

## Kris A. Steinbrecher, PhD

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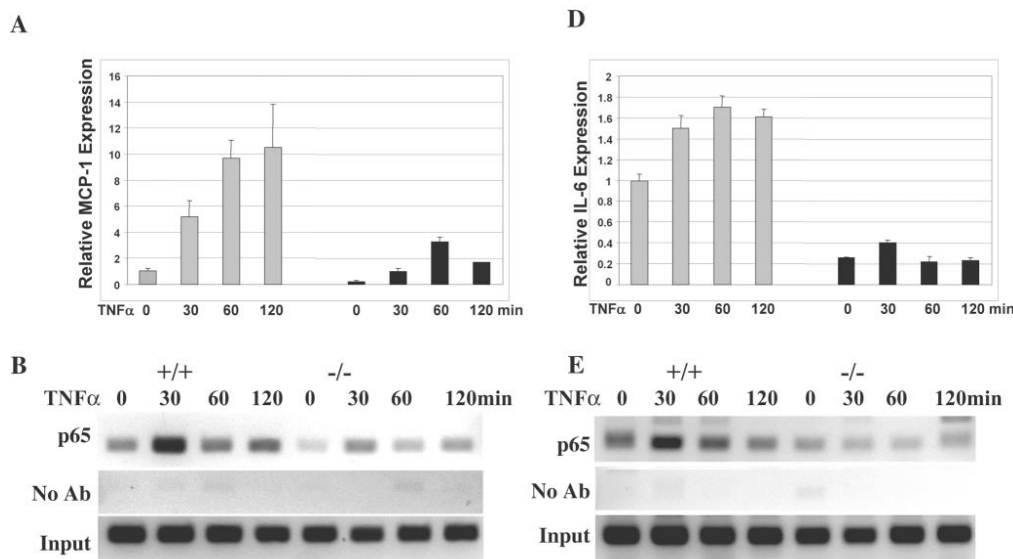
### Description of Research:

A primary goal of Dr. Steinbrecher is to understand the molecular mechanisms through which gut microflora influences both normal intestinal function as well as inflammatory bowel disease (IBD). In the intestine, the presence of commensal or pathogenic bacteria is sensed by Toll-like receptors (TLR) which initiate a signaling cascade that culminates in specific gene expression patterns that are critical for intestinal homeostasis as well as response to infection and injury. He investigates the role of the nuclear factor (NF)- $\kappa$ B family of transcription factors in this process. Recent data show that specific components of the TLR signal transduction pathway dictate which set of NF- $\kappa$ B-activated, pro- and anti-inflammatory genes are expressed in response to commensal or pathogenic microbiota. Ongoing studies utilize both *in vitro* molecular studies as well as tissue-specific, gene targeted animal models to investigate the manner in which TLR signaling pathways regulate intestinal gene expression. This approach will then inform complementary studies aimed at determining the effects of blocking specific TLR signaling proteins within the context of animal models of IBD to discover potential therapeutic targets.

### Collaborations:

Dr. Steinbrecher collaborates with Dr. Denson on defining the role of NF $\kappa$ B in promoting mucosal repair following gut injury using the **Integrative Morphology Core**. He also works with Dr. Rudolph on investigating the role of NF- $\kappa$ B in cAMP-mediated anti-apoptotic signal transduction mechanisms. He also collaborates with Dr. Cohen on mechanisms of GC-C induced apoptosis and intestinal differentiation.

### Representative Figure:



GSK-3 $\beta$  is required for TNF- $\alpha$ -induced transcription and promoter recruitment of p65 to a subset of NF- $\kappa$ B-regulated genes. (A) Real-time RT-PCR for MCP-1 expression was performed on wild-type and GSK-3 $\beta$  null MEFs. (B) ChIP assays to determine p65 localization to the MCP-1 promoter were performed on TNF- $\alpha$ -treated MEFs. The negative control and input are shown in the lower panels. (D) IL-6 mRNA levels following TNF- $\alpha$  stimulation were measured by real-time RT-PCR. (E) ChIP assays in GSK-3 $\beta$  wild-type and null MEFs were used to measure recruitment of p65 to the IL-6 promoter. In this figure, gray bars indicate GSK-3 $\beta$  wild-type and black bars represent GSK-3 $\beta$  null samples ( $\pm$  standard error of the mean,  $n = 3$ ; these data are representative of 3–6 separate experiments). Fig. 6 from *Mol Cell Biol*, 2005; 25:8444-8455.