Combatting Zika Virus Infections: Teaching Old Drugs New Tricks

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Funding: Florida Department of Health (7ZK30)

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Optimize Antiviral Therapy

- What is the **minimal effective dose** of a drug and **how often** do we need to give that drug to maximize viral suppression and prevent resistance.
- Antiviral therapies for Zika virus DO NOT exist!

- Drug Repurposing Strategy: New use for existing drug(s).
  - Safety and Pharmacokinetics (drug metabolism) profiles are defined
  - Formulation and bulk manufacturing process are complete

Focused on Antiviral Agents with Broad-Spectrum Activity

Ribavirin

Interferon-Alfa

Favipiravir

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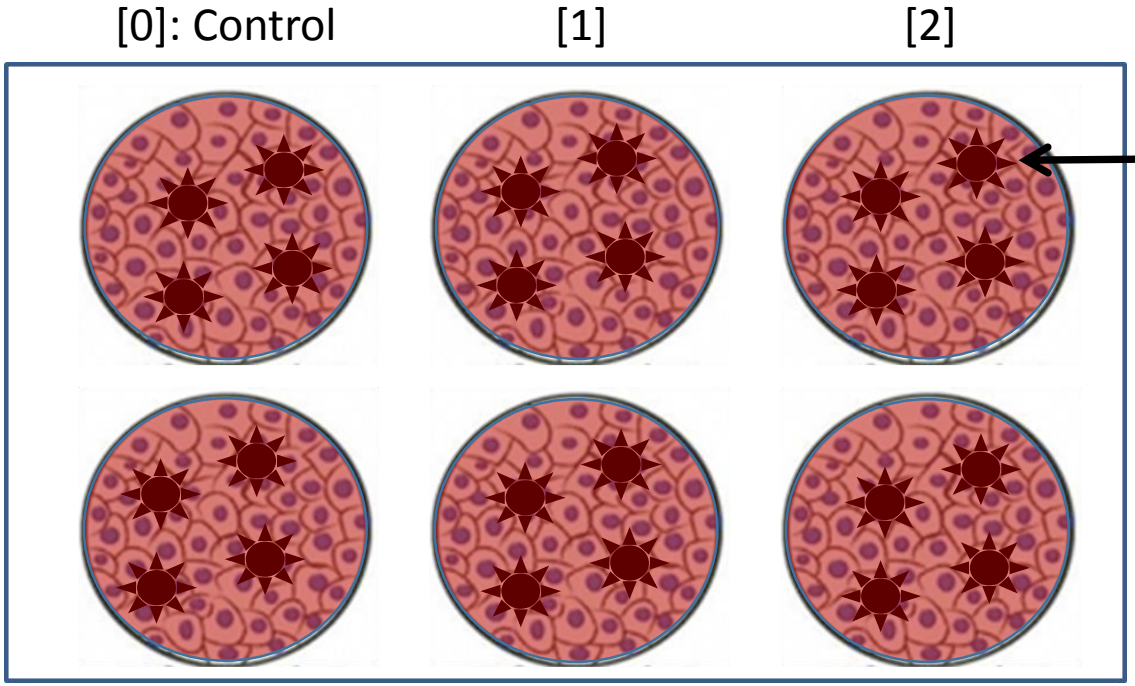
Antiviral Evaluation Methods



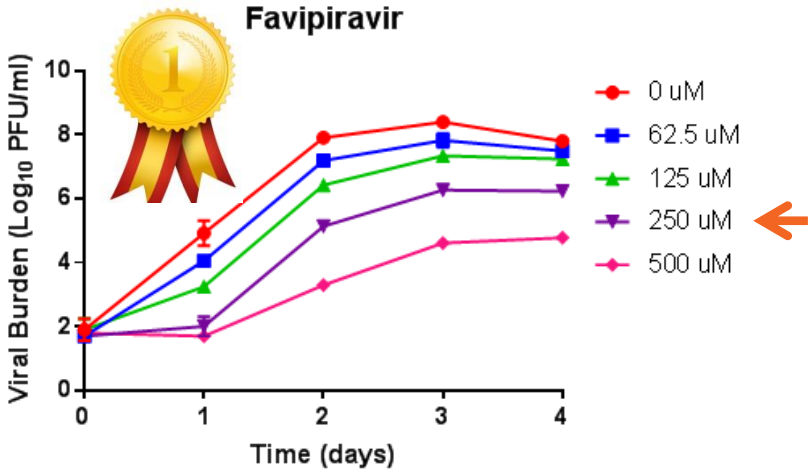
Medium with varying concentrations of drug

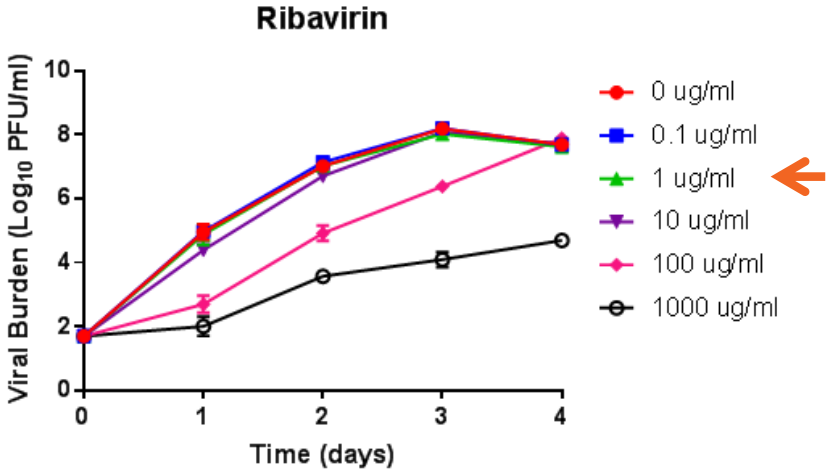
Three drugs:

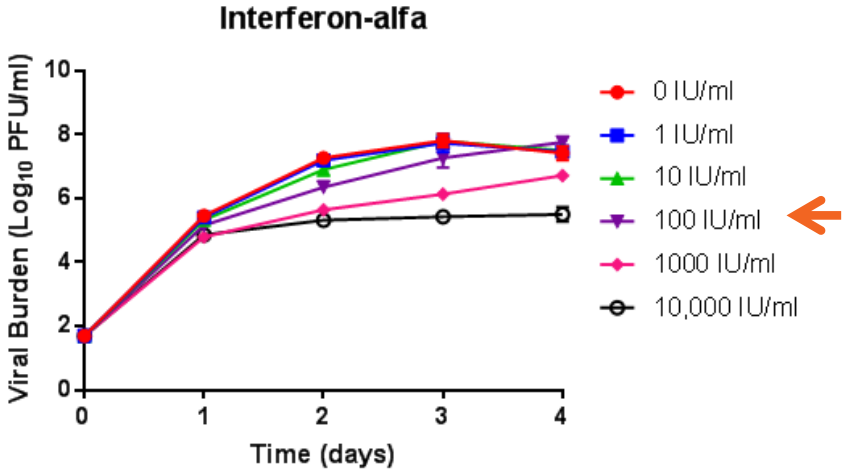
- **Favipiravir,**
- **Ribavirin, and**
- **Interferon**

evaluated as single agent therapy and as all two drug combinations.

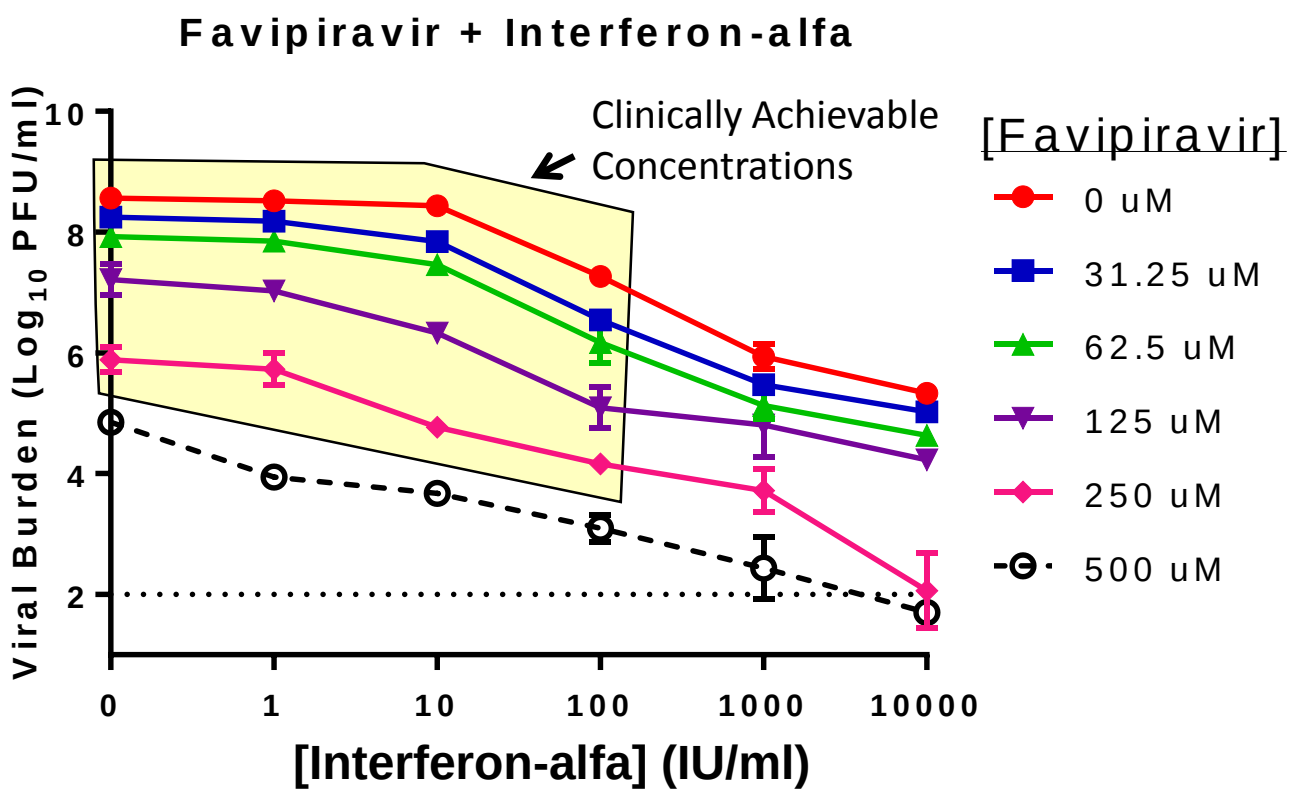
Single Agent Therapy Results



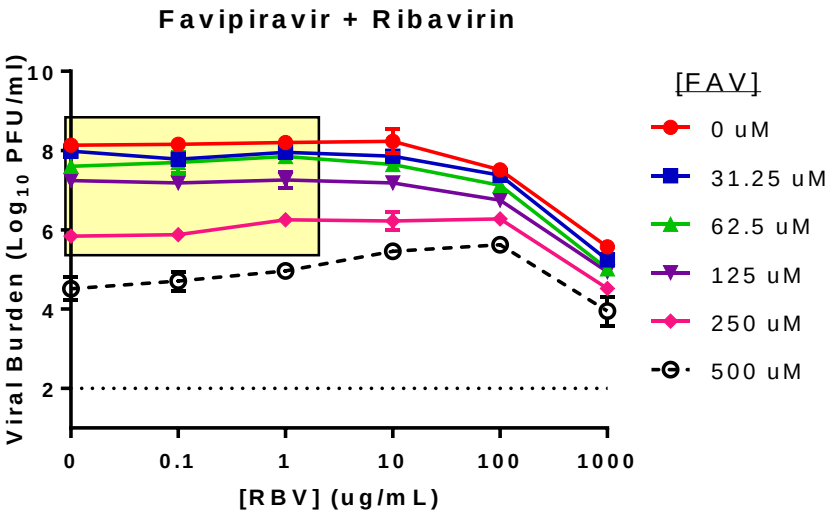


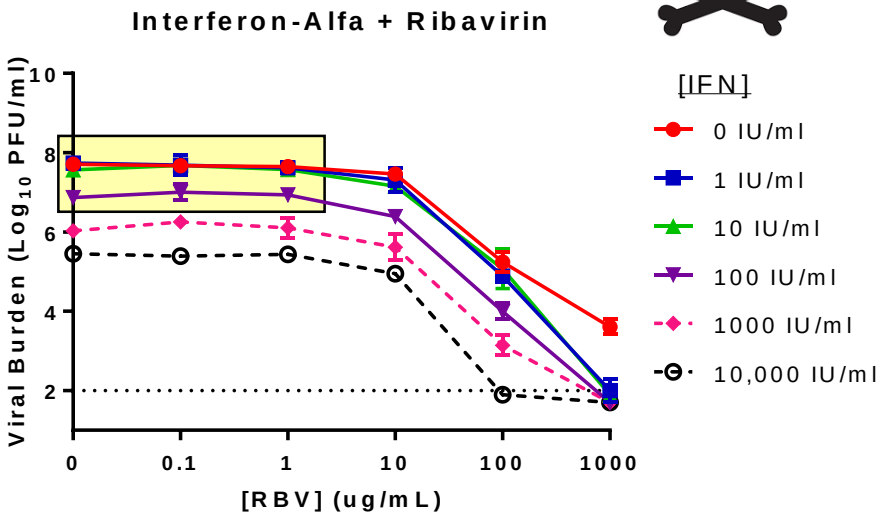


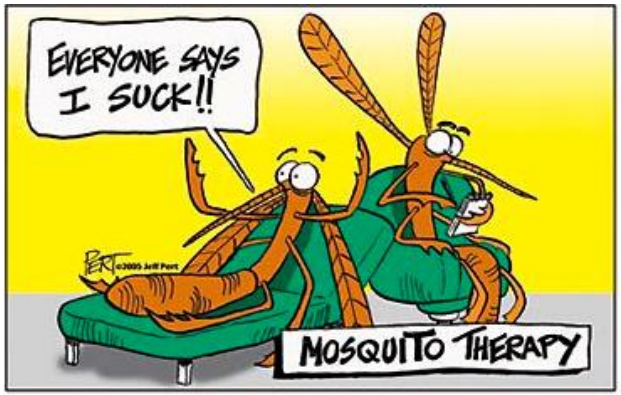
Combination Therapy Results



Combination Therapy Results

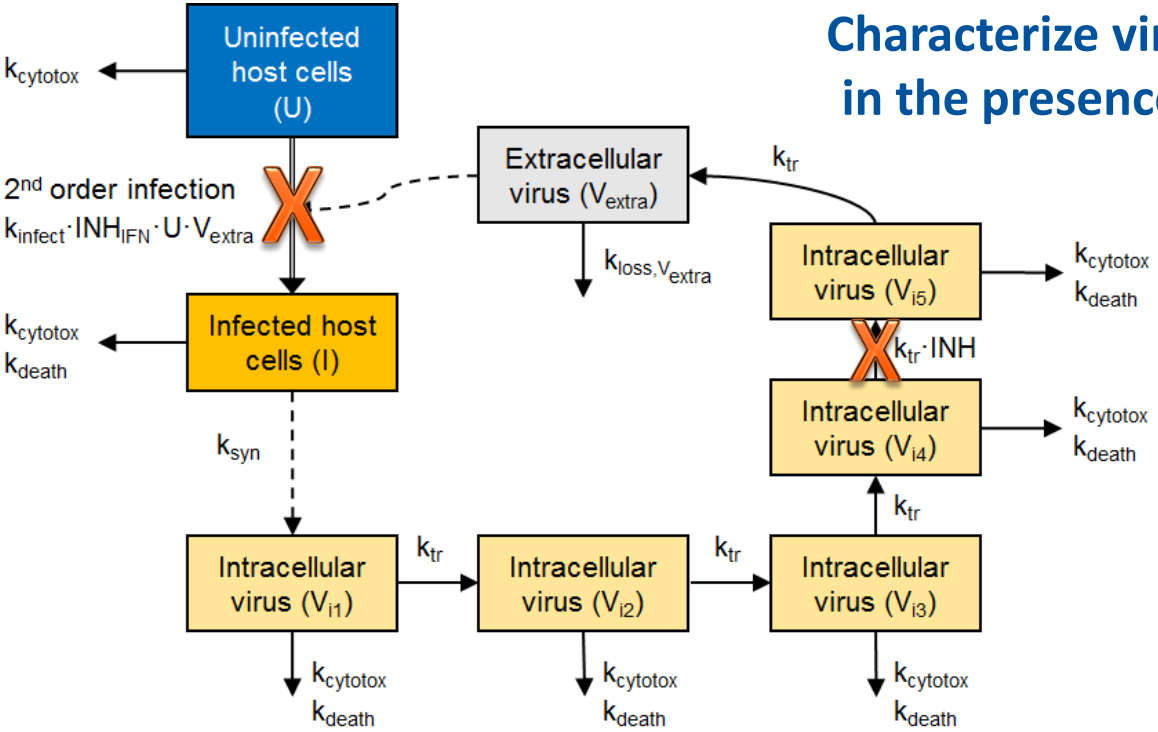




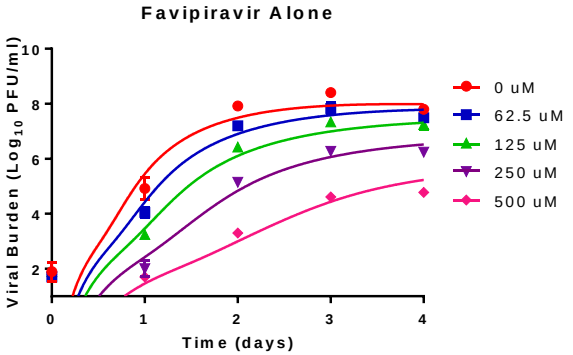


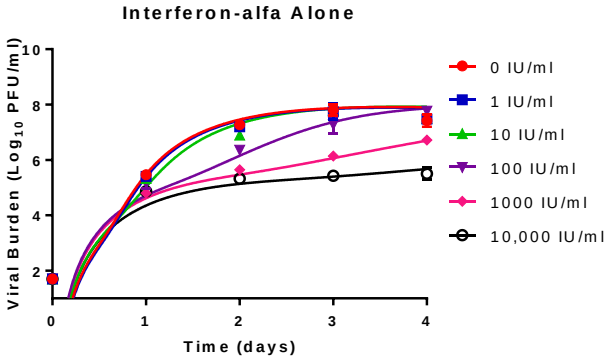
Which dose – how often – for how long? Answered via mathematical modeling

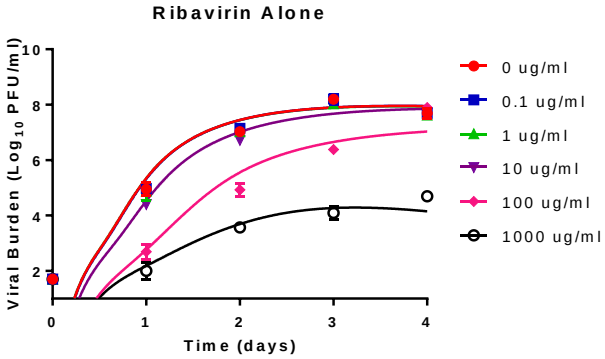
Characterize viral burden over time in the presence of drug treatment

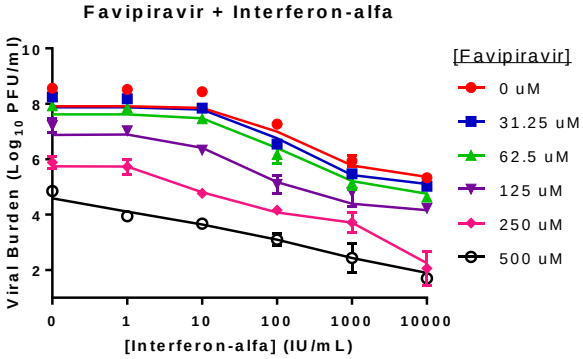


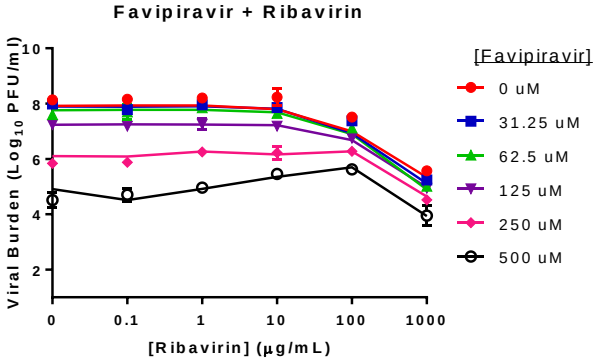
Model excellently described the data

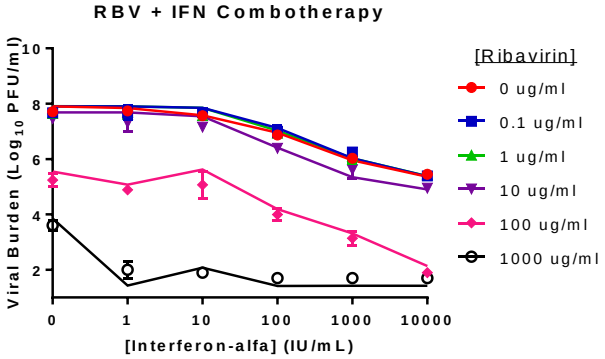






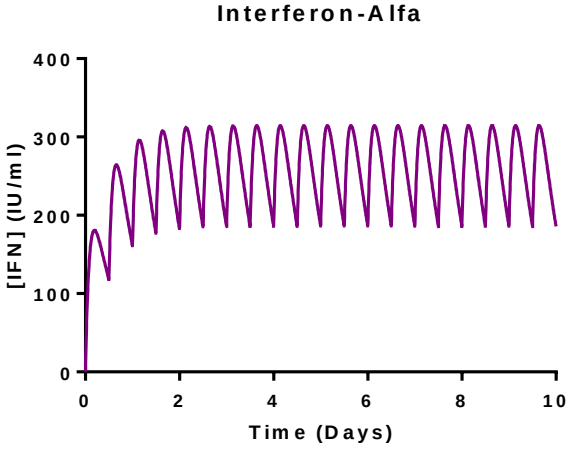


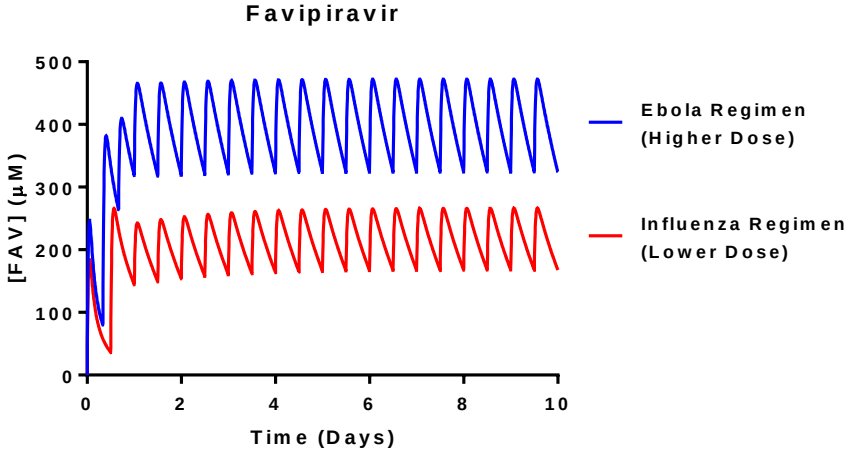




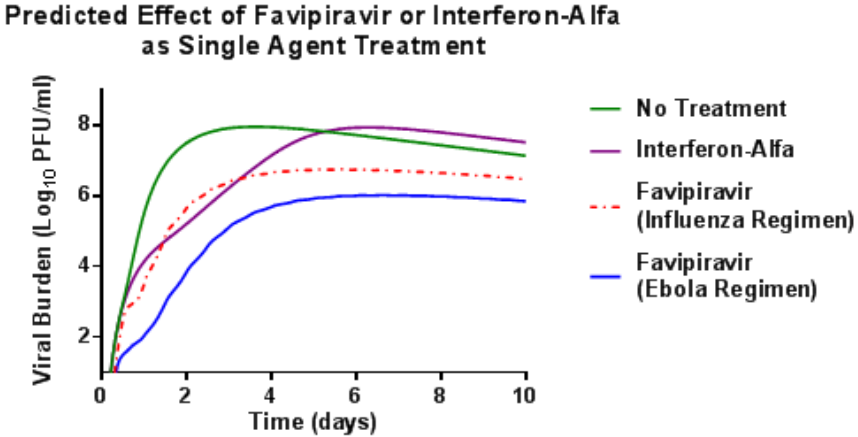
Simulating drug effects for combination therapy

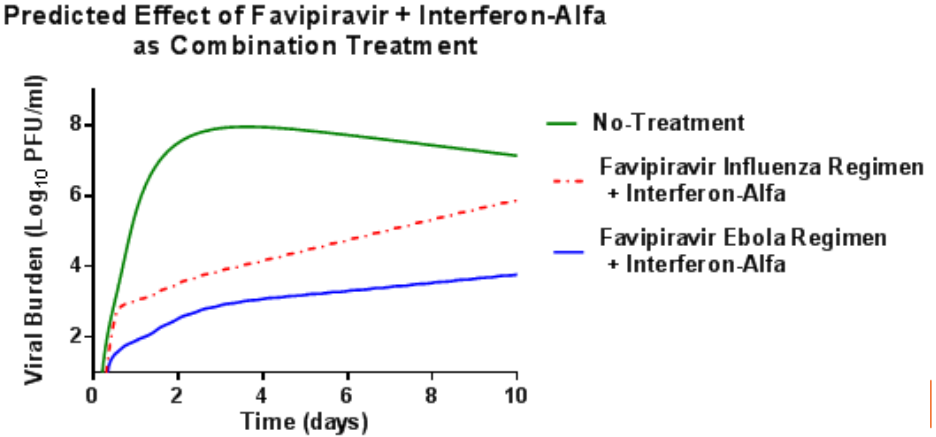
Blood Drug Concentrations in Man are dynamic due to metabolic processes





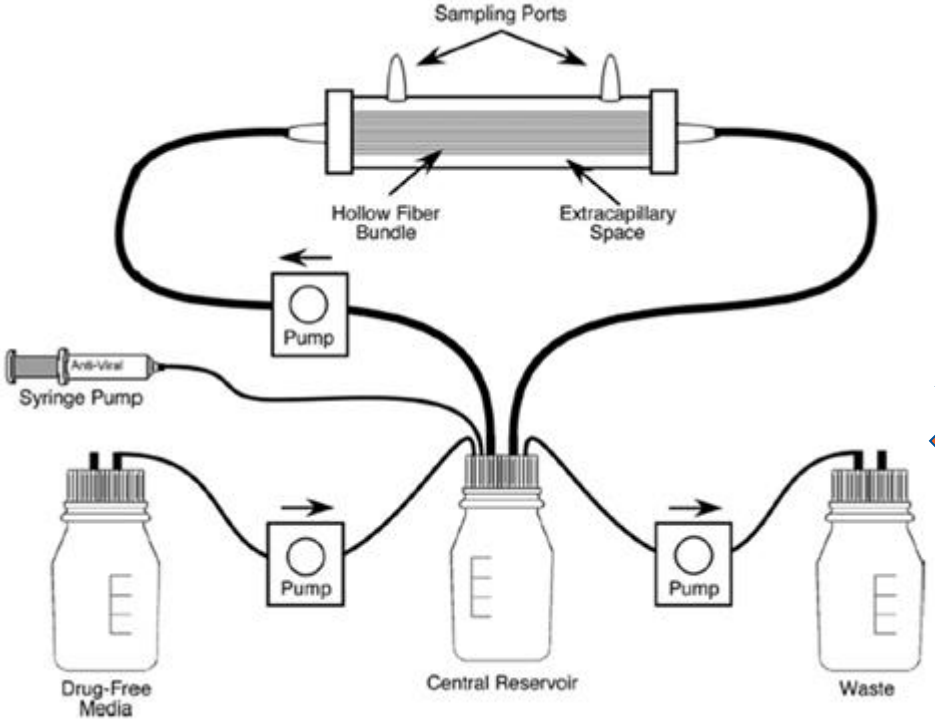
Concentration-Time Profiles Associated With Clinical Regimens

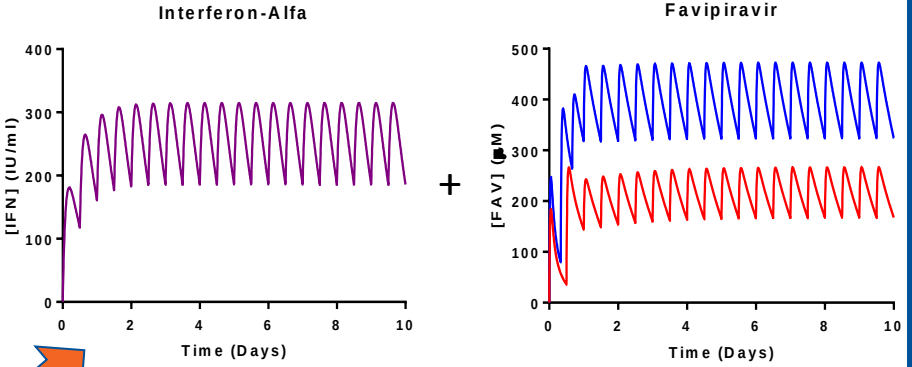


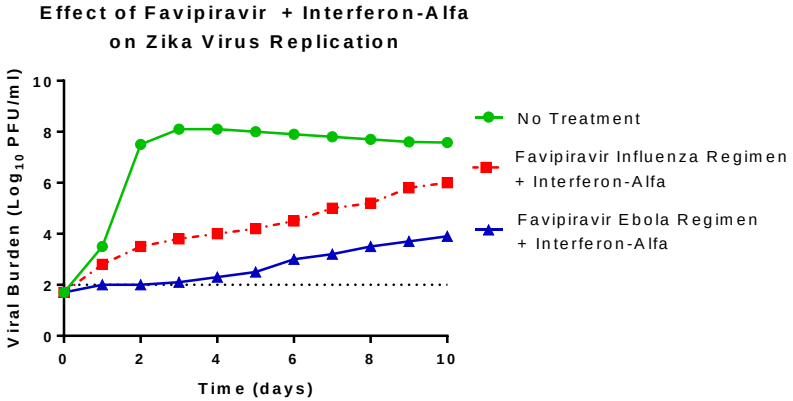


Favipiravir + Interferon-Alfa shows promise as a Therapy for Zika Virus Infections: What Next?

Experimentally Validate the Model Simulations Predicting Antiviral Effect







Future Directions

- **Determine whether antiviral treatment allows for the emergence of viruses that contain mutations conferring resistance to treatment (currently under investigation).**
- **Continue to evaluate other promising repurposed agents against Zika virus as single agent therapy and in combination.**
- **Optimize dosage regimens for new promising agents.**

" ... and, with the proper medication, they lived happily ever after."

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