O99

Genome RNA Replication Dependent Is Required for Betanodavirus-Induced Necrotic Cell Death

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Betanodaviruses are the causative agents for viral nervous necrosis (VNN), an infectious neuropathological condition characterized by necrosis of the central nervous system, including the brain and retina, which presents with clinical signs including abnormal swimming behavior and darkening of the fish. This disease is capable of causing massive mortality in the larvae and juvenile populations of several marine teleost species worldwide. The betanodavirus induces phosphatidylserine (PS) externalization and promotes host secondary necrosis cell death. To determine virus replication whether can trigger necrotic cell death, the inhibitors of endosomal acidification and RNA interference for specific knockdown of viral RNA polymerase expression will be tested. In the results, in the endosomal acidification inhibitor can affect virus replication and delay necrotic cell death in grouper fish cell. On the other hand, in the knockdown of RNA polymerase expression assay, we found that effectively knockdown the RdRp protein can reduce the PS exposure, mitochondrial membrane potential (MMP) loss and two viral death protein (protein-α and B2) expression very well. Furthermore, we have found that the viral titers from 7.5 dropped into 3.2 in TCID 50 at 48 h post-infection time (p.i.). Taken together our results suggest that betanodavirus-induced necrotic cell death may require for viral genome replication and two viral death gene expressions, which trigger mitochondria-mediated cell death in fish cells that may provide new insights into RNA viral control and treatment.