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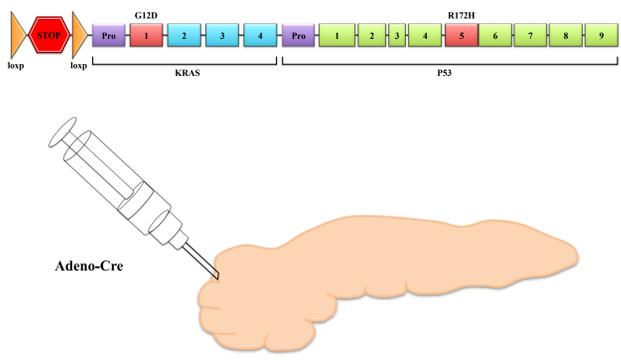
## Abstract # 4178

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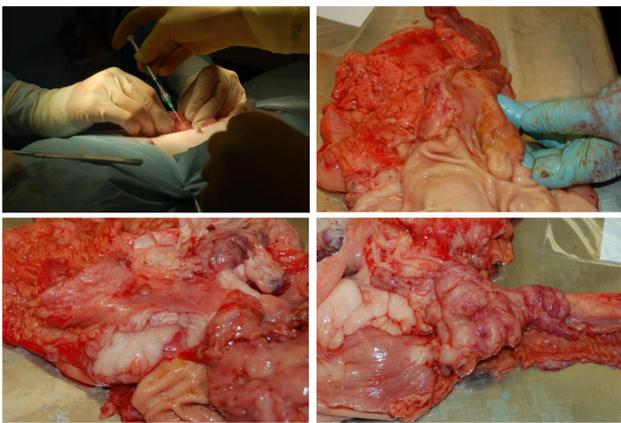
### Introduction:

- Genetically modified mice have provided valuable insight into pancreatic tumorigenesis, yet have distinct limitations in anatomy, physiology, and size when compared to human.
- Porcine models have the potential to alleviate these shortcomings and provide a more faithful recapitulation of human disease.
- Therefore, we generated a pig model with cre-responsive alleles encoding *Kras*<sup>G12D</sup> and *TP53*<sup>R167H</sup> using an Adeno-Cre viral vector to induce tumorigenesis in the pancreas.

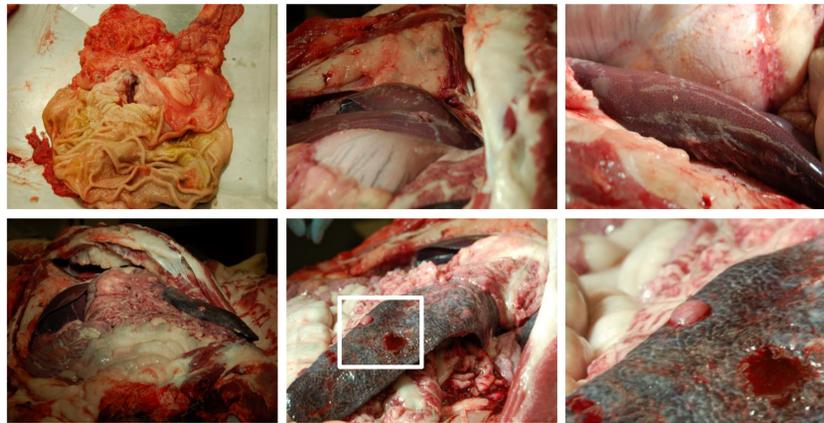
**Figure 1:** Intra-Pancreatic Injection of Adeno-Cre in *Kras*<sup>G12D</sup>/*TP53*<sup>R167H</sup> Pig



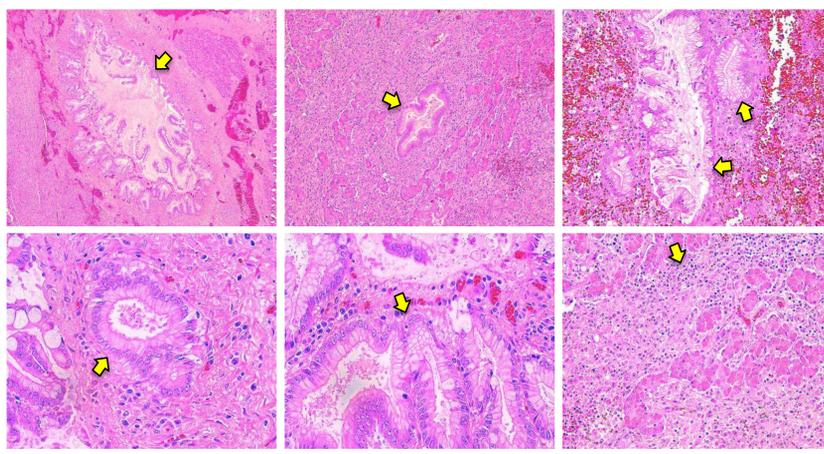
**Figure 2:** Intra-Pancreatic Cre/*Kras*<sup>G12D</sup>/*TP53*<sup>R167H</sup> Pigs Present with Smooth Muscle Derived Tumors



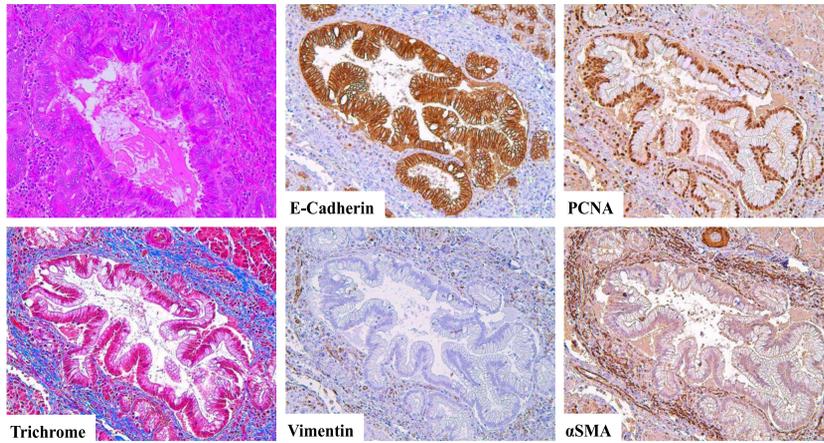
**Figure 3:** *Kras*<sup>G12D</sup>/*TP53*<sup>R167H</sup> Induced Tumors Invade Distant Organs Including the Liver and Spleen



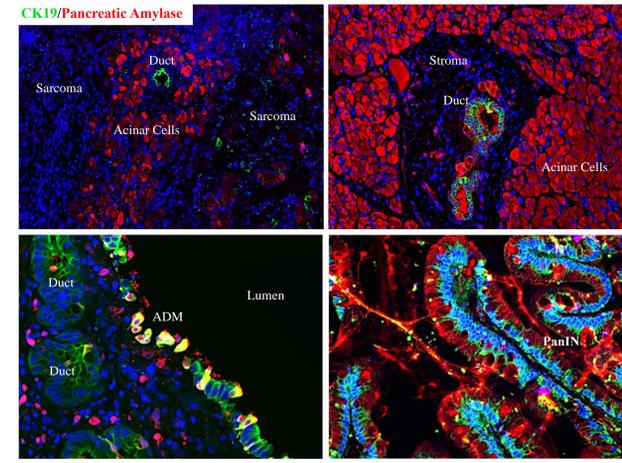
**Figure 4:** Pathological Analysis of the Pancreas Induces Both Leiomyosarcoma and PanIN Disease Forms



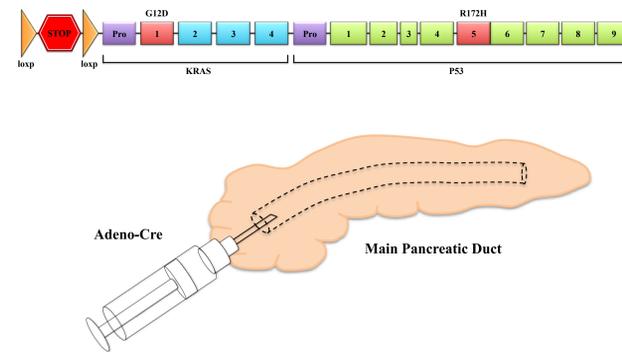
**Figure 5:** PanIN Lesions Display Several Hallmark Features of Pancreatic Tumorigenesis



**Figure 6:** Lesions Show Model-Capability for Acinar-to-Ductal Metaplasia



**Figure 7:** Main Pancreatic Duct Injection of Adeno-Cre in *Kras*<sup>G12D</sup>/*TP53*<sup>R167H</sup> Pig



### Summary:

- Pancreatic Parenchymal Body Injection:**
- Predominant histotype is leiomyosarcoma
  - Limited PanIN Histotype

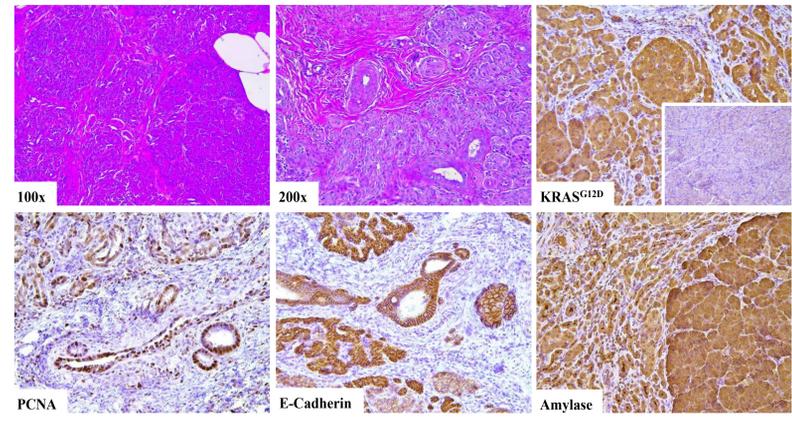
### Main Pancreatic Duct Injections:

- Development of locally invasive tumor
- Potential neuroendocrine involvement

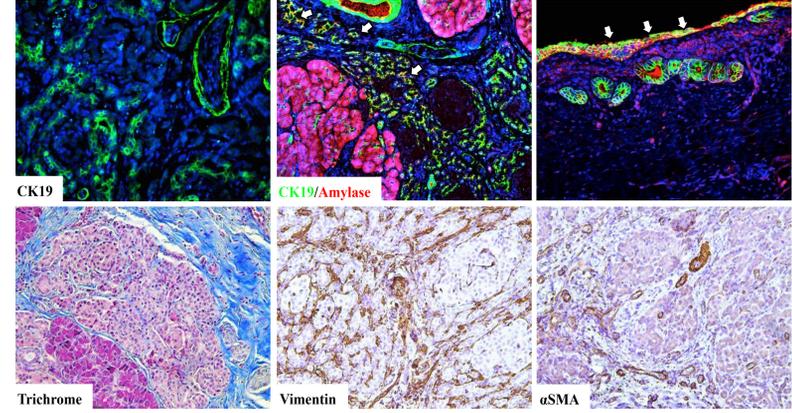
### Conclusions:

*Cre/Kras*<sup>G12D</sup>/*TP53*<sup>R167H</sup> Pigs are sufficient to generate clinically relevant pancreatic histotypes, yet Cre-delivery requires further specificity.

**Figure 8:** Restriction of Cre to Pancreatic Duct Induces Pancreatic Tumorigenesis without Leiomyosarcoma



**Figure 9:** Tumor is Highly Positive for Ductal/ADM Markers and Negative for Mesenchymal Markers



### Future Directions:

- Evaluate liver and GI Tract for metastatic disease
- Generate models of other solid tumors with high rates of KRAS and p53 mutations
  - i.e. Breast, Brain, Liver, Muscle
- Create duct specific Adeno-Cre and deliver to main pancreatic duct
- Generate 3-D pancreatic organoids to assist in further pre-clinical testing

### Acknowledgements:

This work was made possible by Dr. Grippo and his associates. I would like to thank Dr. Rund and Dr. Schook for their guidance and the opportunity to be a part of this project.