

# CPB 69700 RESEARCH SEMINAR

## DEPARTMENT OF COMPARATIVE PATHOBIOLOGY

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Thurs., December 3, 2009  
VPTH 112  
3:30 pm

“Generation Of Th17 Cell Populations Inducing  
Inflammation In Distinct Segments In The Intestine”

### Abstract:

**Background & Aims:** Th17 cells are major effector T cells in the intestine but the regulation of their tissue tropism is poorly understood. We investigated here the generation of inflammatory Th17 cells with distinct tissue tropisms within the intestine. **Methods:** We used *in vitro* and *in vivo* mouse models to study the factors that determine the tissue tropism of Th17 subsets and its impact on intestinal inflammation. **Results:** We found that Th17 cells with distinct tissue tropisms and pathogenic activities are generated depending on the available concentration of retinoic acid (RA). In contrast to the widespread perception that RA would suppress the generation of Th17 cells, we provide evidence here that retinoid acid is actually required for generation of Th17 cells with specific tissue tropisms within the gut. Th17 cells induced with low RA concentration migrated and induced moderate inflammation mainly in the large intestine, whereas Th17 cells induced with optimal levels of RA migrated to the small intestine and induced more severe inflammation. The two subsets of Th17 cells differentially expressed the gut homing receptors CCR9 and  $\alpha 4\beta 7$ . CCR9 is required for Th17 cell migration to the small intestine, while  $\alpha 4\beta 7$  is required for the migration of Th17 cells throughout the whole intestine. **Conclusions:** Our results identified gut Th17 cell subsets with distinct capacities in migration and inflammatory activities. The specific gut tropism of Th17 cells is determined by the combination of gut homing receptors regulated by the RA signal.