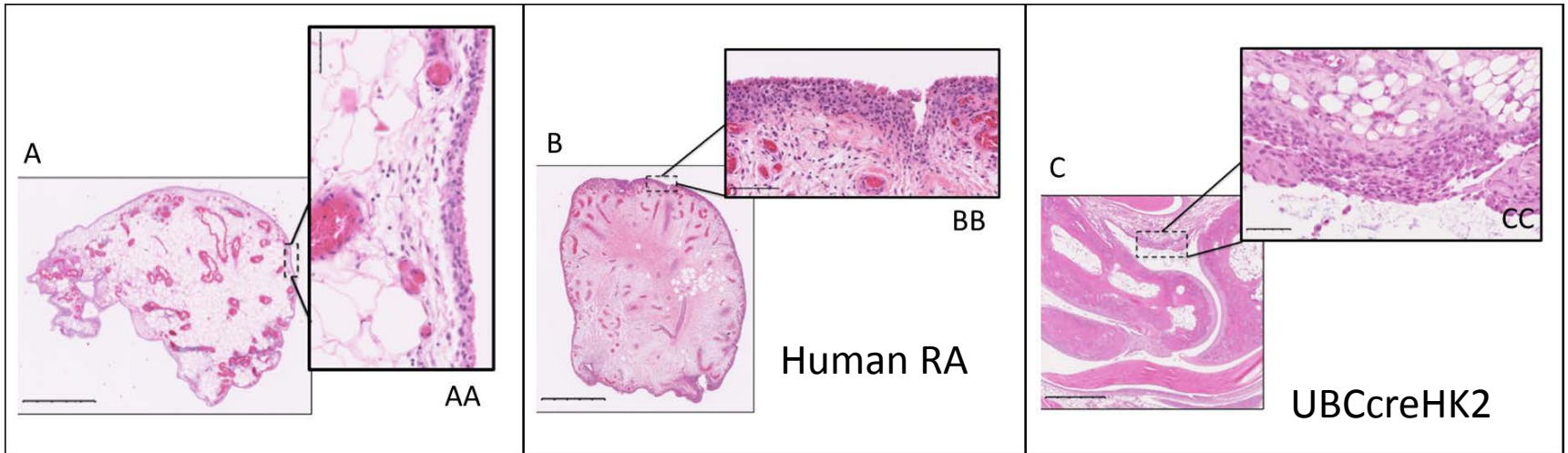
Rx with K/BxN
serum

Evaluate by PET
scan, histology,
RT PCR

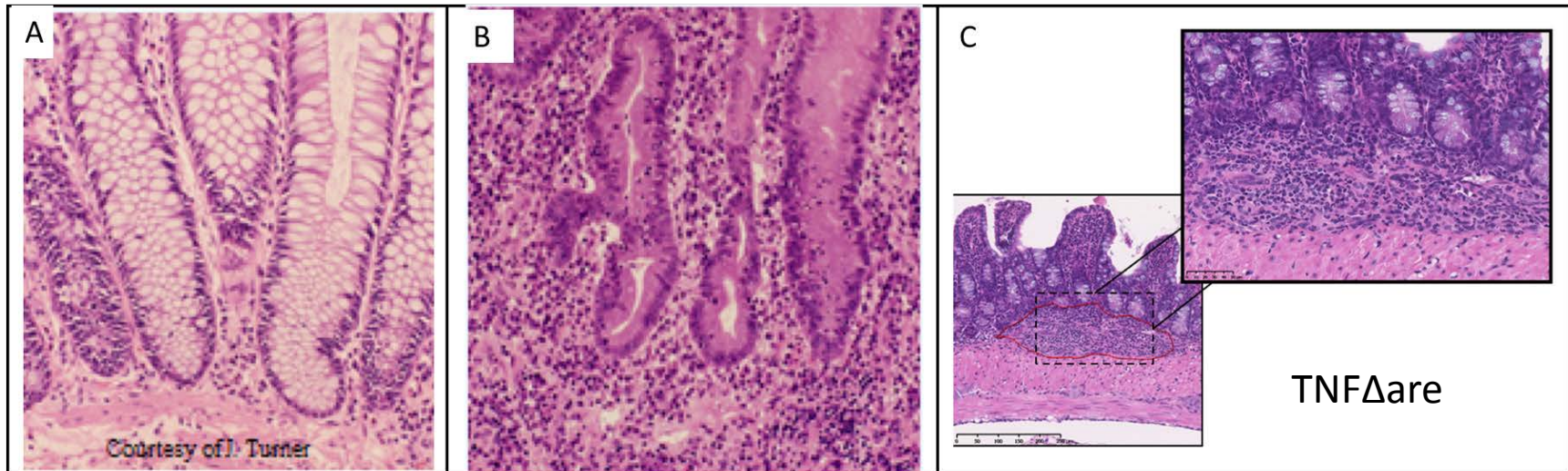
PET/CT with ^{18}F -FDG



Comparison of Human and Murine Tissues



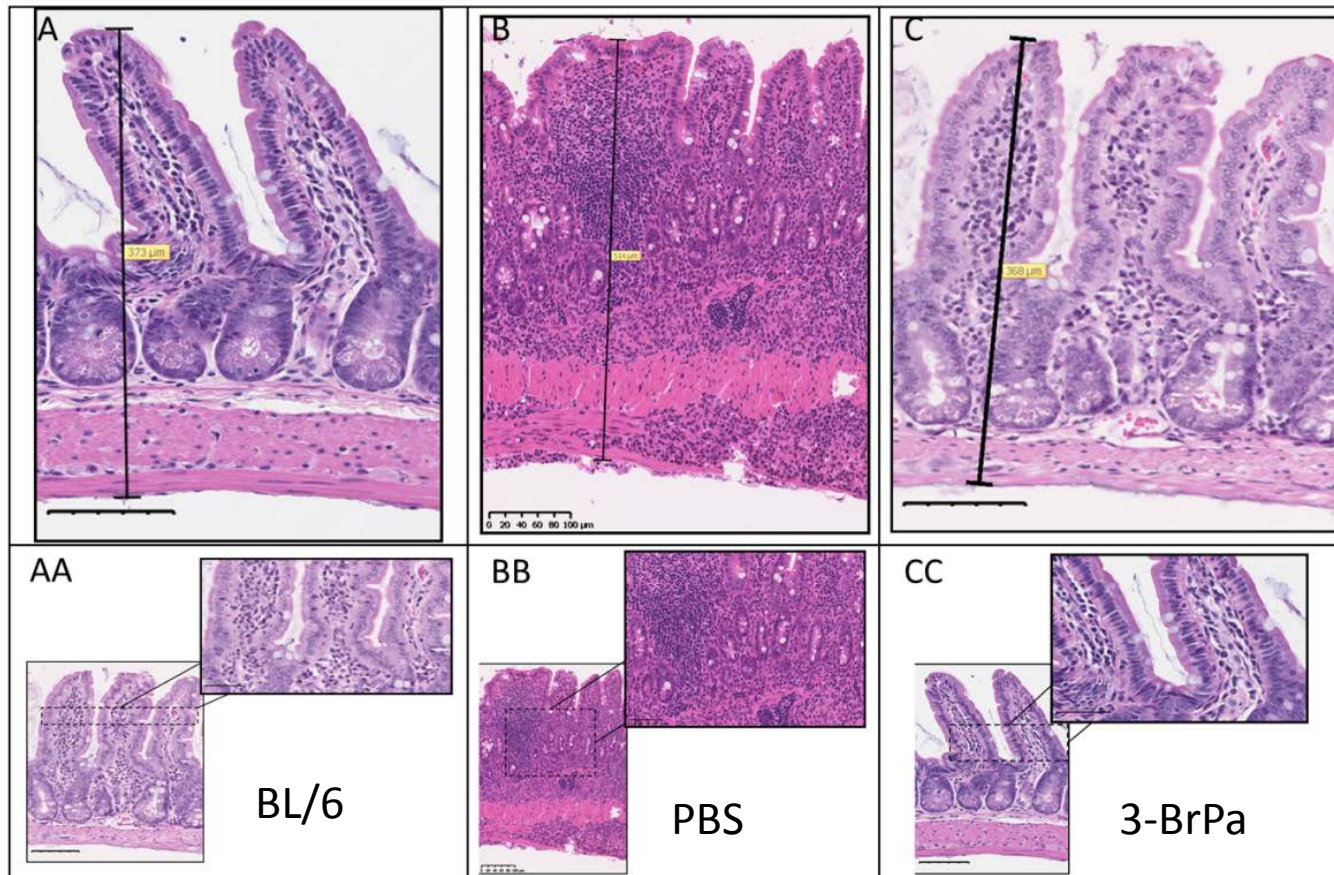
Normal Human

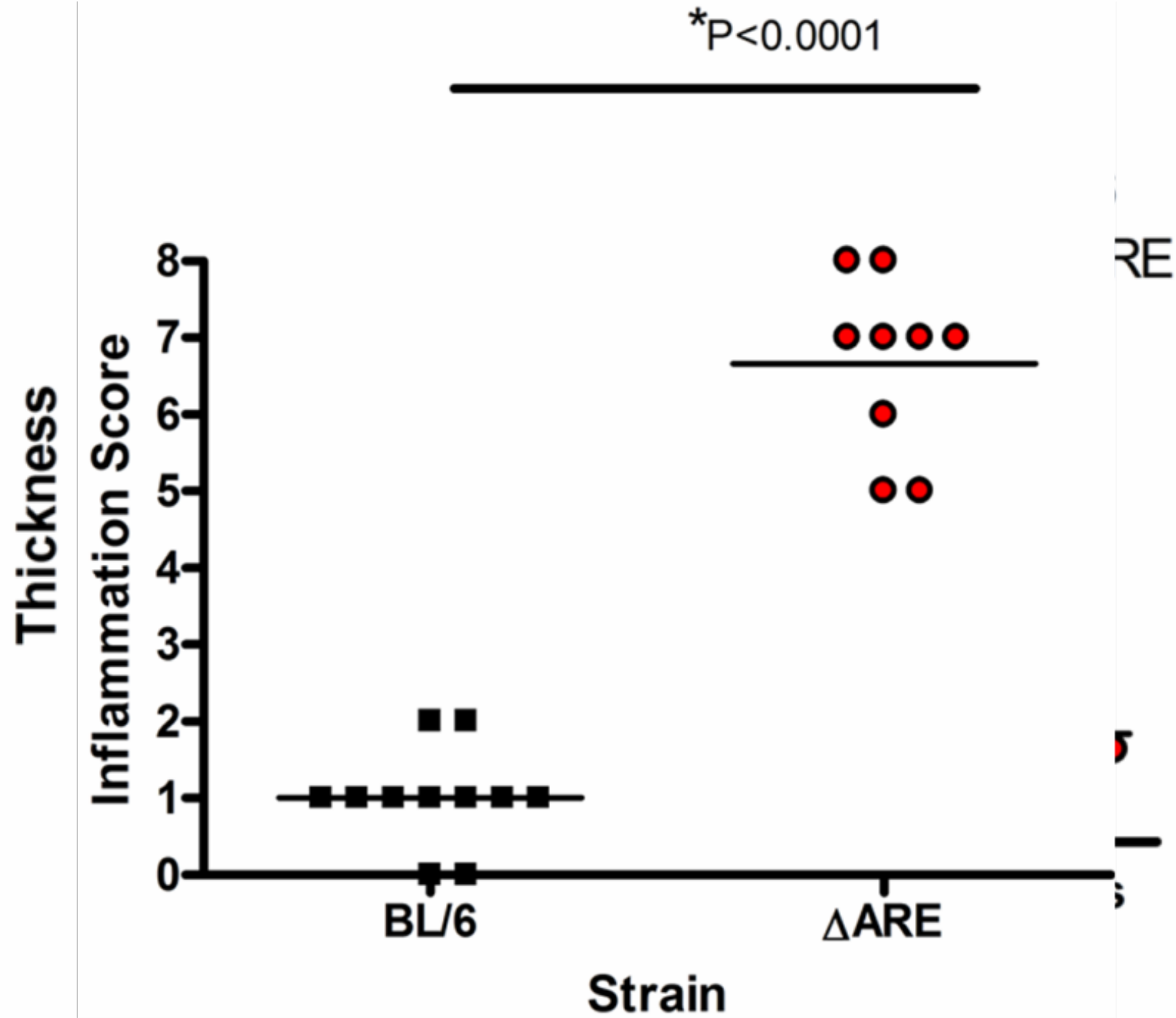


Normal Human

Ulcerative Colitis

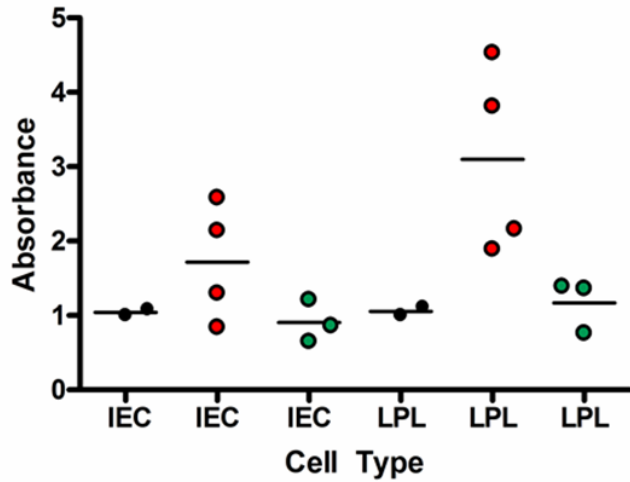
Ileum Histology Scoring Criteria				
Score	0	1	2	3
Tissue Full Thickness	< 450μm	>450μm	>600μm	>800μm
Acute Inflammation (PMN)	Normal	Focal	Multiple focal	Diffuse aggregate or crypt abscesses
Chronic Inflammation (MN)	Normal	Focal	Aggregate	Diffuse aggregate
Other Inflammation	Normal	Loss of goblet cells; bulging villi	N/A	N/A



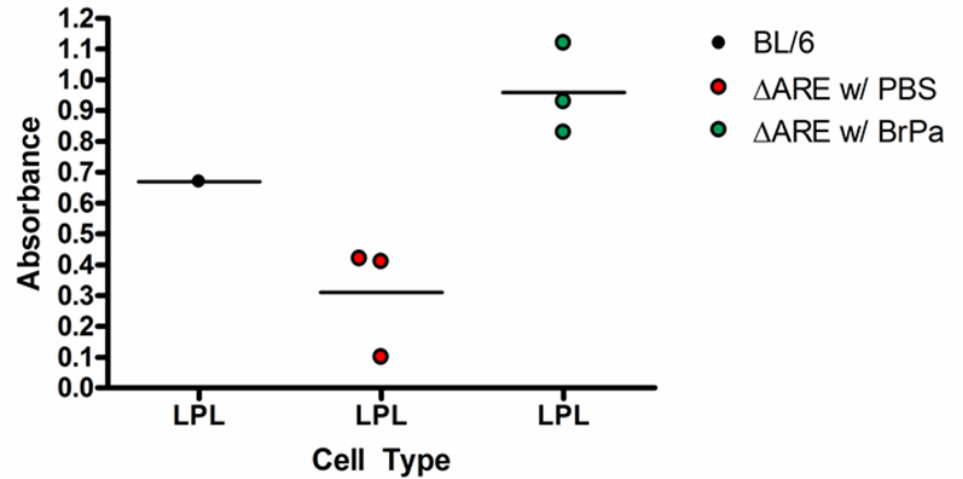


RT-PCR

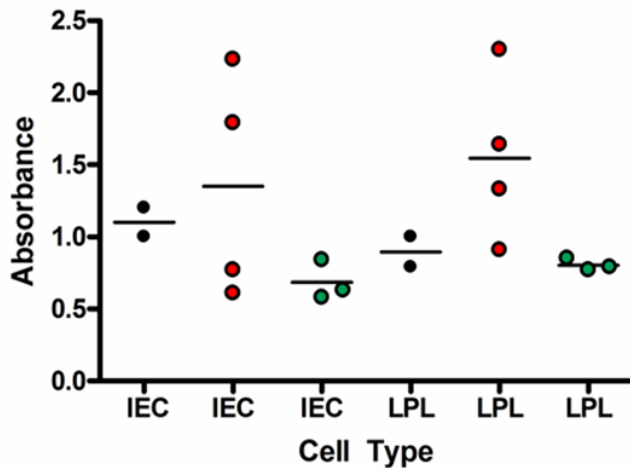
GLUT-1



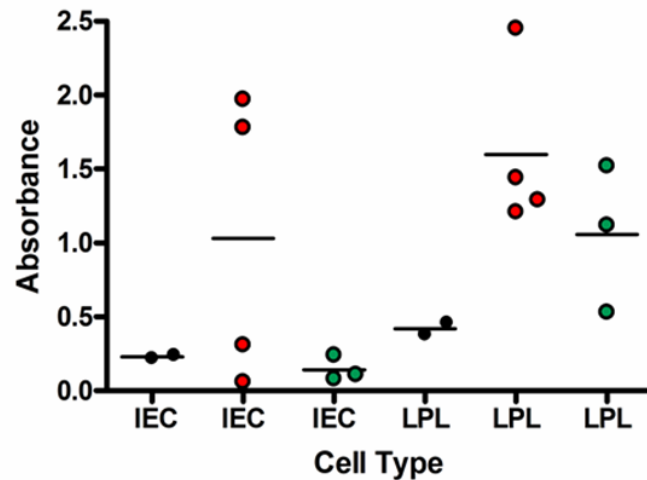
IL-10



HK2



TNF



Conclusions

- Both murine models showed similar cellularity and inflammatory changes to the diseases they are meant to represent
- Glycolysis is increased under inflammatory conditions and inhibition of components of the pathway such as HK2 could be effective treatment strategies

Acknowledgements

- Mentors: Dr. Peter Ernst, Dr. Monica Guma
- NIH 5 T35 OD 10956-17
- Collaborators: Dr. Anilton Vasconcelos, Dr. Marta Fernandez Baustamante
- UCD SVM STAR Program

