GENOME WATCH

Fishy business

Mohammed Sebaihia

Abstract | Three new genome sequences of bacterial fish pathogens are considered in this month's Genome Watch that, together with the previously published sequence of *Flavobacterium psychrophilum*, give insight into interactions of pathogens with aquatic hosts.

Aeromonas salmonicida subsp. *salmonicida* is a Gram-negative bacterium that causes an infectious septicaemia in salmonid fish called furunculosis. Its genome[1] consists of a 4.7 Mb chromosome and five plasmids that together contain 4,758 coding sequences (CDSs). Of these CDSs, 170 are pseudogenes, and there are also 88 insertion sequence (IS) elements — both of these features are hallmarks of a genome that is undergoing reduction. For example, mutations or IS elements in flagellar genes explain why *A. salmonicida* is non-motile even though it contains an entire suite of flagellar genes. The genome encodes multiple virulence factors, including siderophores, toxins, secreted proteases, adhesins, type III secretion systems, a type VI secretion system and an array of antibiotic resistance proteins.

The Gram-positive bacterium *Renibacterium salmoninarum* causes a kidney disease in salmonid fish. Its 3.1 Mb genome[2] contains 3,507 CDSs and, in common with *A. salmonicida*, contains many pseudogenes (730) and IS elements (80). It encodes virulence factors, such as iron-sequestering proteins, polyketide and capsular polysaccharide synthesis enzymes, haemolysins and the major surface antigen (MSA), the most important virulence factor, which is encoded by two identical genes. MSA is unique to *R. salmoninarum* and constitutes ~70% of all proteins on the cell surface. It is processed by a serine proteinase of >100 kDa, but no candidate gene was identified in the genome.

Comparative analyses show that *R. salmoninarum* and *Arthrobacter* spp. share 1,562 CDSs and support the previously held view that *R. salmoninarum* evolved from an *Arthrobacter*-like ancestor through genome reduction. However, most of the *R. salmoninarum* virulence genes do not have orthologues in *Arthrobacter* spp., and therefore might be responsible for the differences in the diseases caused by these bacteria. Renogen, a vaccine used in Atlantic salmonid, consists of live, lyophilized *Arthrobacter* spp. but does not provide significant protection to Pacific salmonids. The *R. salmoninarum* genome might therefore help identify novel vaccine candidates.

Mycobacterium marinum, a close relative of *Mycobacterium tuberculosis*, causes a tuberculosis-like disease in fish and amphibians, and can cause fish-tank or aquarium-tank granuloma in humans following direct contact, through skin cuts and scratches, with infected fish or contaminated aquatic environments. The genome of *M. marinum*[3] comprises a circular chromosome (6.6 Mb) that encodes 5,424 CDSs and a 23 kb plasmid (pMM23). Multilocus sequence typing identified nine distinct sequence types, which have <3% nucleotide variation. Genome comparisons confirmed the close relationship between *M. marinum* and *M. tuberculosis*, and suggested divergence of these two organisms from a common generalist, environmental *Mycobacterium* ancestor. But in contrast to *M. tuberculosis*, *M. marinum* has maintained a stable genome, which is necessary for its dual lifestyle: persistence within a broad host range and environmental survival.

M. marinum shares several important virulence factors with *M. tuberculosis* and other mycobacteria. It has 29 *esx* genes, which encode specialized secretion systems required for the export of specific members of the 6-kDa ESAT-6 (early secreted antigenic target) protein family, compared with 23 *esx* genes in *M. tuberculosis*. Genes that encode polyketide synthases and non-ribosomal peptide synthases that are responsible for the production of a diverse range of polyketide secondary metabolites, some of which are important virulence factors, are also present in higher numbers in *M. marinum* than in *M. tuberculosis*. Furthermore, *M. marinum* has a large repertoire of gene families that encode acidic or asparagine- or glycine-rich proteins, called PE and PPE proteins, which are involved in several aspects of host–pathogen interactions.

Mohammed Sebaihia is at the Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK.
e-mail: microbes@sanger.ac.uk

doi:10.1038/nrmicro2055

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2. Wiens, G. D. *et al.* Genome sequence of the fish pathogen *Renibacterium salmoninarum* suggests reductive evolution away from an environmental *Arthrobacter* ancestor. *J. Bacteriol.***190**, 6970–6982 (2008).
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DATABASES

Entrez Genome Project: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj
Aeromonas salmonicida subsp. *salmonicida* | *Mycobacterium marinum* | *Mycobacterium tuberculosis* | *Renibacterium salmoninarum*

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