

## Type III secretion systems in *Vibrio parahaemolyticus*

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*Vibrio parahaemolyticus* is an important pathogen causing food-borne gastroenteritis worldwide. An 80-kb pathogenicity island (Vp-PAI), which contains two *tdh* (thermostable direct hemolysin) genes and a set of genes for the type III secretion system (T3SS2), is closely related to the pathogenicity of this bacterium. However, the regulatory mechanisms of Vp-PAI's gene expression were poorly understood. Here we report that two novel ToxR-like transcriptional regulatory proteins (VtrA and VtrB) regulate the expression of the genes encoded within the Vp-PAI region, including those for TDH and T3SS2-related proteins. Expression of *vtrB* was under control of the VtrA, as vector-expressed *vtrB* was able to recover a functional protein secretory capacity for T3SS2, independent of VtrA. Moreover, these regulatory proteins were essential for T3SS2-dependent biological activities, such as *in vitro* cytotoxicity and *in vivo* enterotoxicity. Enterotoxic activities of *vtrA* and/or *vtrB* deletion strains derived from the wild-type strain were almost absent, showing fluid accumulation similar to non-infected control. Whole genome transcriptional profiling of *vtrA* or *vtrB* deletion strains revealed that the expression levels of over 60 genes were downregulated significantly in these deletion mutant strains and that such genes were almost exclusively located in the Vp-PAI region. These results strongly suggest that VtrA and VtrB are master regulators for virulence gene expression in the Vp-PAI and play critical roles in the pathogenicity of this bacterium.