

## Targeting pancreatic calcineurin to prevent post-ERCP pancreatitis

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## Post-ERCP pancreatitis (PEP) is still a problem

- Despite recent preventative modalities, PEP still occurs with a frequency of 3-8%
- Why does ERCP cause pancreatitis?




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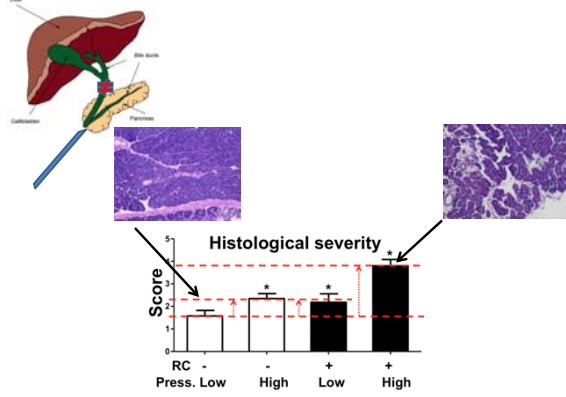
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## Both pressure & radiocontrast contribute to PEP




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## Why does radiocontrast exposure cause PEP?

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## Radiocontrast on $\text{Ca}^{2+}$ and $\text{Ca}^{2+}$ targets

- Radiocontrast causes faint  $\text{Ca}^{2+}$  changes in renal cells  
*(Humes et al. Am J Physiol 1987; Yang et al. Am J Nephrol 2013)*
- Aberrant  $\text{Ca}^{2+}$  is an early pathologic signal in pancreatic acinar cell injury
- A key  $\text{Ca}^{2+}$  target in pancreatitis is calcineurin
  - $\text{Ca}^{2+}$ -activated serine/threonine phosphatase

## Does radiocontrast trigger aberrant acinar cell $\text{Ca}^{2+}$ signals?

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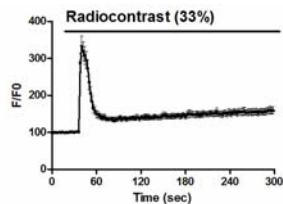
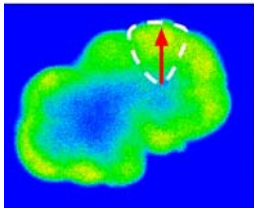
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## Radiocontrast induces high amplitude $\text{Ca}^{2+}$ signals in pancreatic acinar cells

Peak fluorescence



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Do these  $Ca^{2+}$  signals activate the phosphatase calcineurin?

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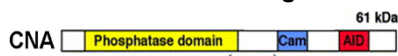
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The phosphatase calcineurin is a target of  $Ca^{2+}$



**Calcineurin (Cn)**

Activators

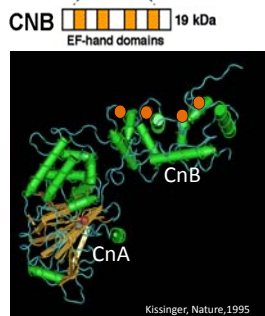
- $Ca^{2+}$
- Calmodulin (CaM)

Inhibitors

- FK506, CsA

Targets

- NFAT, several others




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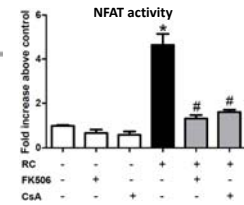
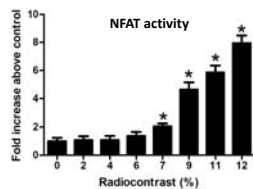
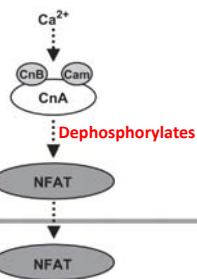
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**Radiocontrast induces calcineurin activation**




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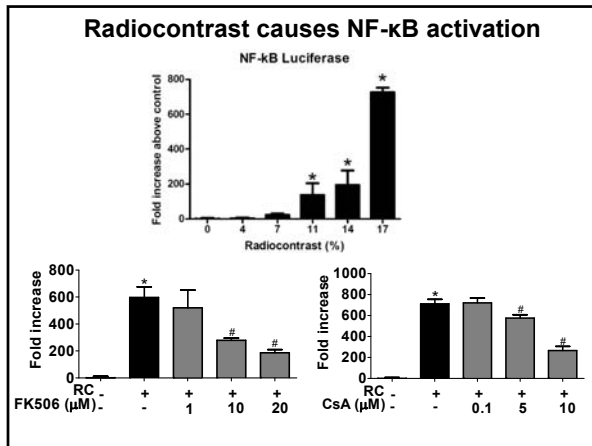
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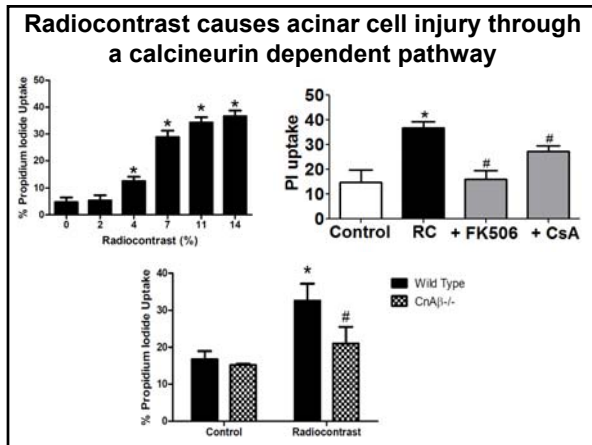
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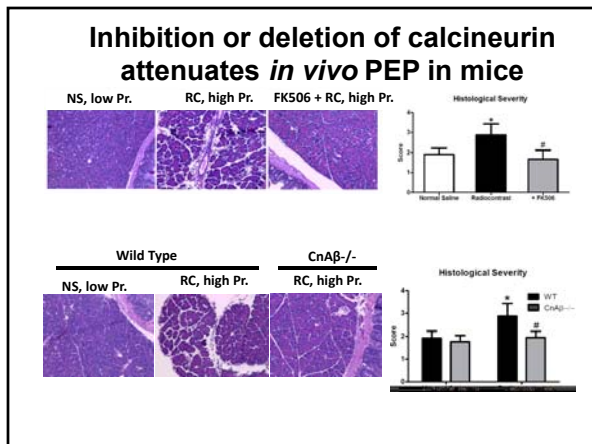
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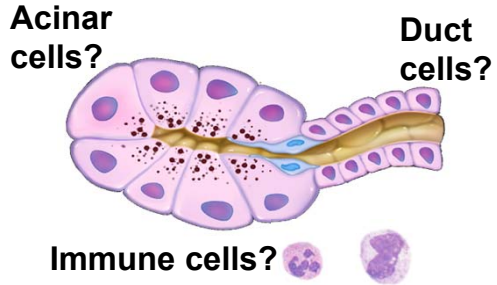
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Which cellular source of calcineurin is involved in PEP?




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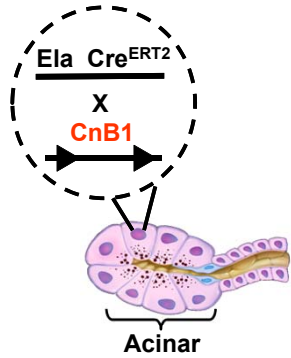
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Designing an acinar cell-specific calcineurin knockout




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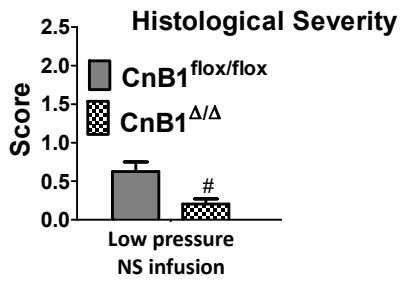
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Acinar cell calcineurin mediates PEP




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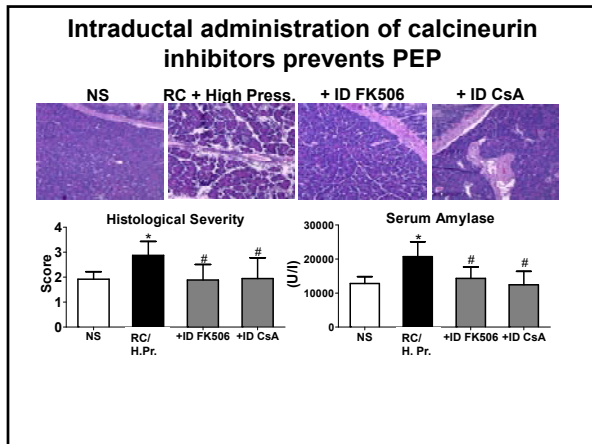
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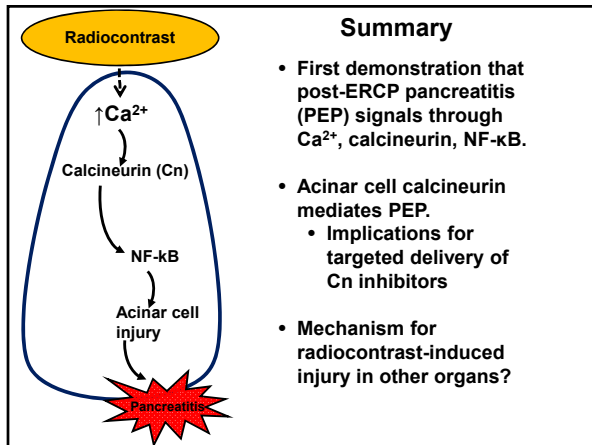
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### Acknowledgments





**Husain Lab**

- Shunqian Jin
- Tanveer Javed
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- Swati Sah



**Collaborators**

- George Gittes
- Rita Bottino
- Jeffery Molkenkin
- Ping Guo



National Institute of Diabetes and Digestive and Kidney Diseases

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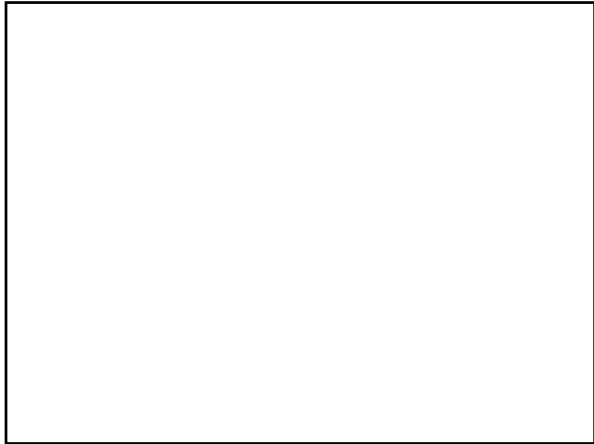
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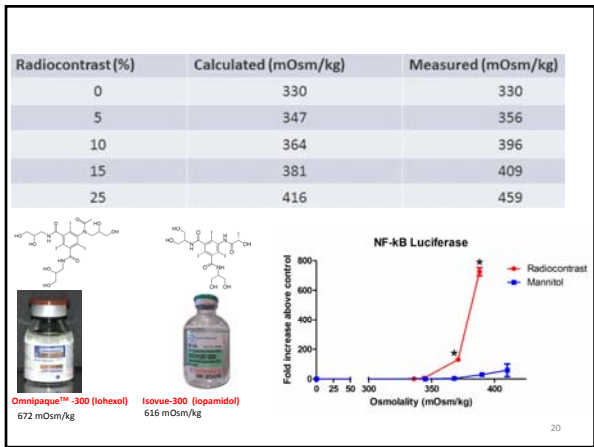
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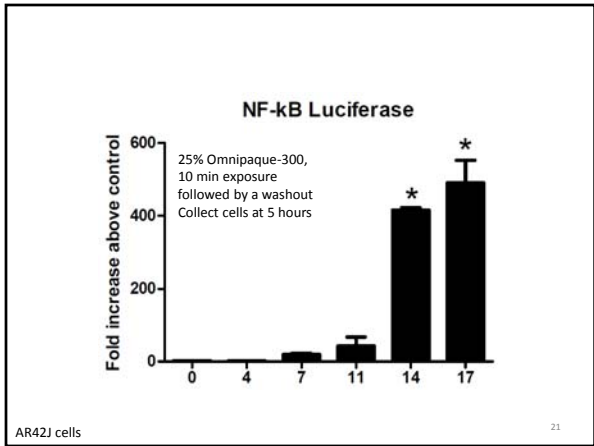
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