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Species-specific mechanisms of cytotoxicity toward immune cells determine the successful outcome of *Vibrio* infections in oysters

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Introduction. *Vibrio* species cause infectious diseases in human and animals, but they can also live as commensals within their host tissues. How *Vibrio* subverts the host defenses to mount a successful infection remains poorly understood, knowledge which is critical for predicting and managing disease.

Objectives. Characterize the cellular and molecular mechanisms underpinning infection and colonization of two virulent *Vibrio* species, in an ecologically-relevant host model, oyster, to study interactions with marine *Vibrio* species.

1 Immune cell lysis is a trait common to virulent strains

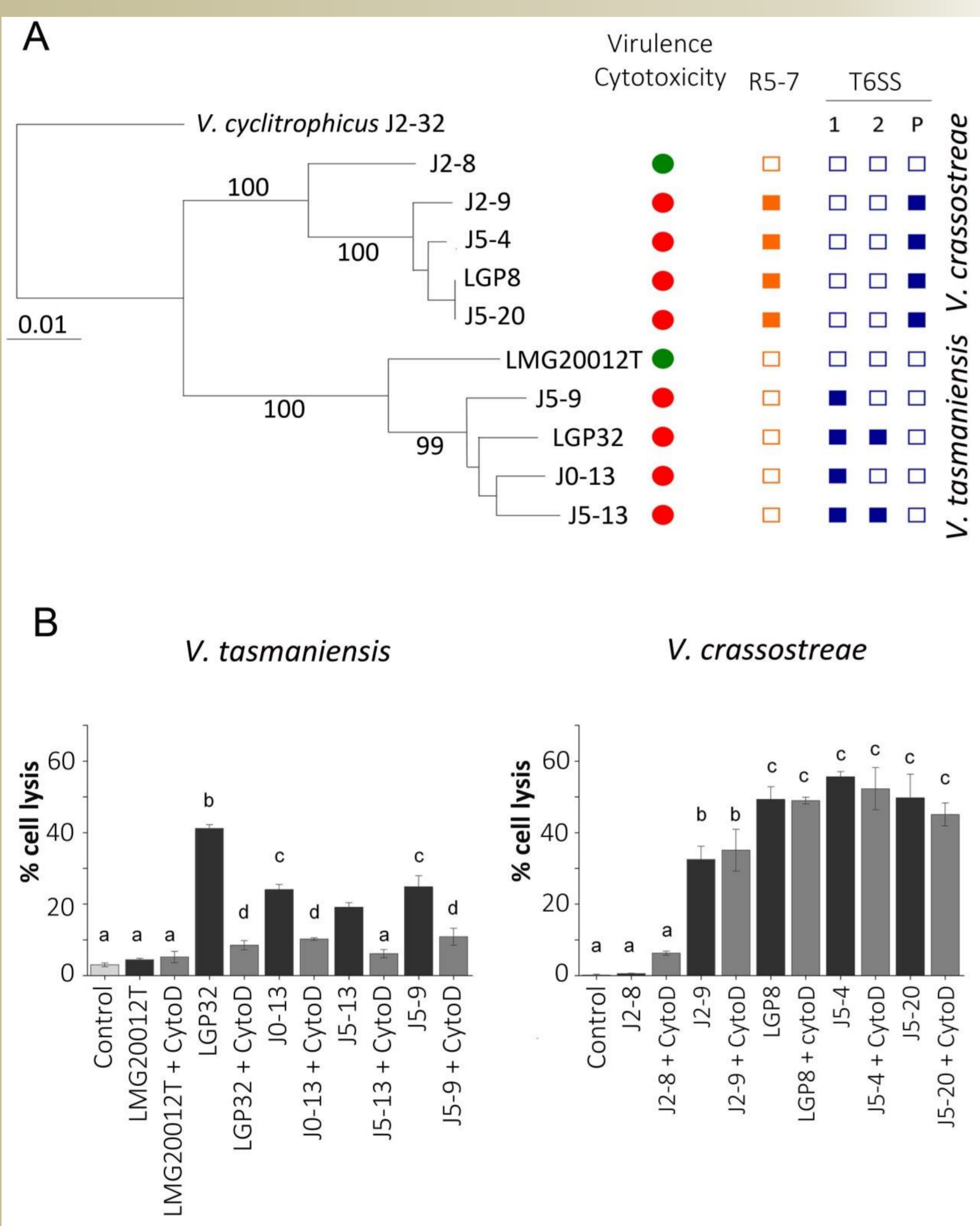


Figure 1. Species-specific mechanisms of cytotoxicity in *V. crassostreae* and *V. tasmaniensis*. (A) MLST on 6 core genes. Strain cytotoxicity and virulence correlate (red/green). Presence/absence of potential virulence factors T6SS and R5-7 is displayed. (B) In vitro cytotoxicity toward immune cells is phagocytosis-dependent for *V. tasmaniensis* only.

2 Virulent strains escape from hemocyte control and cause systemic infections

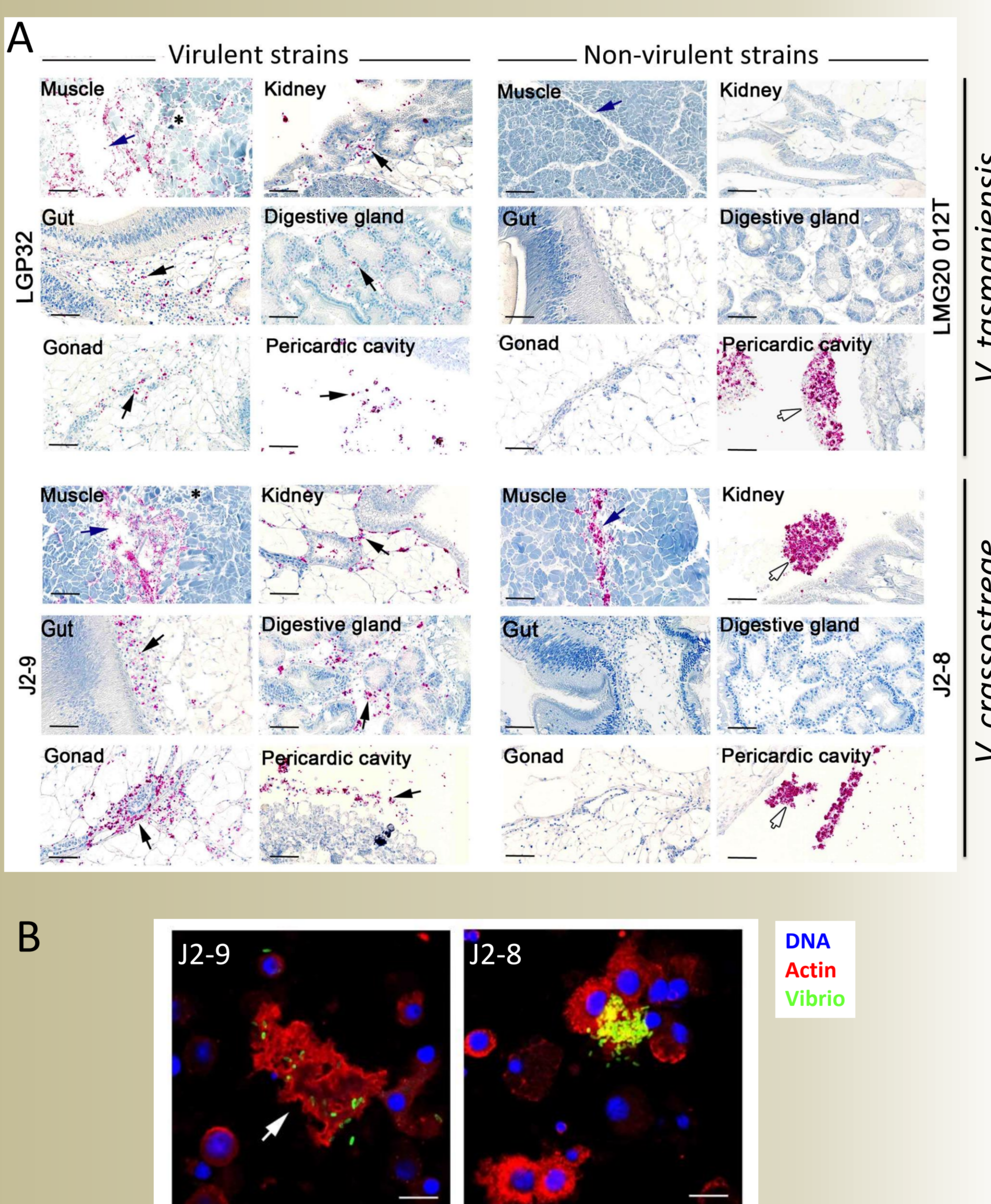


Figure 2. Virulent strains cause damage to hemocytes and escape hemocyte aggregates in vivo. (A) Histological sections of oysters infected with vibrios (pink). (B) Immune cell lysis induced by virulent strains in oyster hemolymph. Non-virulent strains are controlled by hemocytes.

4 Species-specific mechanisms of cell lysis compromise oyster immunity

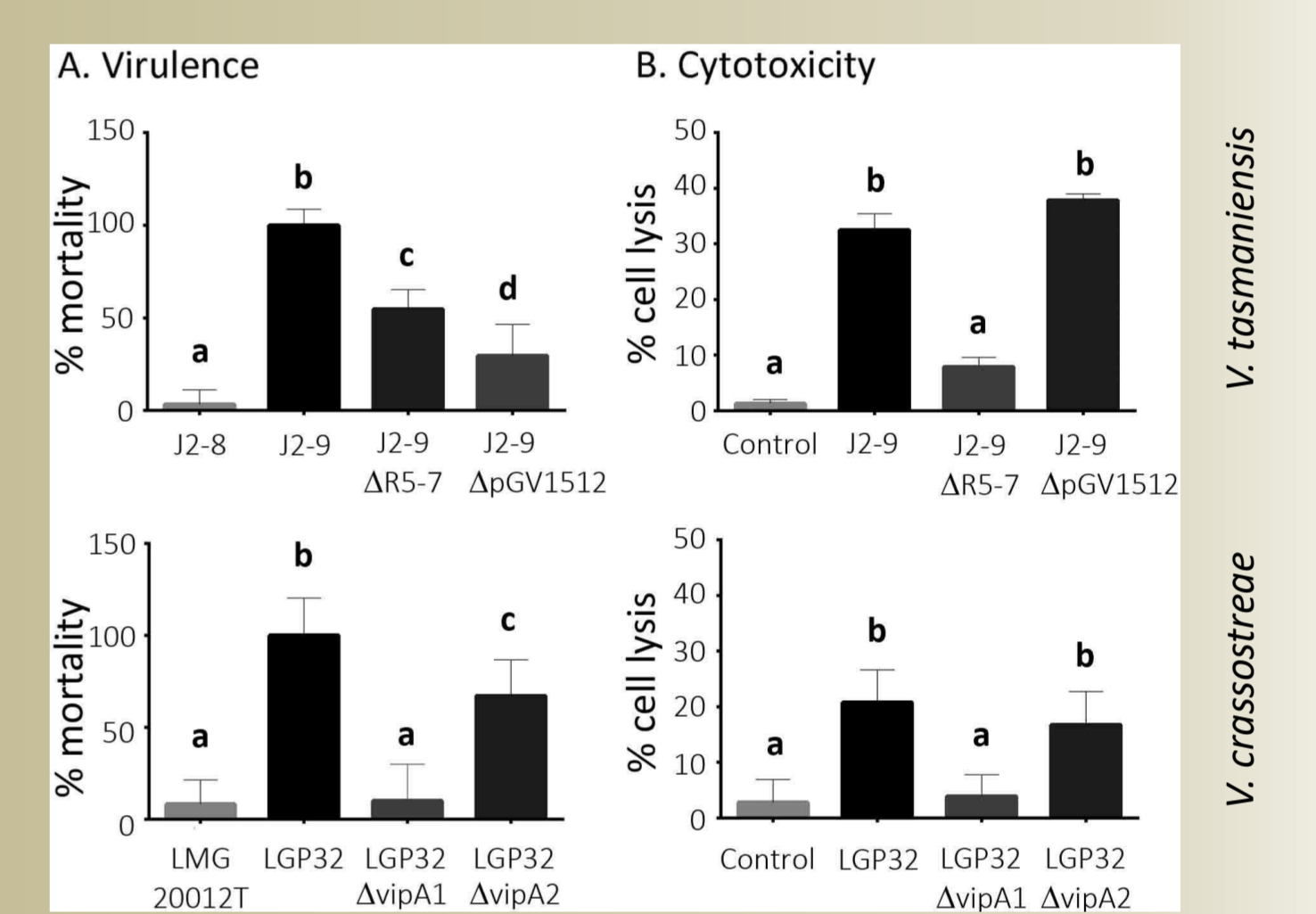


Figure 3. Species-specific virulence factors are needed for immune cell lysis. Mutants were phenotyped for (A) virulence in oyster experimental infections and (B) Immune cell lysis.

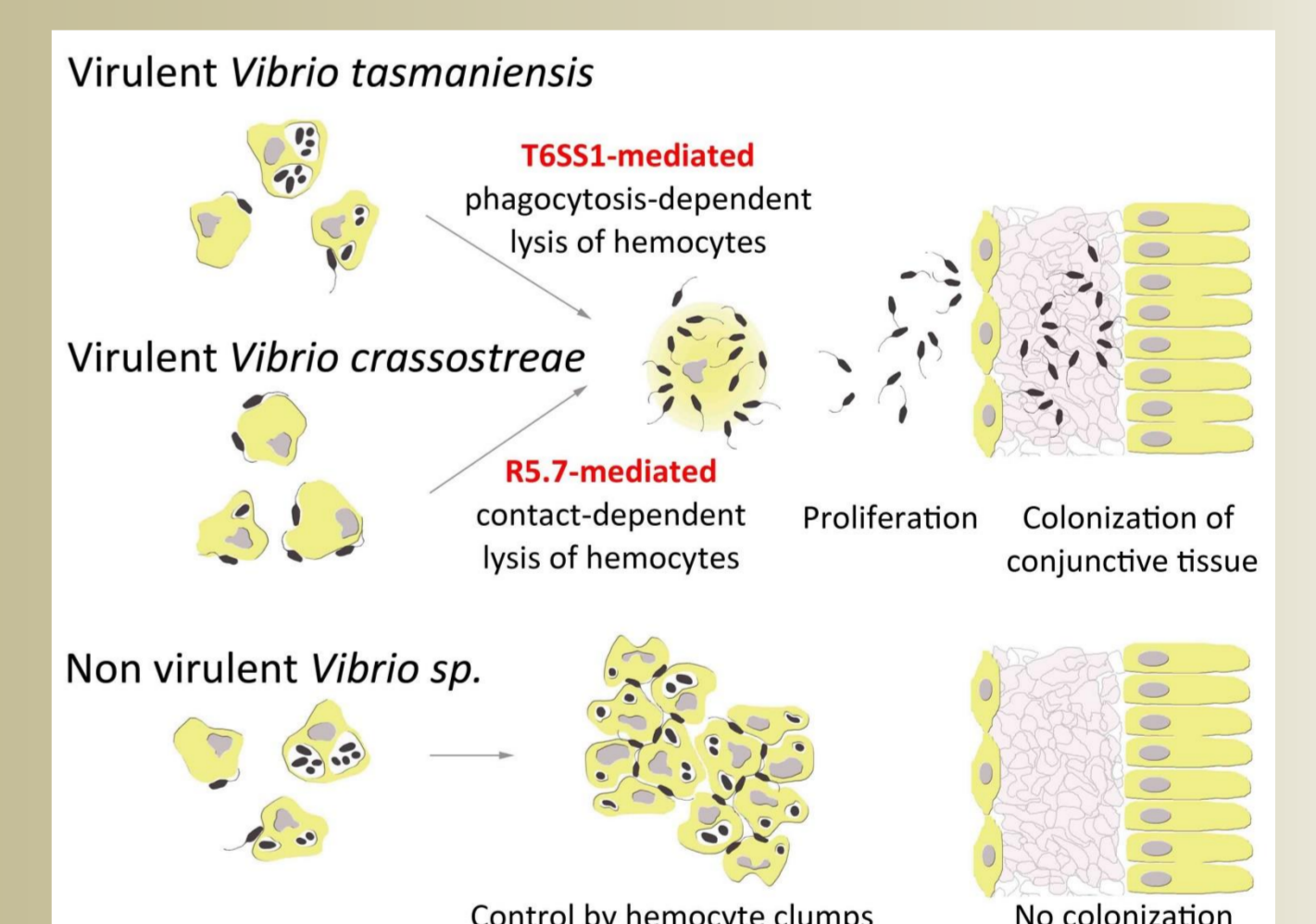


Figure 4. Impairment of oyster cellular immunity as a common strategy of immune evasion

3 DualRNAseq and comparative genomics identify distinct candidate virulence factors in both species → Functional validation is performed through gene knock-out

Conclusions → Proliferation of commensal vibrios is controlled by the host immune system, preventing systemic infections in oysters, whereas the successful infection of virulent strains relies on species-specific molecular determinants that converge to compromise host immune cell function.

→ *Vibrio crassostreae* and *V. tasmaniensis* use distinct mechanisms to cause hemocyte lysis. *V. crassostreae* requires an ancestral gene encoding a protein of unknown function, R5-7, whereas *V. tasmaniensis* (which lacks R5-7) requires intracellular secretion of T6SS effectors.

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