Xenotransplantation of Porcine Lungs

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How many people do you know have lung problems?
Population Affected by Lung Problems

- Lung Cancer in the U.S. (2011)†
  - 207,399 diagnosed
  - 156,953 died

Sustained function of genetically modified porcine lungs in an ex vivo model of pulmonary xenotransplantation
What’s the big picture?

- Think about future endeavors in the field of xenotransplantation
- Why xenotransplant a lung?
- Where to go from here?
Why Xenotransplantation?

- Xenotransplantation
  - Transplanting any biological tissue, in this case organ, from one species to a different species.

- Possibility of providing a fix to donor shortages across the medical field by utilizing livestock that are abundant in numbers.
What is the paper proving?

- Difference between $H_0$ and a hypothesis
- $H_0$ – It is not possible to overcome immunological barriers when xenotransplanting porcine pulmonary lungs to an ex vivo model of a human biological system.
Key Terms

- Wild Type
- Pulmonary Vascular Resistance (PVR)
- Hyperacute Rejection
- Homologous Recombination
- GTKO - α1,3-galactosyltransferase gene knockout
Methods – Generation of Transgenic Pigs

- Transgenic pigs produced through homologous recombination
- CD55-59 expression generated through oocyte microinjection
- CD39 expression generated through transfection in pig fetal fibroblasts
Lungs obtained through cross-bred Large White/Landrace pigs after being anesthetized, intubated, paralyzed and ventilated.
Methods – Ex Vivo Lung Rig

- Lung and heart were set up with a mechanical ventilator, centrifuge pump and membrane deoxygenator.
Methods – Study Design

- 6-hour time period (240 minutes)
- Perfusion of Steen solution
  - Contains Human Serum Albumin (Type-A)
  - Dextran
  - Extra-cellular K+ (electrolyte)
- 600 mL Steen solution
- 10 Experiments
  - 3 Wild-type
  - 2 GTKO
  - 3 GTKO/CD55-59
  - 2 GTKO/CD55-59/CD39
Methods – Tissue Biopsies

- Immunohistochemistry used to determine if coagulation activation occurs among...
  - IgG
  - IgM
  - C3
  - C5b-9m
  - CD6
  - C4d
Methods – Assessment of Perfusate

- Perfusate was assessed for levels of...
  - Neutrophils
  - Lymphocytes
  - Monocytes
  - Macrophages
  - platelets
Methods – Statistical Analysis

- ANOVA and Chi-square tests performed on data
- Statistical significance was defined as p < 0.05
• What is shown here?

• Are there any trends?

• What conclusions can be made based on these data?
Data - 2

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Data - 4

- What is shown here?
- Are there any trends?
- What conclusions can be made based on these data?
After the addition of human blood...
- All WT lungs failed rapidly (21 +/- 4 mins)
- All but one genetically modified lung succeeded (240 mins)
Failed Tests

- All WT Lungs
- One Genetically Modified Lung
- Why?
  - Hyperacute Rejection
  - Antibodies in the introduced human blood
Successful Tests

- 6 Genetically Modified Lungs
- Why?
  - No rejection from antibodies in the introduced human blood
  - No attack complexes found
  - Possible result of CD39, CD55 and CD59.
Conclusions - 1

- After looking at the scatter plot with variables dAV Oxygenation/mmHg (Independent) and Perfusate Platelet Count % change (Dependent)...
  - $R^2 = 0.64$
  - $p < 0.01$

- What does this mean statistically?
Conclusions - 2

- What do these results say about $H_0$?
  - Due to great statistical significance ($p < 0.01$), we can reject the null hypothesis.

- But what does that mean?
Questions?