Effect of Diabetes on Prostate Inflammation and Epithelial Hyperplasia

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Background

- Men diagnosed with symptomatic benign prostatic hyperplasia have a higher incidence of diabetes than the general population.
- Clinical studies indicate significantly increased risk of BPH and symptomatic progression in men with diabetes.
- Animal studies examining the effect of diabetes on prostate growth have yielded inconsistent findings. The observations have varied with the model used and seem to involve changes in the hormonal axis as well as the effects of hyperglycemia and/or hyper-insulinemia.
- The goal of this proposal is to use one or more TG animals to examine the effect of diabetes on the prostate.

Research Aims

- Aim 1

  Test hypothesis that diabetes is associated with increase prostatic inflammation.

  -Quantitative histological scoring

  -RT-PCR

- Aim 2

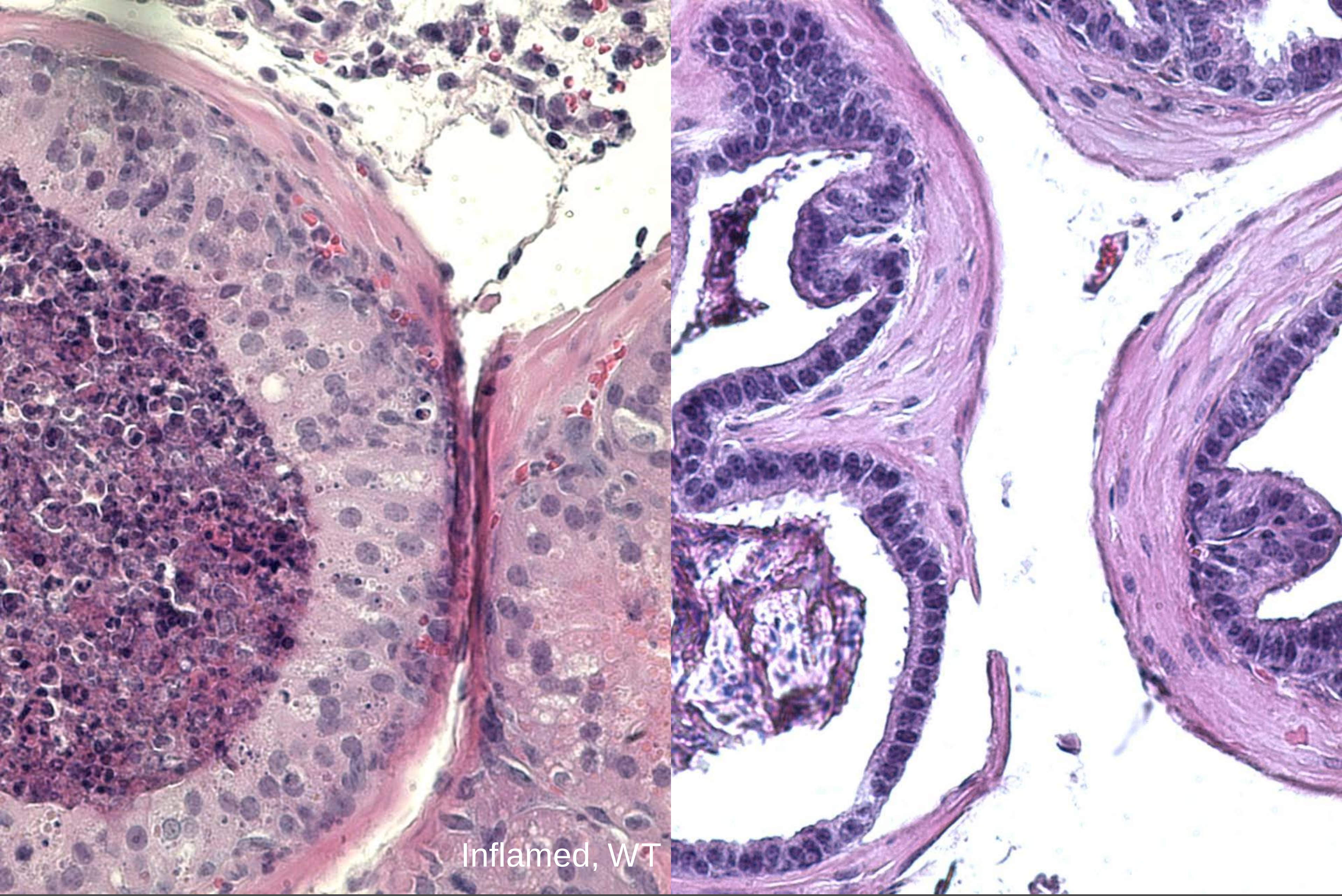
  Test hypothesis that diabetes is associated with epithelial hyperplasia.

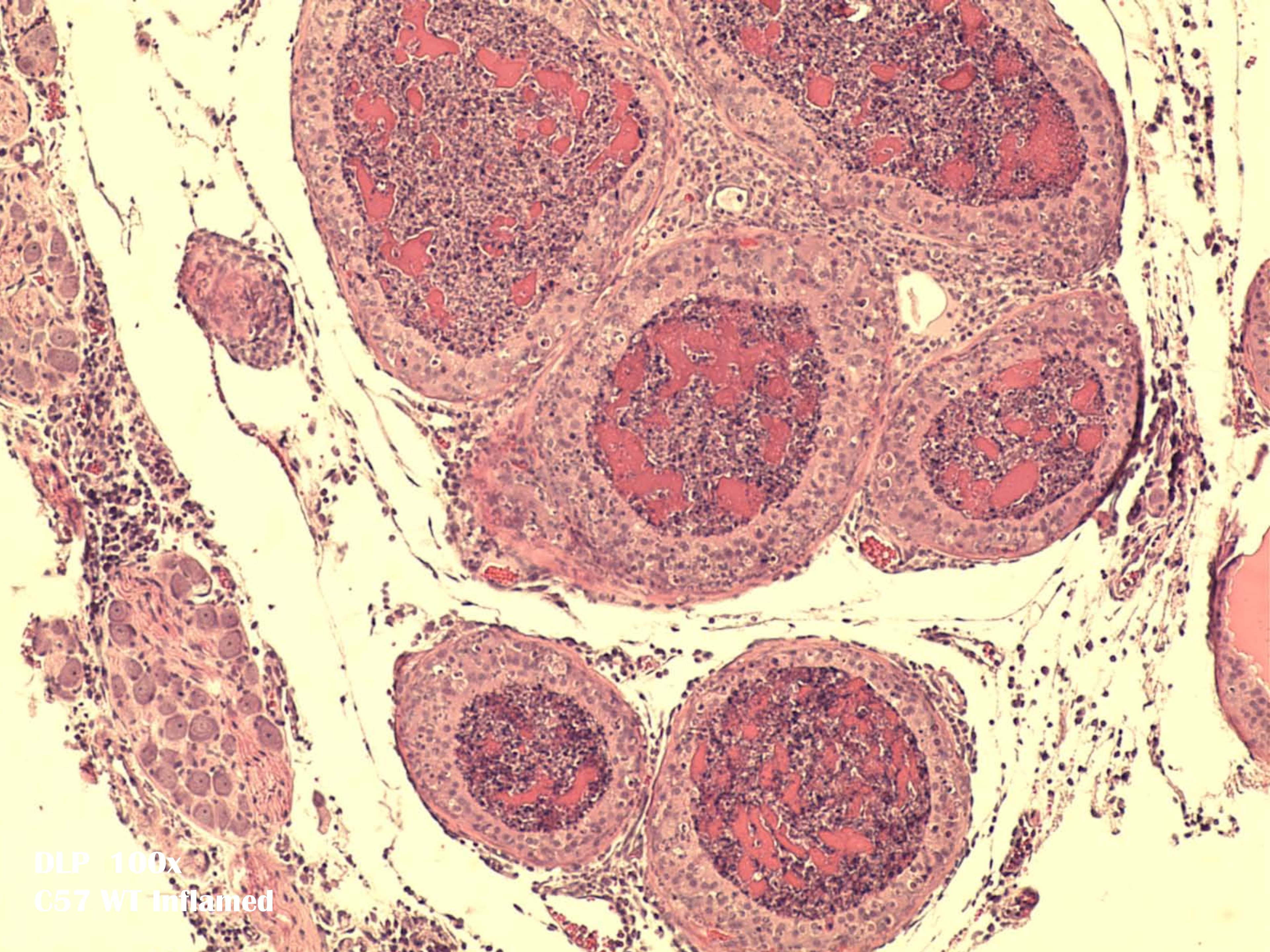
  -Quantitative histological scoring

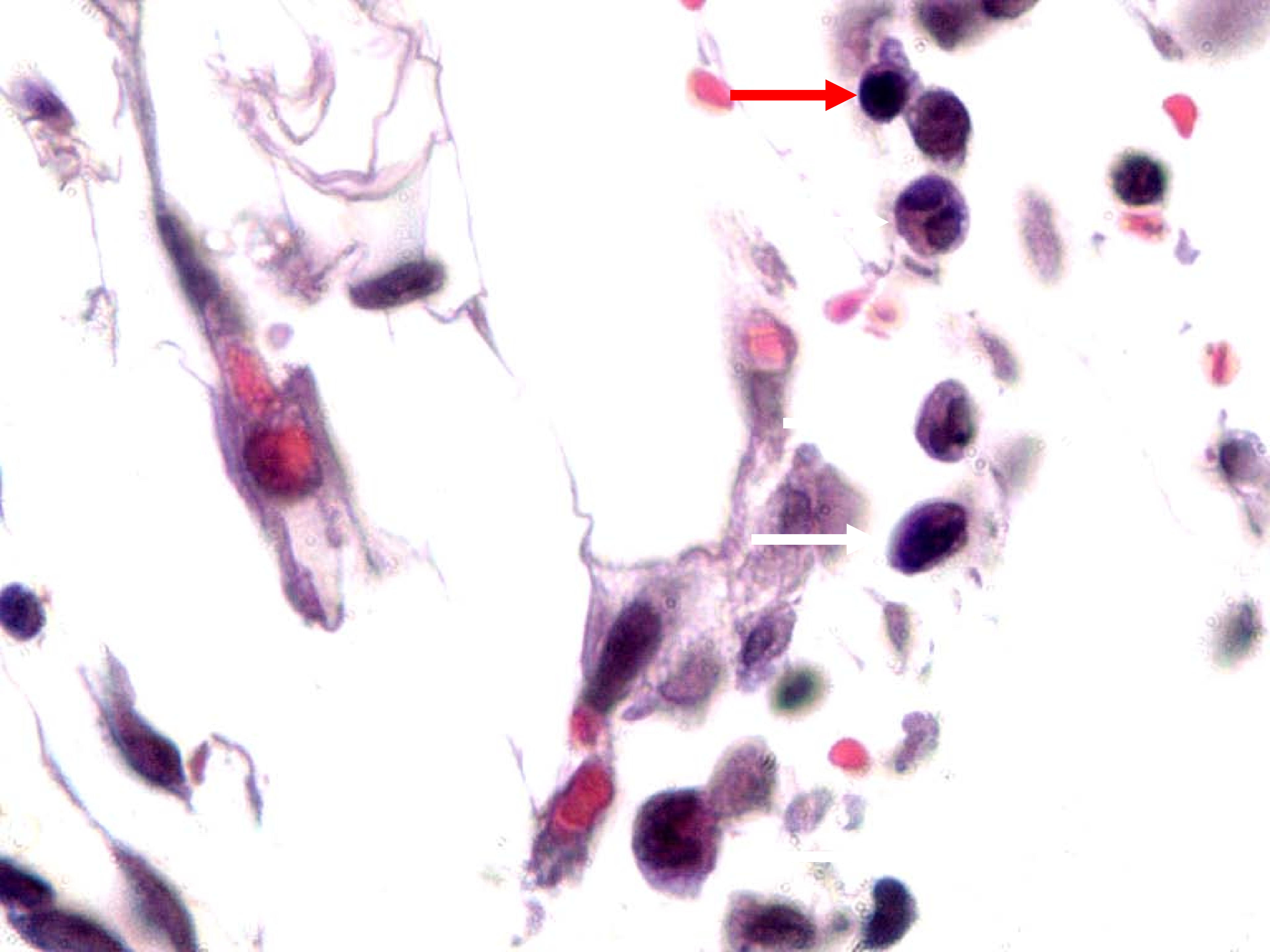
  -Quantitative measurements

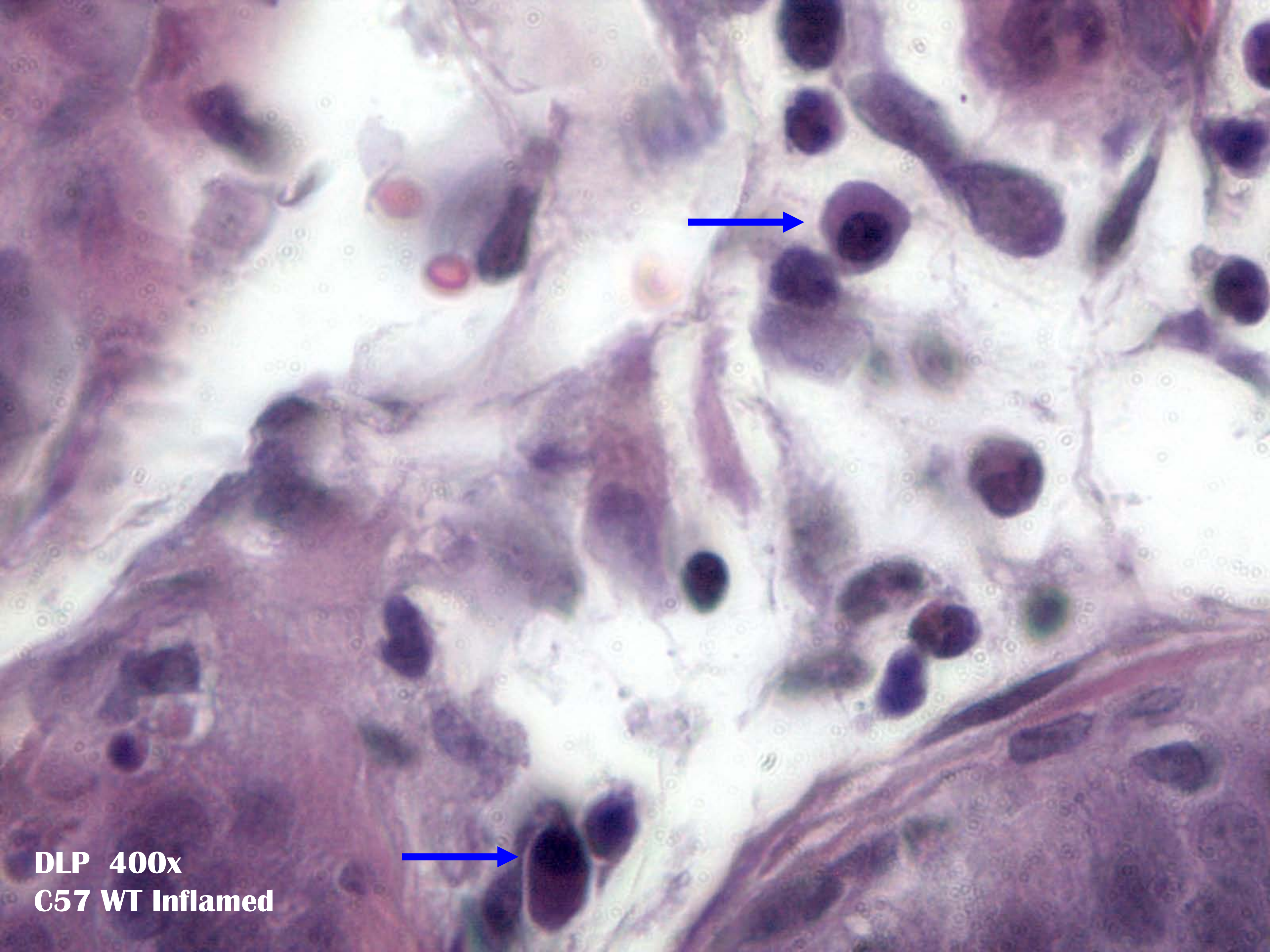
Mouse model of reactive hyperplasia

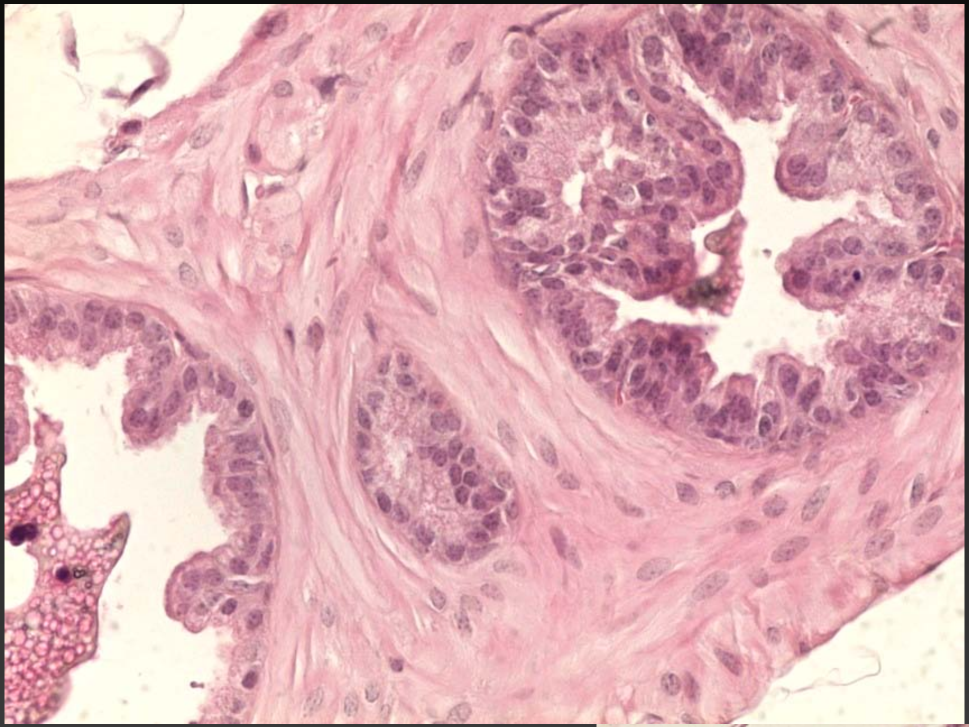
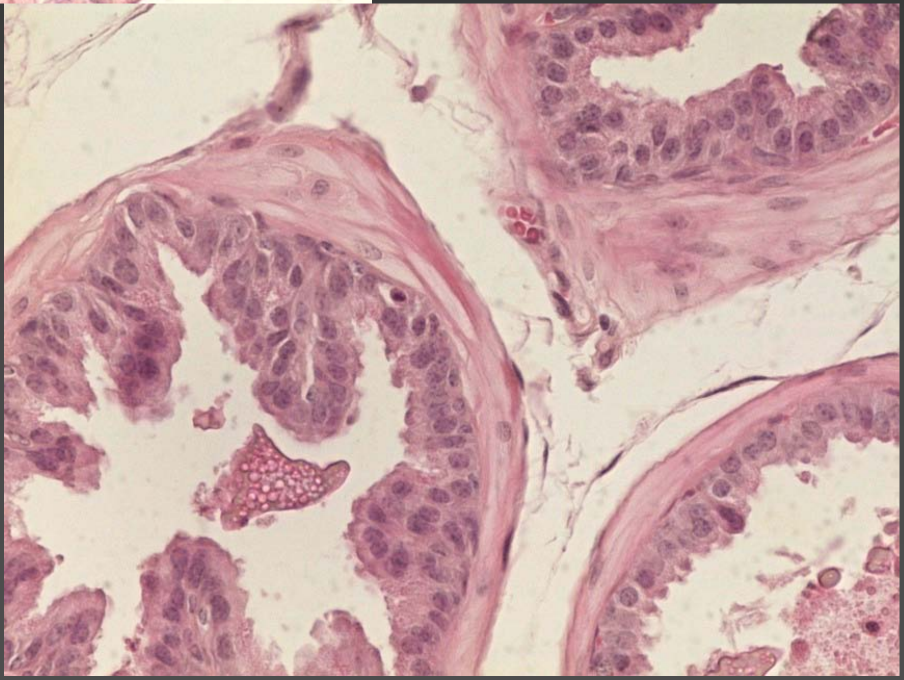
- Inflammation induced by *E. coli* 1677 first characterized by Walt Hopkins lab.
- Mouse strain specific effects
- In C57 BK mice, infection and substantial inflammation days 1-5; clearing by day 7
- Reactive hyperplasia days 3-7
- *"Reactive hyperplasia"* is the response of the tissue to inflammation-believed to precede cancer.


Inflamed, WT


DLP 100x
C57 WT Inflamed



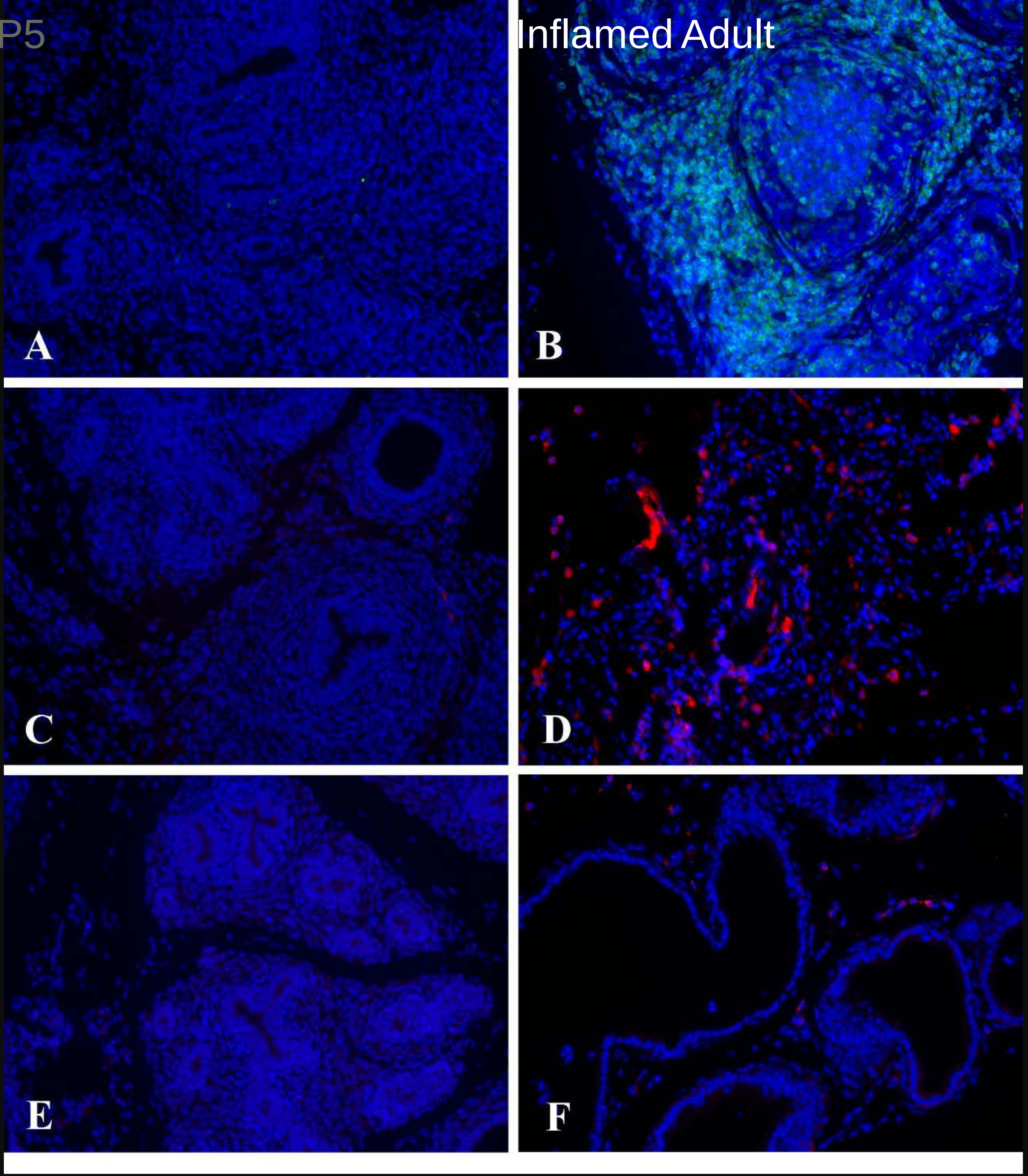

DLP 400x
C57 WT Inflamed

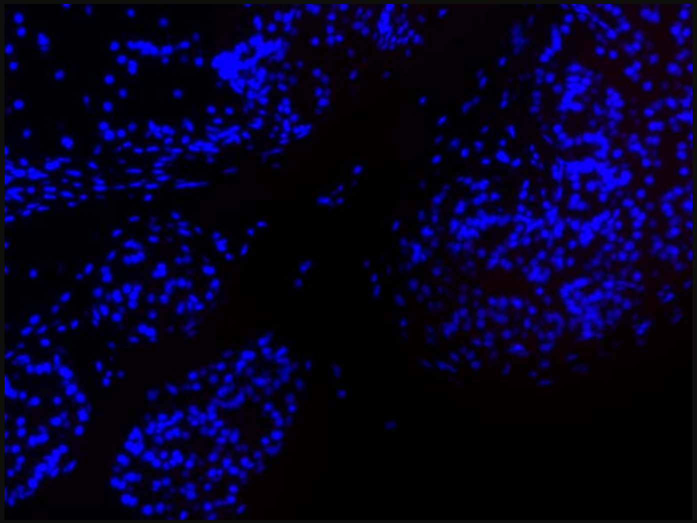
CD-3
(T-Lymphocytes)

F4-80
(Monocytes)

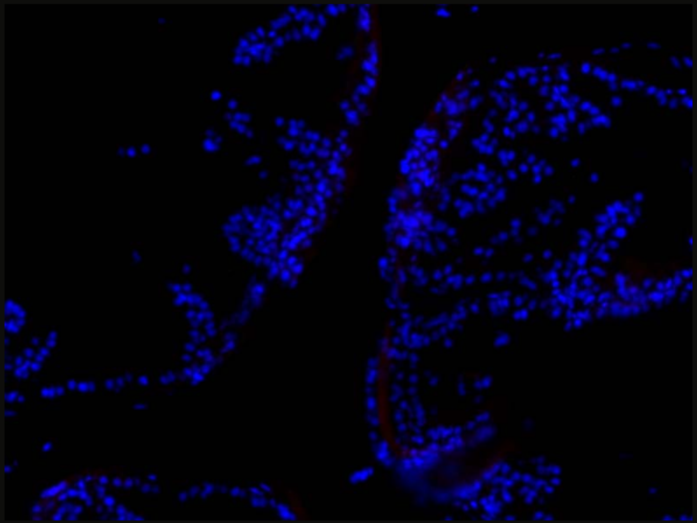
CD-20
(B-Lymphocytes)



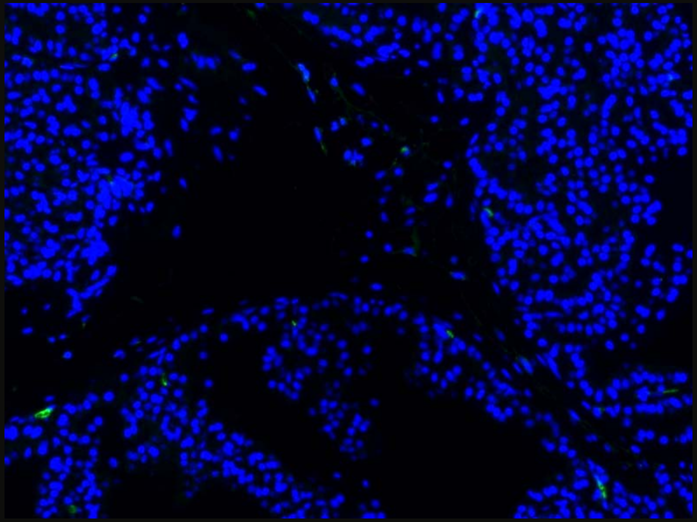
Jerde and Bushman, *Science Signaling*, 2009



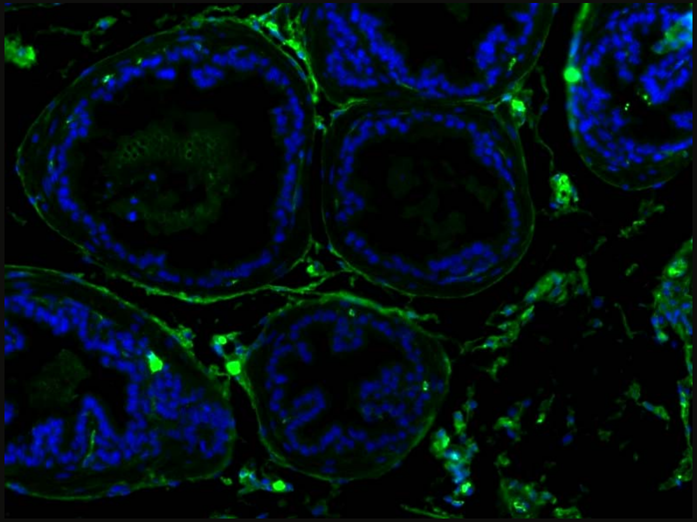
WT ki67 + hoechst



TG 1 KI67 + hoechst



WT CD45 + hoechst



TG 1 CD45 + hoechst

Choice of Mice Model

- Insulin resistance?
- What are the instructive lessons from similar studies performed in other tissues?