

# Characterization of HaPV Coinfection in Hamster Model of ZIKV Pathogenesis



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## Background

### Zika Virus (ZIKV)

The ongoing Zika virus (ZIKV) epidemic has produced unique and severe clinical outcomes including neurological diseases and birth defects. This has brought about the urgent need for an animal model that replicates human ZIKV infection and has comparable reproductive anatomy.

### Animal Model for ZIKV

#### Mouse (A129):

The mouse is the model that is typically used to study ZIKV, there are flaws with this model. The wild type mouse is not infected with ZIKV the same way that humans are. In an attempt to fix this issue mice were engineered to be susceptible to ZIKV. These immune compromised mice do not accurately model the human infection because the mice perish very quickly. Due to the short lifespan, the mouse is not a good reproductive model.

#### Golden Syrian hamster:

The STAT2 KO hamster respond to ZIKV more like humans than mice do. This includes surviving infection, which means it is possible to do reproductive studies with them. The biggest flaw with this animal was that many developed tumors. The tumors seemed to present similarly to hamster polyomavirus (HaPV).

### HAPV

HaPV, a DNA virus that can integrate into the genome of the host animal, is seen almost exclusively in research colonies. It is speculated that HaPV can be transmitted vertically through breast milk or by integration into a heritable portion of the host genome. If the latter is true, it is possible that most, if not all, research hamsters carry HaPV.

## Methods

### Overall direction

- Determine presence of HAPV in tumors, then livers, then terminal blood

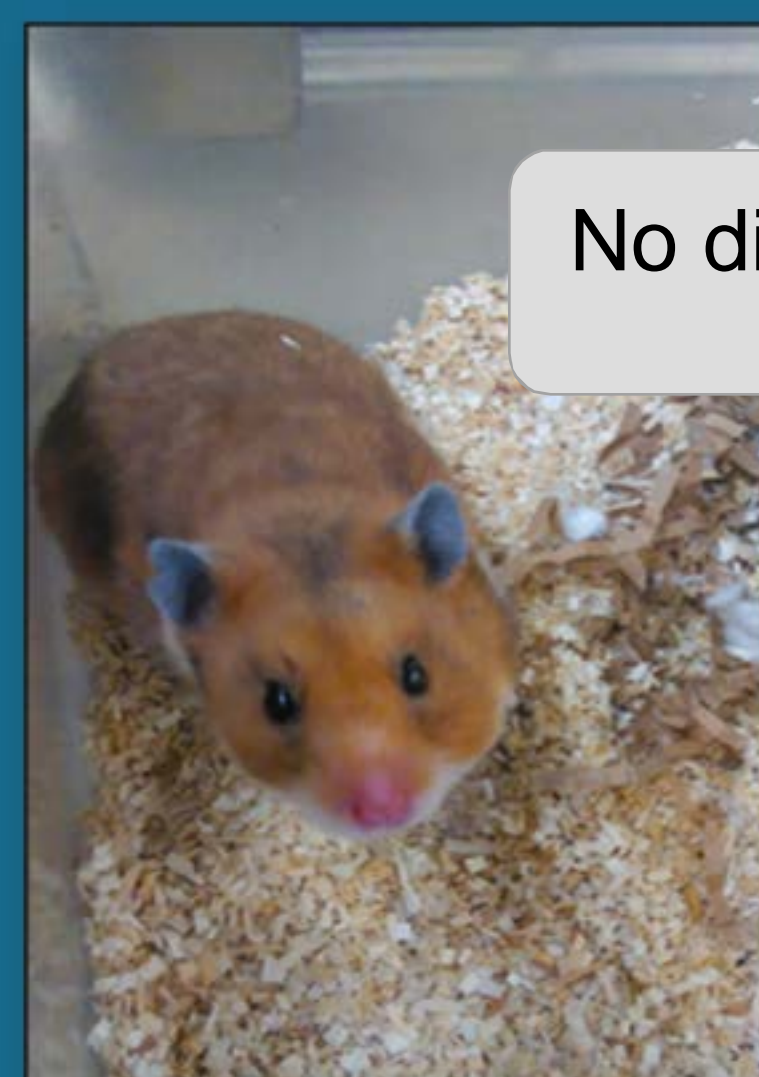
### Assay Design

- Design primers using NCBI Blast system
- Determine positive control through IDEXX test
- Compare designed primer with paper primer
- Optimize

### Trouble Shooting

- Change one variable at a time
- Agarose, decide primer, volume, Denaturing temp, annealing temp, enzyme, more cycles, gel/buffer interaction

## Results



No display of illness 3 dpi with I-44



Outward display of illness 3 dpi with MR-766



Cheek pouch tumor in I-44 infected tumor 5 dpi



Liver mottling in I-44 infected tumor 5 dpi

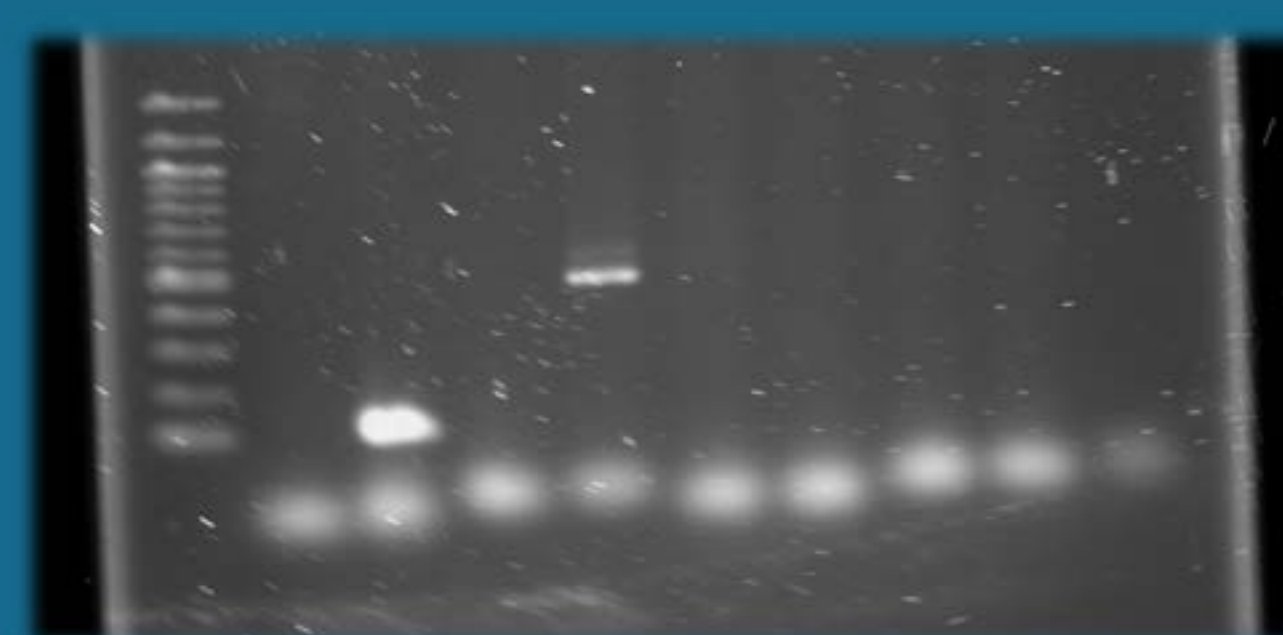


Figure 1. DNA extracted from HaPV positive tumors using MAD and SIM primers.

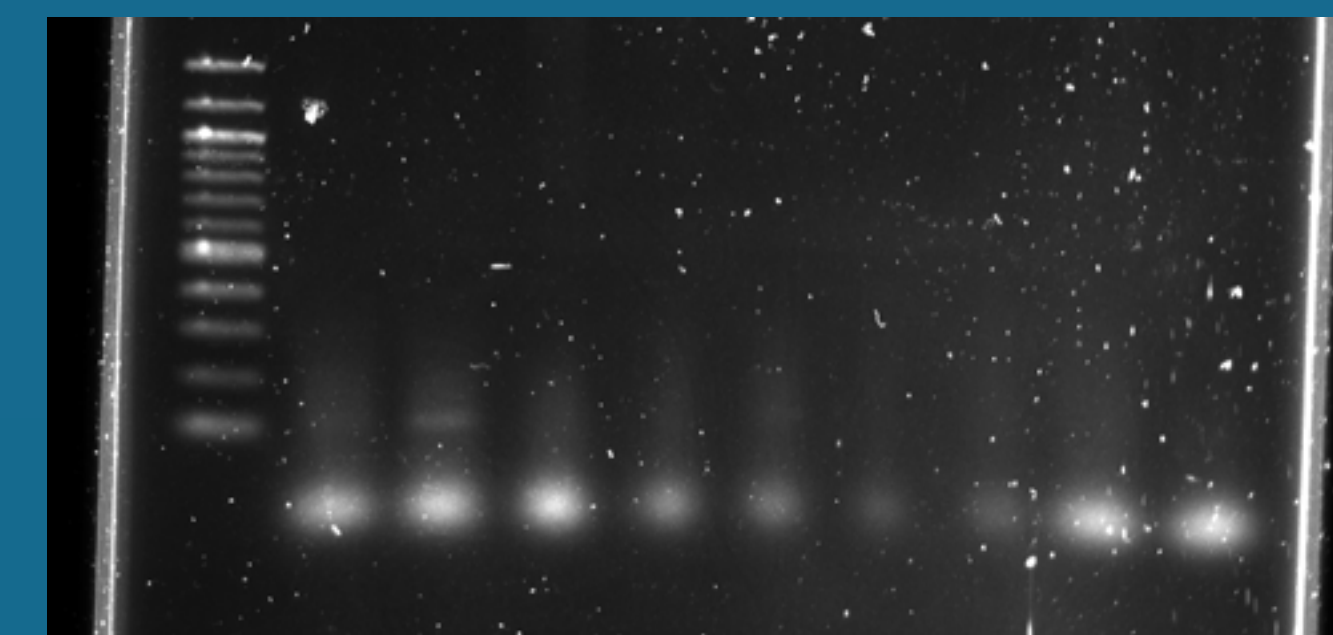


Figure 2. DNA extracted from livers using MAD primers



Figure 3. DNA extracted from positive control, optimizing volume of PCR mix.

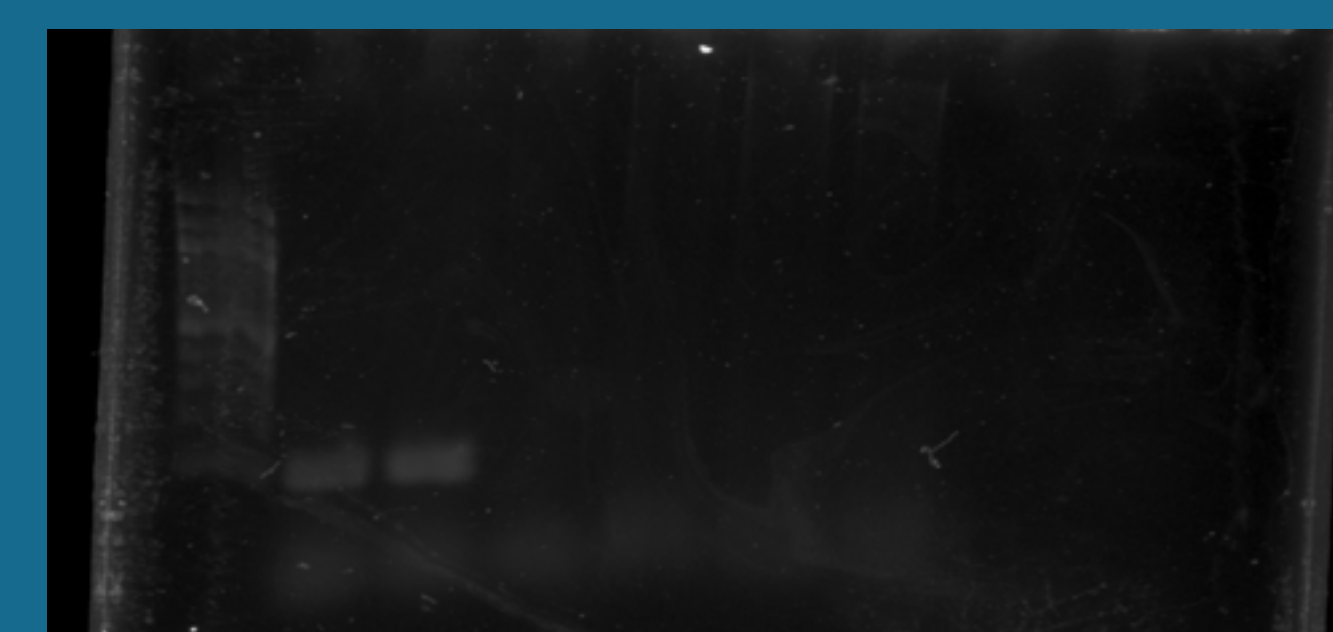


Figure 4. DNA extracted from positive controls optimizing denaturing temperature (96°C).

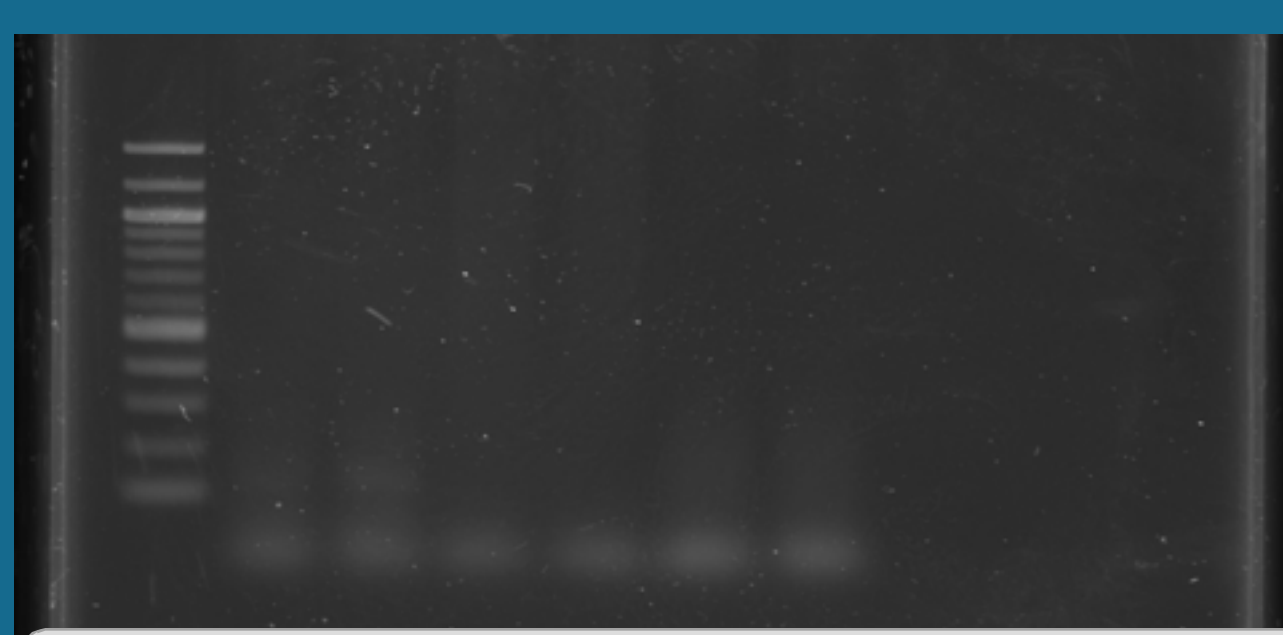


Figure 5. DNA extracted from positive controls, optimizing annealing temperature (53.5).

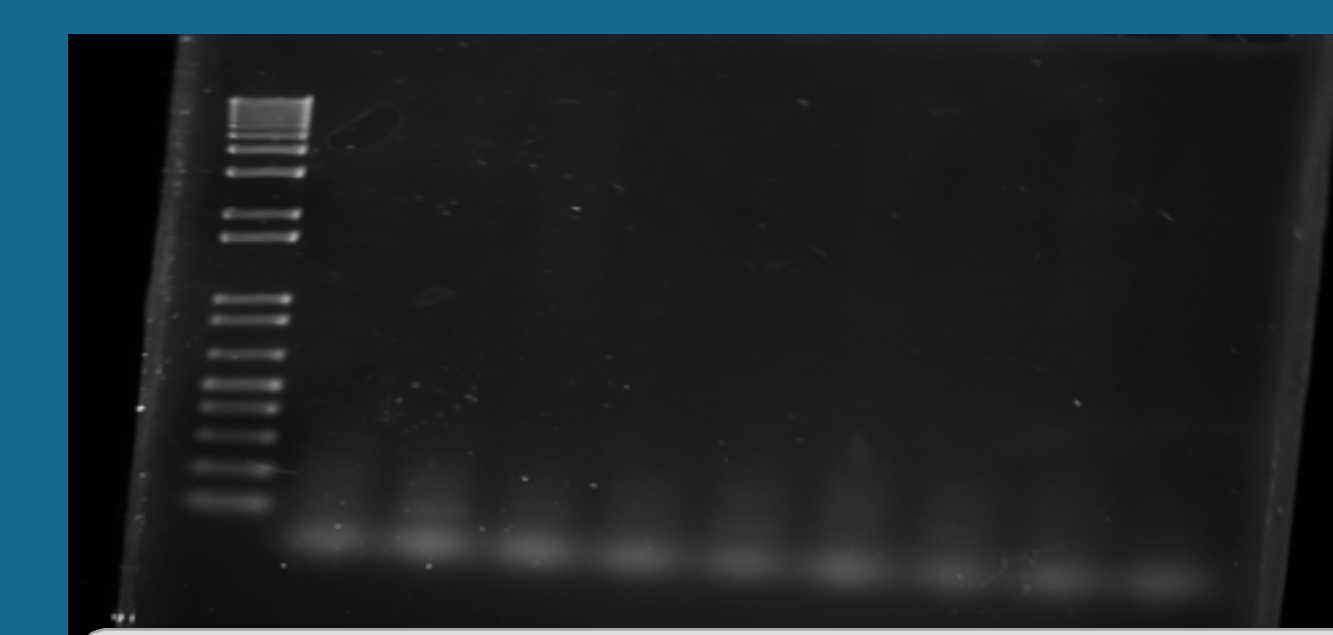


Figure 6. DNA extracted from livers, agarose gel optimization.

## Conclusions

### PCR Assay

- The primers work
- The assay still needs optimization

### STAT2 KO Hamster

- Not a good model due to HaPV coinfection
- HaPV needs characterization

## Future Directions

### PCR ASSAY

- Could be used to screen animals before testing to limit group size
- Help to limit group sizes

### STAT2 KO Hamster

- CRISPR out the HaPV gene to stop coinfection issues

## Acknowledgements

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## References

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