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Lecture: “The Inflammatory Cascade” by Dr. Geert Schmid-Schonbein, part II.

Given August 7, 2006 during the GEM4 session at MIT in Cambridge, MA.

Please use the following citation format:

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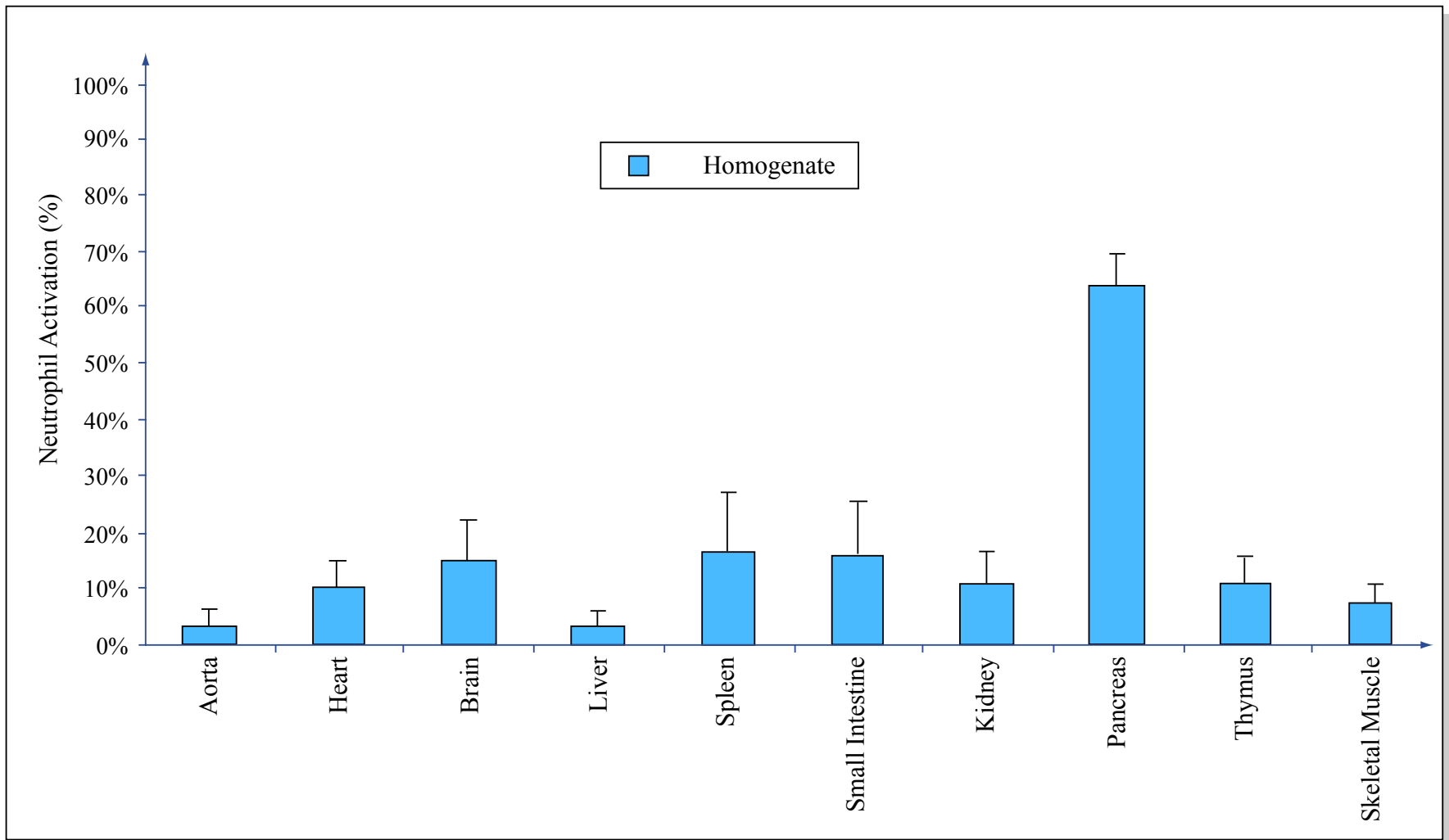


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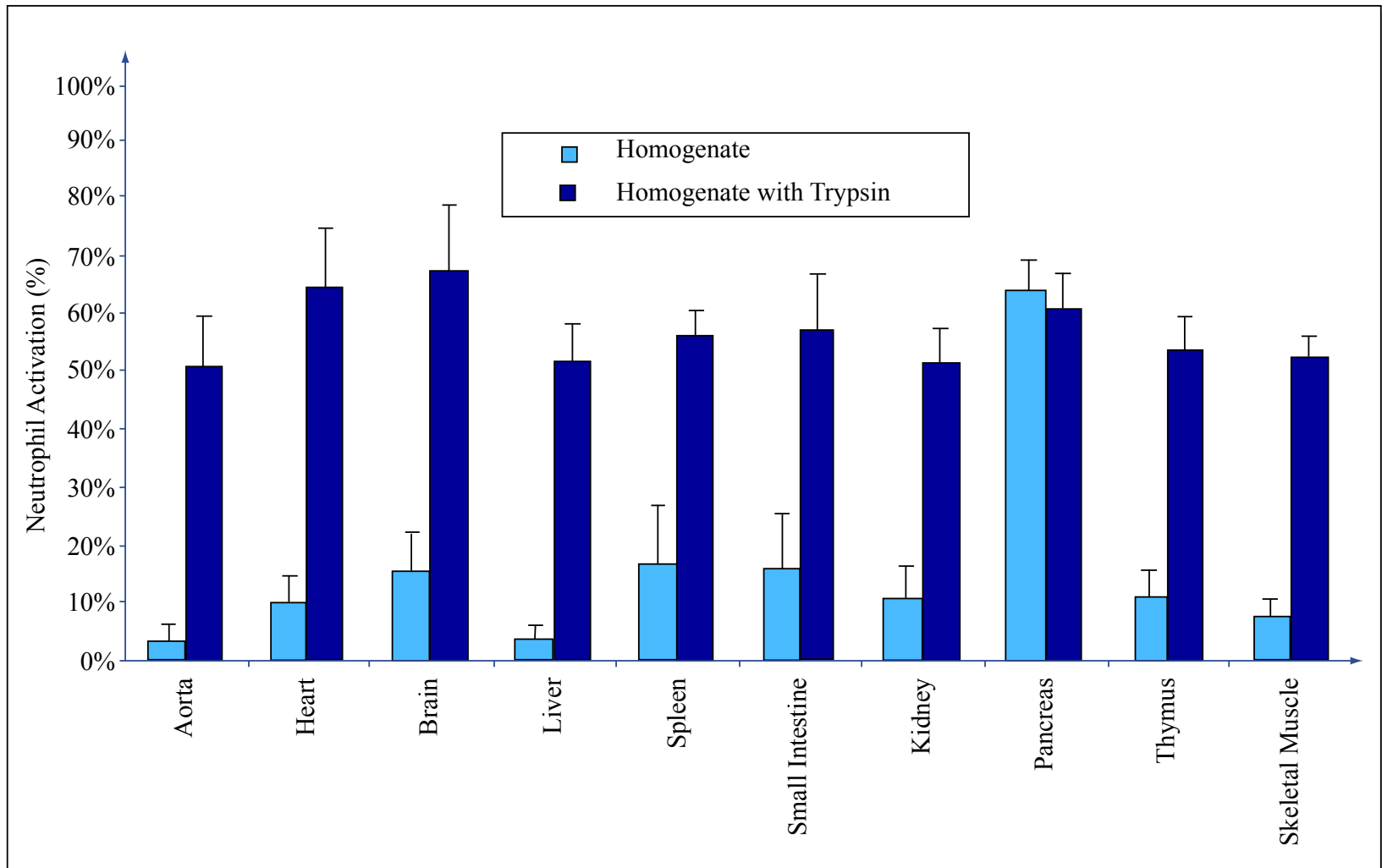


Figure by MIT OpenCourseWare. After Kistler et al., 2000.

Pan

Prote

Trypsinogen

Chymotrypsinogen

Proelastase

Procarboxypeptidase A

Procarboxypeptidase B

Amyl

Amylase

Hydrolyse proteins, carbohydrates, lipids, nucleic acid

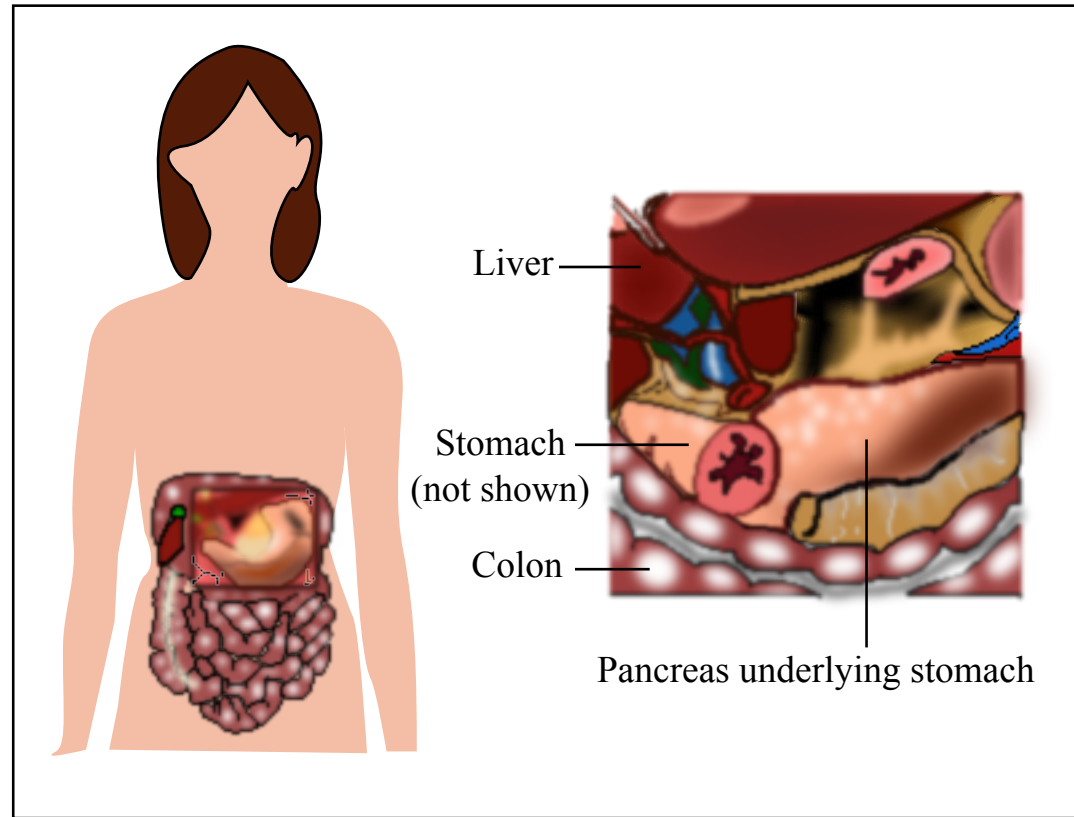


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Waldo et al, 2003

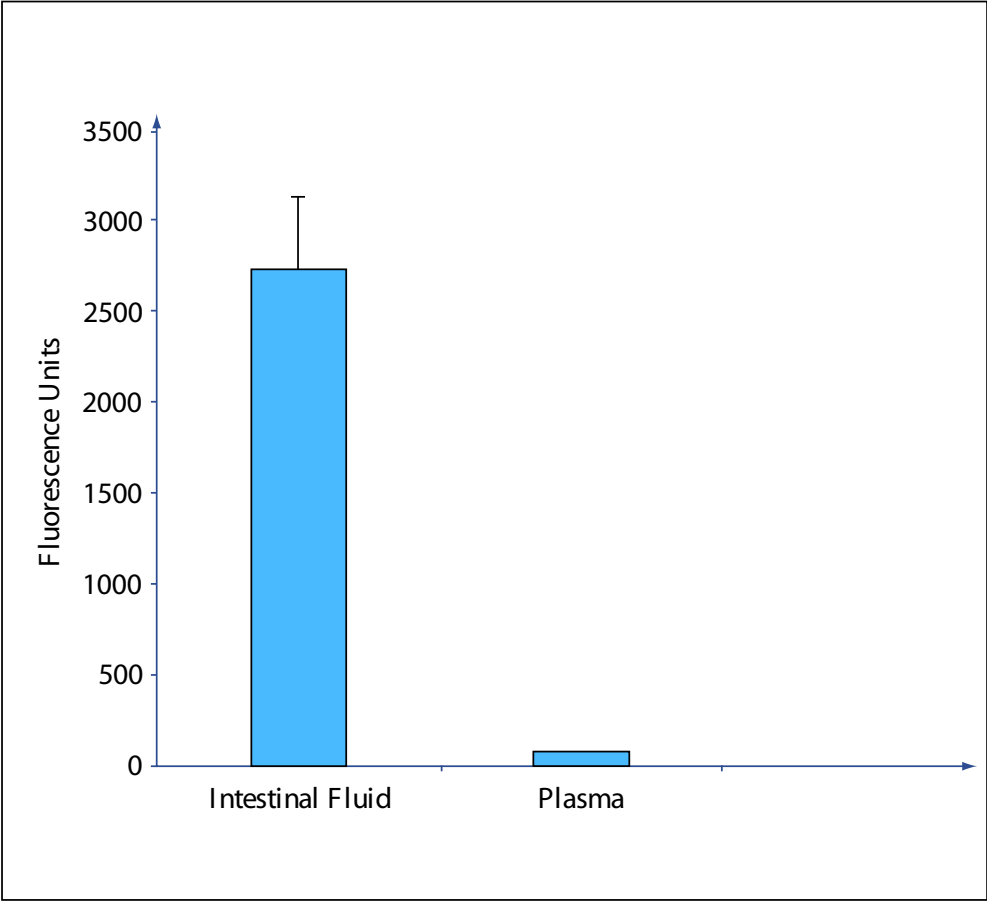


Figure by MIT OpenCourseWare.

Pancreatic Enzyme Derived Inflammatory Mediators

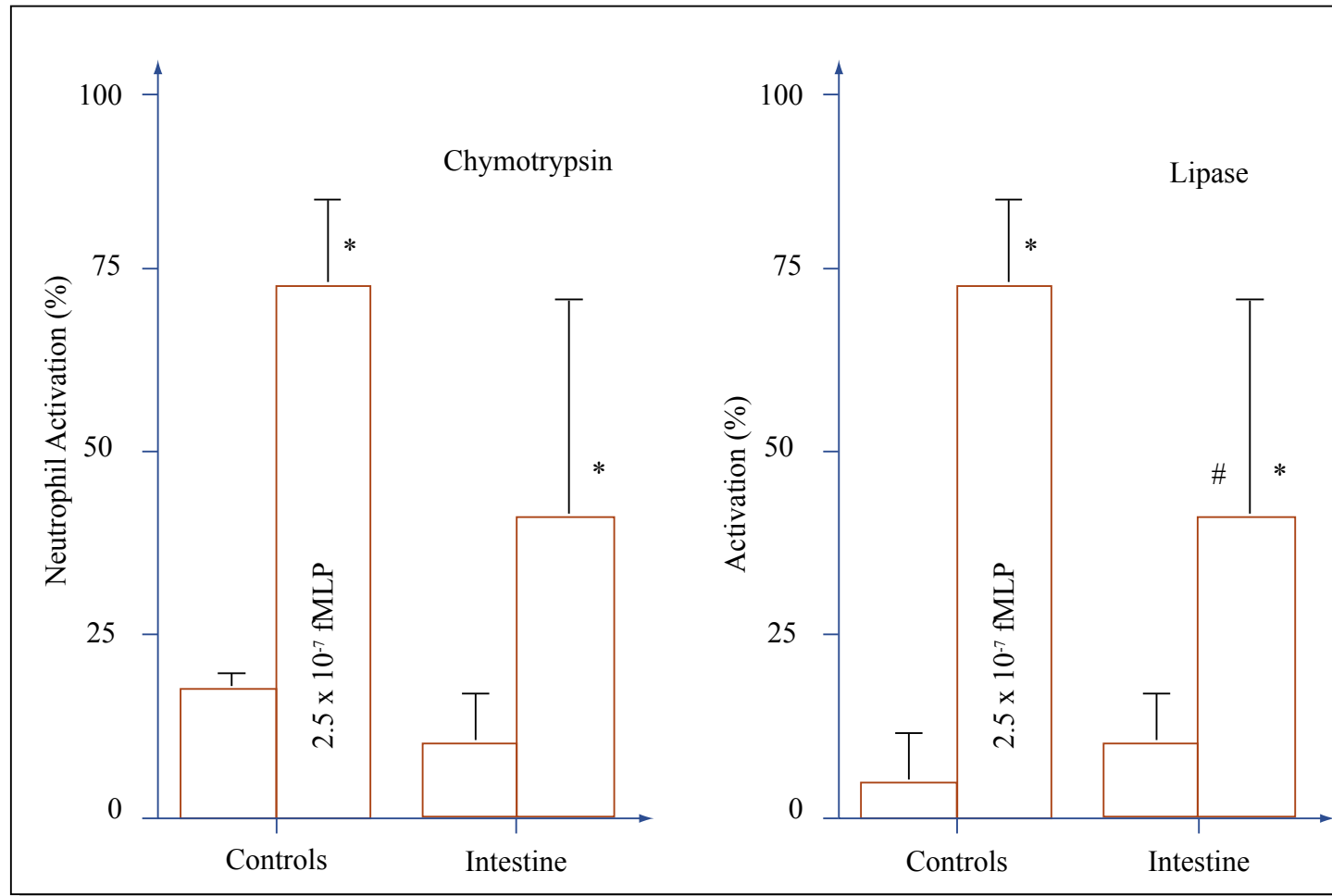


Figure by MIT OpenCourseWare. After Waldo et al., 2003.

Organ homogenates with pancreatic enzymes produce cell death

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Images of cell death from Penn et al., 2006, in review.

Pancreatic Digestive Enzyme Blockade with ANGD, FOY® (Gabaxate mesilate), and Aprotinin

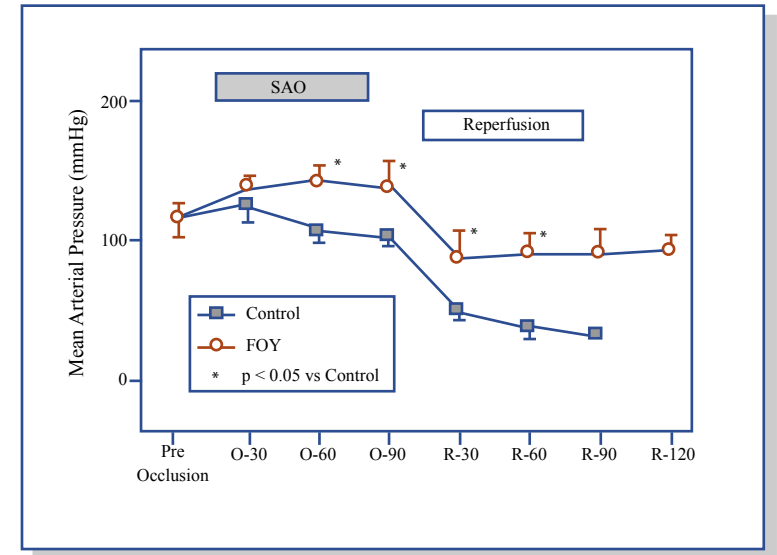
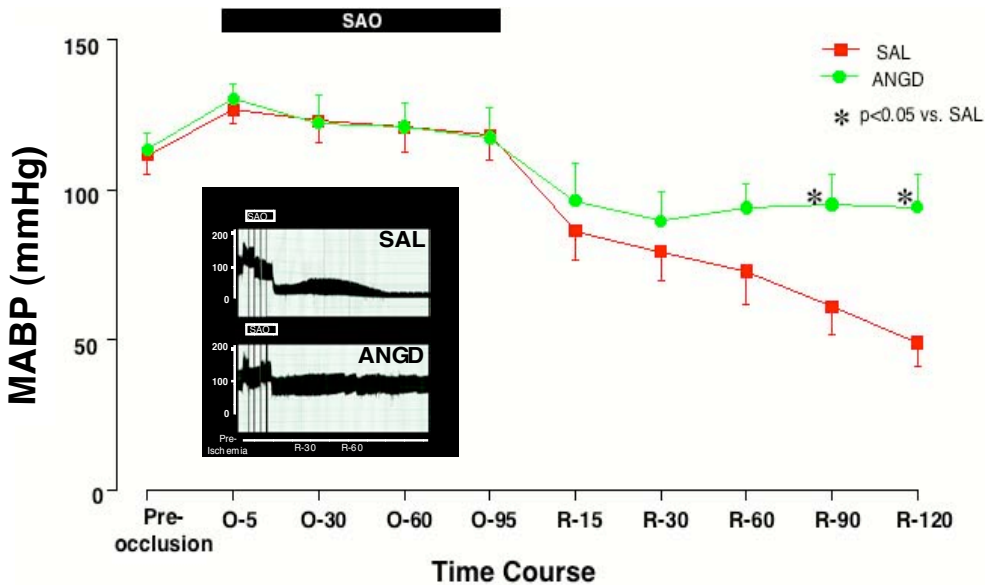


Figure by MIT OpenCourseWare. After Mitsuoka et al., 2002.

Courtesy of National Academy of Sciences, U. S. A. Used with permission.
 Source: Mitsuoka, et al. "Generation of in Vivo Activating Factors in the Ischemic Intestine by Pancreatic Enzymes." *Proc Natl Acad Sci* 97 (2000): 1772.
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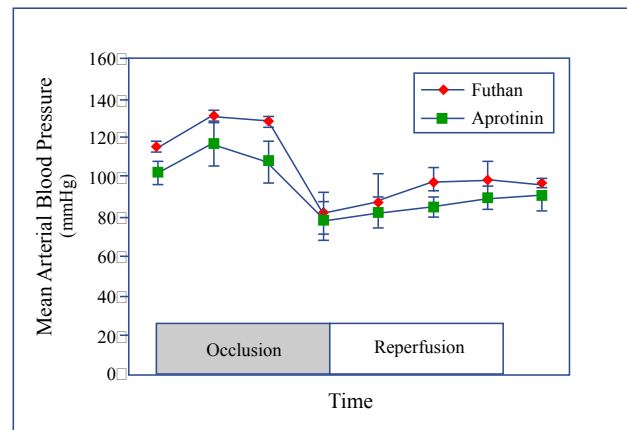
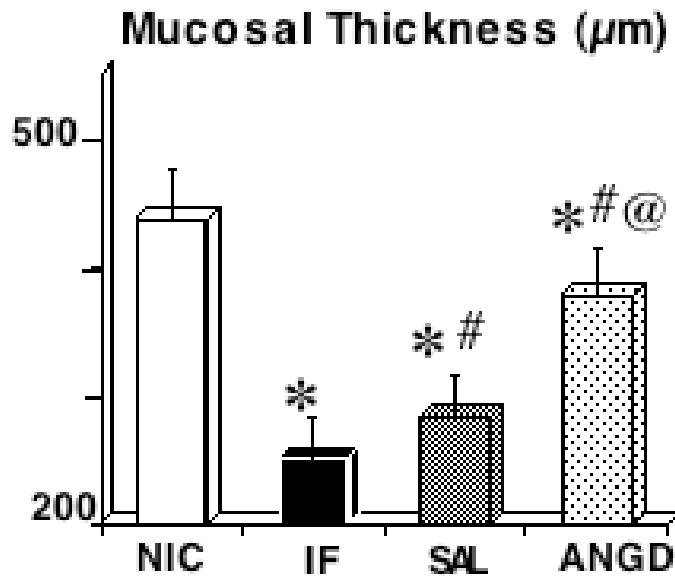


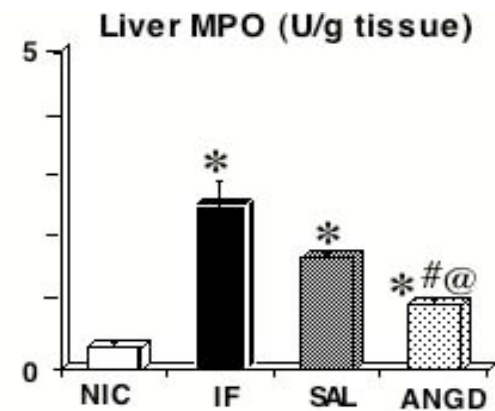
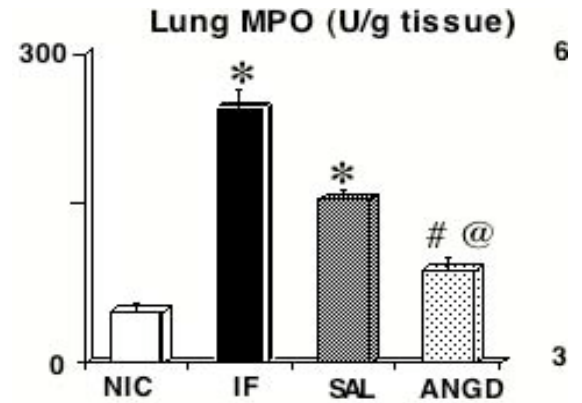
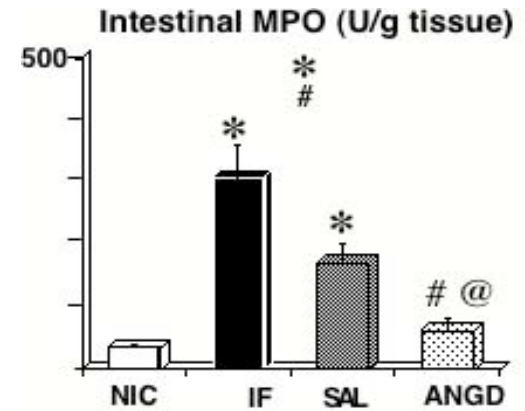
Figure by MIT OpenCourseWare. After Shimmeyer et al., in review.

Intestinal Mucosal Injury

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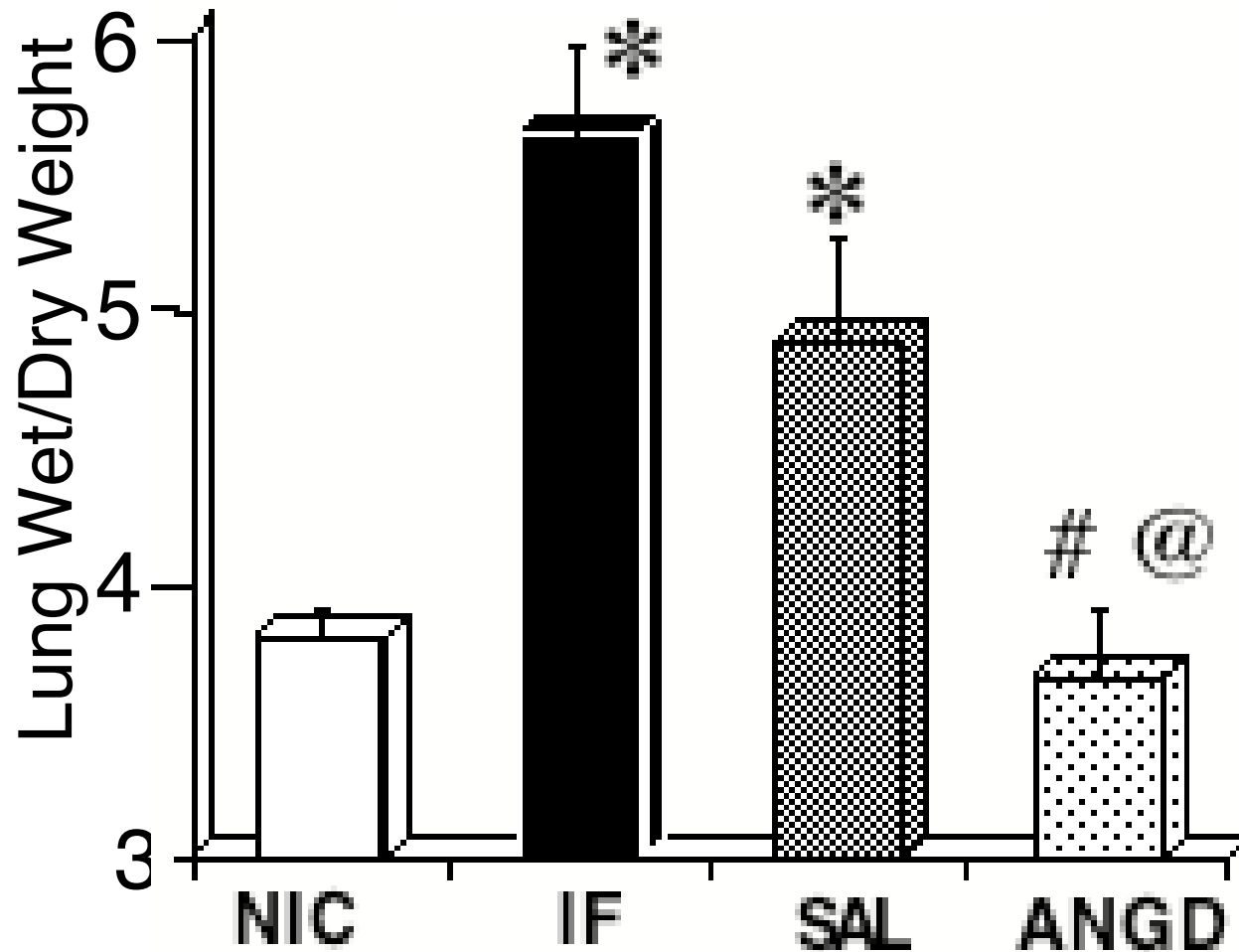


Leukocyte Infiltration



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 Source: Mitsuoka, et al. "Generation of in Vivo Activating Factors in the Ischemic Intestine by Pancreatic Enzymes." *Proc Natl Acad Sci* 97 (2000): 1772.
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Acute Respiratory Distress Syndrome



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Source: Mitsuoka, et al. "Generation of *in Vivo* Activating Factors in the Ischemic Intestine by Pancreatic Enzymes." *Proc Natl Acad Sci* 97 (2000): 1772.

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Intestinal Enzyme Blockade Prevents Cell Death in the Peripheral Microcirculation

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See figures in Fitzal, F., F. A. DeLano, C. Young, H. S. Rosario, and G. W. Schmid-Schonbein. "Pancreatic Protease Inhibition During Shock Attenuates Cell Activation and Peripheral Inflammation." *J Vasc Res* 39 (2002): 320-329.

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See figures in Fitzal F., DeLano F. A., Young C., Rosario H. S., Schmid-Schonbein G. W. "Pancreatic Protease Inhibition During Shock Attenuates Cell Activation and Peripheral Inflammation." *J Vasc Res* 39 (2002): 320-329.

What are the inflammatory mediators ?

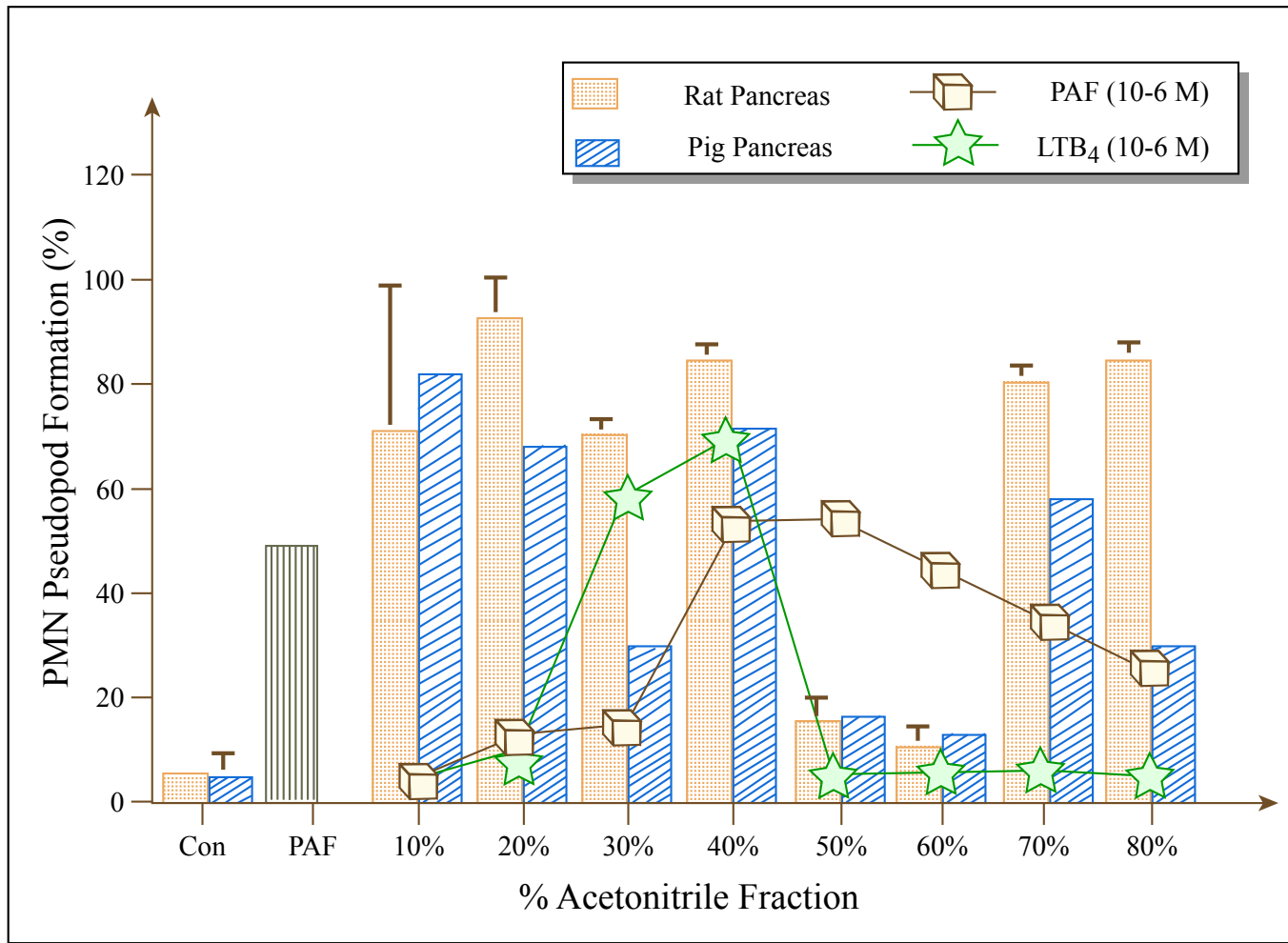
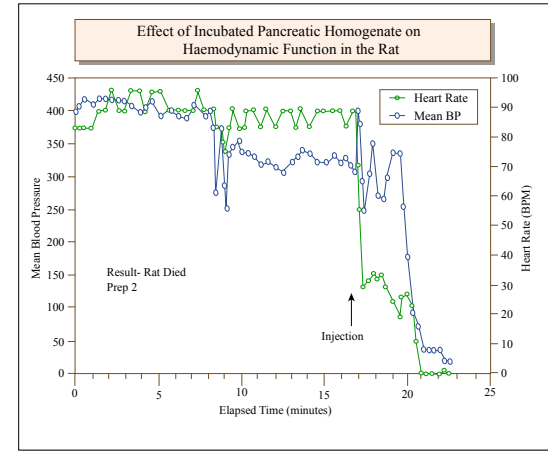
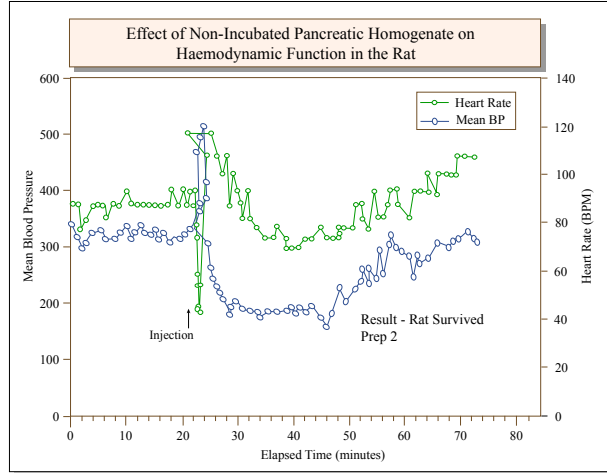
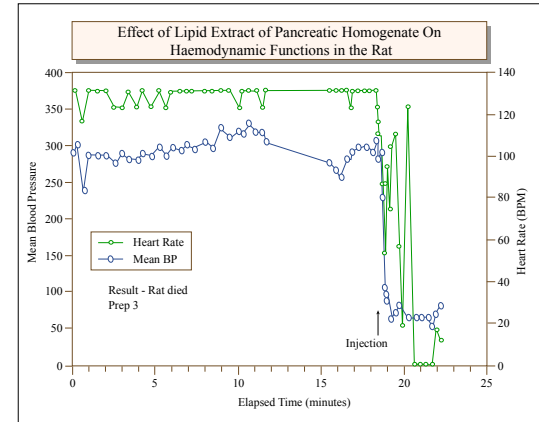
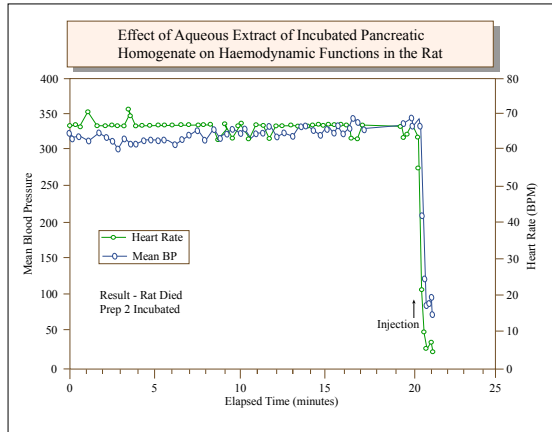


Figure by MIT OpenCourseWare. After Schmid-Schönbein, et al., 2001.



Figures by MIT OpenCourseWare. After Kramp, et al., 2003.



Electrophoresis pattern of aqueous fraction of incubated (I) and non-incubated (N) pancreatic homogenates

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See Fig. 7 in Kramp, et al. "Characterization of Two Classes of Pancreatic Shock Factors: Functional Differences Exhibited by Hydrophilic and Hydrophobic Shock Factors." *Shock* 20 (2003): 356-362.

A breach of the intestinal mucosal barrier causes

**Escape of Digestive Enzymes into the
Wall of the Intestine and Auto-digestion**

**Destruction of the Mucosal
Epithelial Barrier**

Cardiovascular Cytotoxicity

Cell Activation

Swelling of the Lung & ARI

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