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Action in pairs

Two tandem genes in the fish pathogen *Yersinia ruckeri* are virulence factors

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Yersinia ruckeri is a gram-negative rod-shaped bacterium belonging to the family Enterobacteriaceae. It is in the same genus as *Yersinia pestis*, the causative agent of the bubonic plaque and a category A select agent. The taxonomic assignment of *Y. ruckeri*, however, has raised controversy since it appears to have diverged from the rest of the Yersinia genus in phylogenetic analysis.[1]

Y. ruckeri is the causative agent of enteric redmouth (ERM) disease in salmonids, known as yersiniosis, and can cause significant economic losses, particularly in the rainbow trout farming industry.[2] Clinical signs include hemorrhaging around the mouth, intestines and other organs. *Y. ruckeri* is naturally associated with the aquatic environment and is thought to initially infect via adhesion to the gill surface.

While most research effort has been focused on characterizing human pathogens, studies of their closely related non-pathogenic-to-human relatives have been largely overlooked although it has been recognized that many human pathogens have actually emerged very recently from protean environmental, commensal, or zoonotic populations, and there are similarities in the genomic, biochemical levels among these strains.[3,4]

This is also the case for research on *Y. ruckeri* despite its importance in aquaculture. Most research attention in species of the Yersinia genus is focused on the three well-known human pathogens, *Y. pestis*, *Yersinia pseudotuberculosis*, and *Yersinia enterocolitica*. For example, the virulence mechanisms of *Y. pestis* have been well studied[5] because it has caused approximately 200 million human deaths historically, with at least 2000 cases of plague reported annually by the World Health Organization (WHO). However, there are only a few pathogenic mechanisms of *Y. ruckeri* that have been described so far. Some of these mechanisms have been proven to be involved in virulence, such as the iron uptake mechanism via the siderophore natural product ruckerbatin[6] and the YhlA hemolysin[7] and a new type of two-component operon that contains an amino acid permease motif and an L-cysteine desulfidase motif.[8] The operon was confirmed to be involved in the regulation of cysteine uptake, and knockout of this operon abolishes virulence of *Y. ruckeri* in fish. *Y. ruckeri* was also found to produce an antibiotic natural product holomycin,[9] a founding member of a unique family of dithiolopyrrolone natural products.[10] Interestingly, holomycin production was also found to have a connection with the regulation of cysteine uptake.[11] It remains to be shown whether holomycin production is associated with pathogenicity of *Y. ruckeri*.

Featured in the present issue of *Virulence*, Navais et al.[12] reported a potential new virulence factor that includes one pair of tandem genes *yrpA* and *yrpB*, encoding putative peptidases, in the chromosome of *Y. ruckeri*. Their studies demonstrated that these two genes may be transcribed together. The expression of the genes can be induced when the bacterium was cultured with peptone and under microaerobic culturing conditions. More importantly, inactivation of *yrpA*, resulting in the mutant strain Δ*yrpA*, greatly reduced the infection process for this mutant strain. In silico analysis indicated that similar genes with the same genetic arrangement also exist in the genomes of other human-related pathogenic yersiniae, suggesting a possible new virulence mechanism in this genus. The study also highlights the potential for *Y. ruckeri* to be used as a surrogate model for *Y. pestis* because of such similarities at the genomic level between these two species.[13] Since *Y. ruckeri* does not require the biosafety category 3 facilities needed for some of the resistant *Y. pestis* strains it is easier to study and to work with.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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