Warming Mediterranean Waters and Viral Emergence: Dissecting Betanodavirus Outbreaks through Reverse Genetics

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Global warming is drastically altering marine environments, turning the Mediterranean Sea into a climate hot spot where spikes in water temperature are directly linked to surges in viral pathogens. In September 2024, sea surface temperatures reached ~28°C, coinciding with unusual mortality events affecting dusky groupers (*Epinephelus marginatus*).

Nervous Necrosis Virus (NNV), a major viral pathogen of marine fish, was identified in affected specimens through molecular and cell culture analyses. From these events, two betanodavirus isolates were successfully recovered, providing a unique opportunity to investigate viral determinants associated with disease emergence under environmental stress.

Both isolates were fully sequenced and classified in the Redspotted grouper NNV genotype. Despite the high conservation typical of this genotype, comparative analysis revealed distinct amino acid substitutions in the capsid protein, including a mutation in the protruding domain, a key region involved in host interaction and viral entry.

To functionally characterize these differences, we established a reverse genetics system enabling the recovery of infectious viruses and, critically, the generation of homologous and reassortant strains. This approach provides a unique experimental framework to directly link viral genetic variability to phenotypic outcomes.

These findings establish a critical framework for investigating how climate-driven shifts influence viral genomics and evolution. By analyzing these shifts, we can position Betanodavirus as a primary genomic model for understanding how environmental stressors trigger genetic adaptations and the emergence of climate-sensitive viral threats.