

The Role of Host Fatty Acid Synthase in Mayaro virus replication

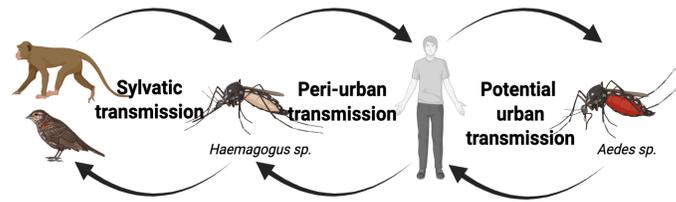
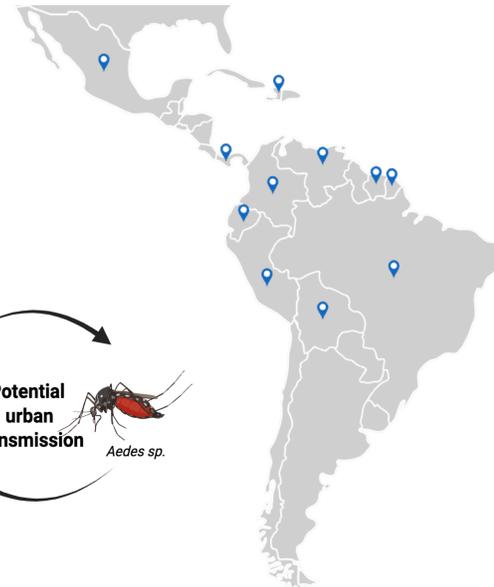
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Introduction

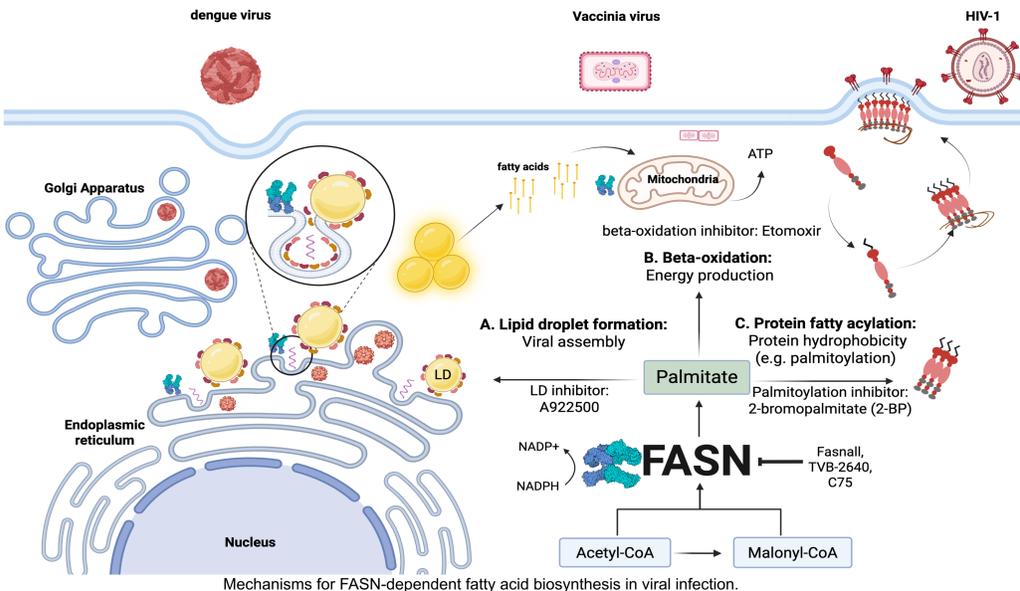
Fatty Acid Synthase (FASN) is a metabolic enzyme required by many viruses

Mayaro virus: alphavirus with potential for global spread

- Characterized by muscle and chronic joint pain.
- Unknown FASN requirement.



Mayaro virus transmission cycle and geographic prevalence

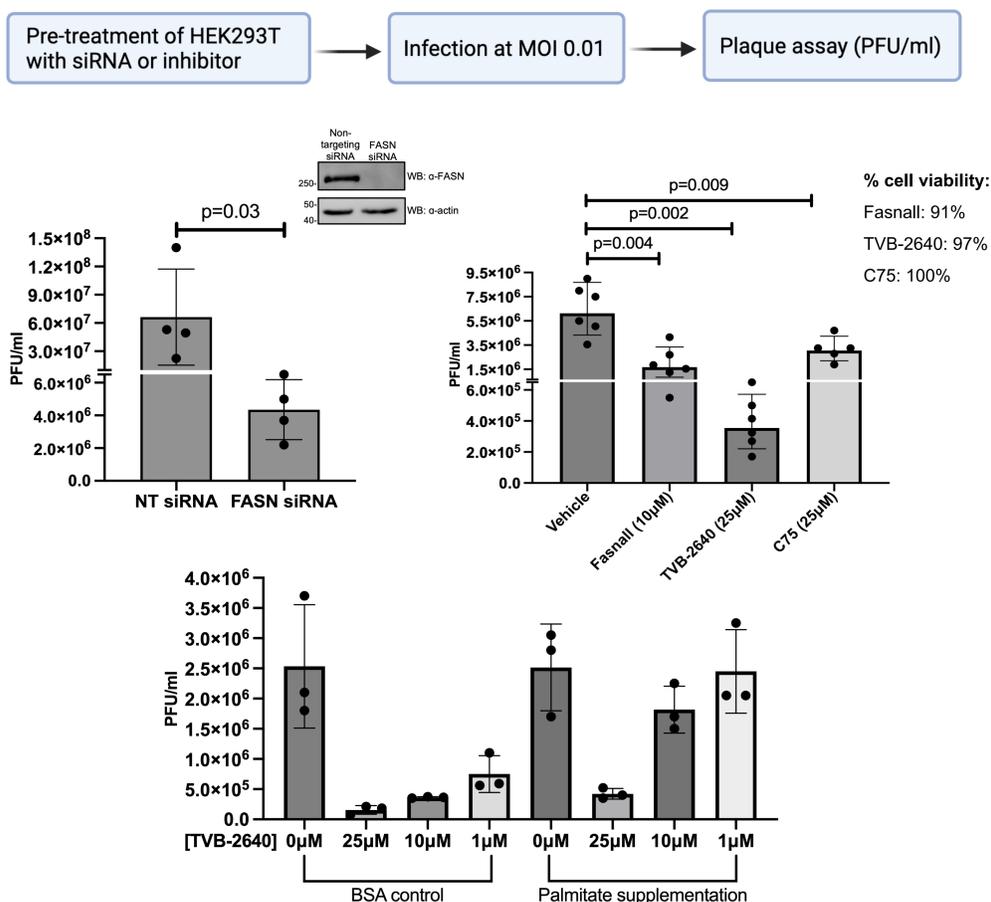


Mechanisms for FASN-dependent fatty acid biosynthesis in viral infection.

Methods and Results

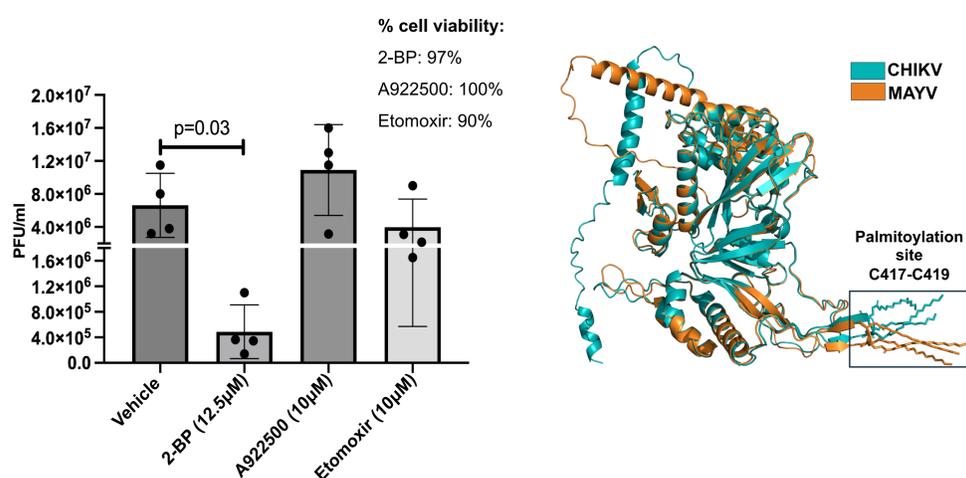
A.) MAYV requires FASN for infection

C.) Click-chemistry detects protein palmitoylation

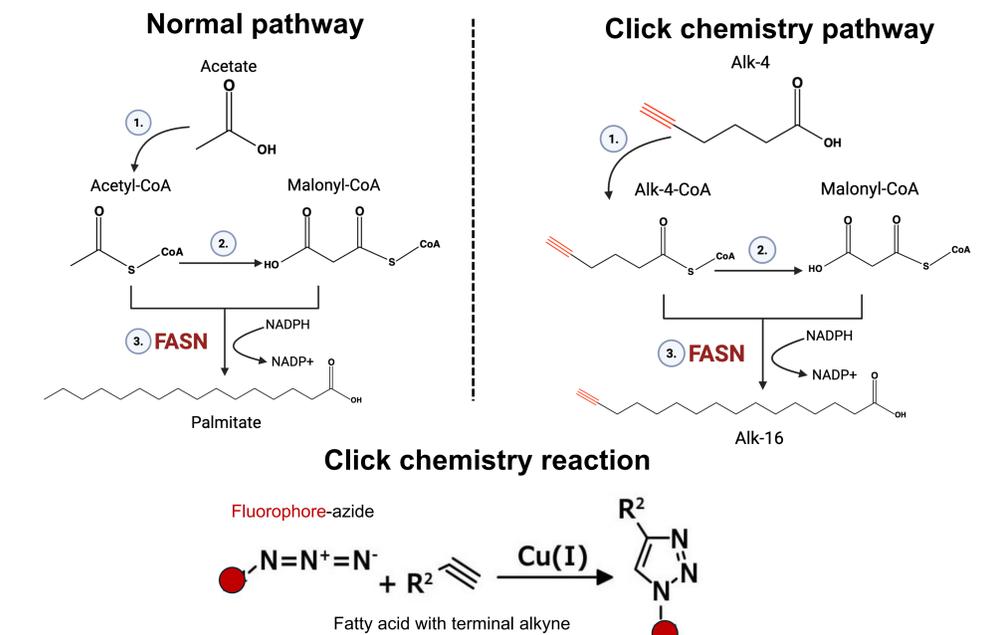


A.) FASN knockdown during MAYV infection in 293T. Pharmacological FASN treatment of MAYV infection in 293T. Rescue of infection with palmitate supplementation upon TVB-2640 treatment. Statistics: Mann-Whitney Test.

B.) MAYV nsP1 requires protein palmitoylation for replication

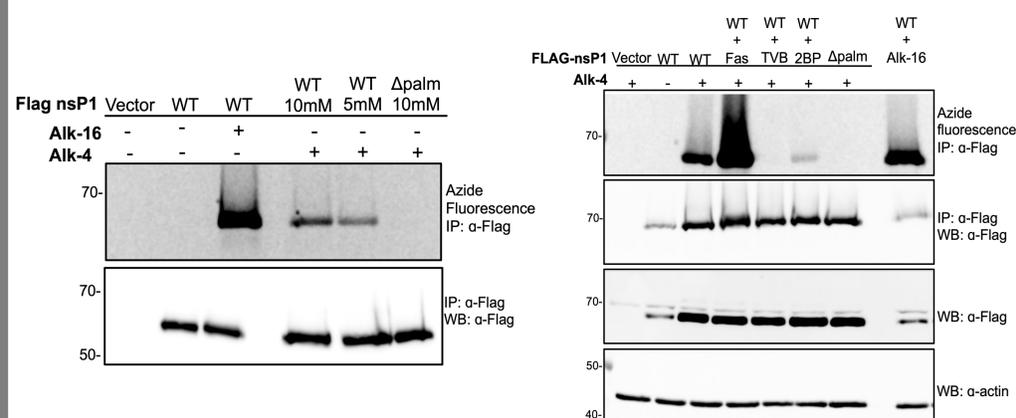


WT nsP1
 FLAG-MAYV CCC nsP1
 Δpalmitate nsP1
 FLAG-MAYV AAA nsp1



C.) The acetate analog, Alk-4, is metabolized by FASN into alkyne fatty acids. Click chemistry of proteins is performed by exposing fluorophore azide with alkyne fatty acids in proteins in the presence of copper to form a triazole structure.

D.) nsP1 is palmitoylated in a FASN-dependent manner



D.) The FASN metabolized acetate analog, Alk-4, labels WT nsP1 only. The FASN inhibitor, TVB-2640, and the palmitoylation inhibitor, 2-BP, reduce Alk-4 labeling of WT nsP1, but not Fasnall.

Conclusion & Acknowledgements

- MAYV requires FASN activity for replication.
- FASN derived palmitate contributes to viral protein palmitoylation in MAYV infection, with MAYV nsP1 studied as a model for palmitoylation.
- The FASN inhibitor currently in clinical trials, TVB-2640, is a promising pharmacological target to treat MAYV infection.



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