Most bacteria synthesize polyphosphate by unknown mechanisms

We comment on the recent paper by Sanyal et al. (2013) in Microbiology describing how the ppk1 gene of Mycobacterium tuberculosis plays a crucial role in stress responses by integrating a pair of two component signalling pathways encoded by senX3–regX3 (regulating phosphate import) and mprAB (ultimately controlling transcription of the stringent response regulator rel). Hence, PPK1 represents an essential determinant of pathogenicity by regulating the supply of phosphate groups for the activation of signalling pathways. Inorganic poly P is present in all organisms (Kulaev & Vagabov, 1983) and is vital in numerous cell metabolic processes, structures and stress responses and also in virus replication (Brown & Kornberg, 2008).

It is widely believed that bacteria express just one or two PPKs, namely PPK1 or PPK2 (Rao et al., 2009; Moreno & Docampo, 2013). Consequently, the important mechanism described by Sanyal et al. (2013) could have profound significance for other bacterial diseases. We have tested the widespread assumption of the universal distribution of PPK1 and/or PPK2 in bacteria. In common with all genomics-based approaches, the majority of genes detected via DNA sequence will never have been phenotype tested for function. Nonetheless, when knockout mutants have been constructed, such as in Escherichia coli and Pseudomonas aeruginosa, dramatic declines in poly P content have been noted (Brown & Kornberg, 2008). Table 1 summarizes a recent search of the bacterial genome databases for the presence of PPK1 and PPK2 encoding sequences. The NCBI genome database was analysed through BLASTP (http://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE_TYPE= BlastSearch&BLAST_SPEC= MicrobialGenomes). A BLASTP search using either E. coli PPK1 (UniProt P0A7B1) or P. aeruginosa PPK2 (GenBank NP_248831) was performed against all complete genomes on the database except Candidatus isolates. Where more than one genome of the same species was available then only one was analysed. If an isolate was only classified to genus level it was included in the analysis only if no other species of that genus was available for analysis. The smallest expect (e) value determined as a match was 0, whilst the largest for PPK1 and PPK2 was only 5e-14 and 1e-12, respectively. The vast majority of significance values were 1e-20 or less. A tiny proportion of bacterial genomes produced identity values of 0.1 to 1e-12, all of which showed no conserved regions and were concluded not to contain either PPK. Almost all those bacterial species that were classified as containing no PPKs returned no hits whatsoever. Generally PPK1 searches produced matches with lower e significant values than PPK2 searches.

Surprisingly, the table shows that both PPK1 and 2 are present only in less than half of taxa and that a third of taxa have neither enzyme. PPK2 is rarely found alone and significantly, several taxa show all four possible states. There is no PPK1 in about 40% of taxa. Consequently, the important mechanism described by Sanyal et al. (2013) could have profound significance for other bacterial diseases. It adds urgency to the need to identify those unknown enzymes responsible for synthesizing polyphosphate (poly P) in the sizeable minority of bacteria that lack both PPK1 and PPK2. We propose that the actin-like Arp homologues in bacteria, may be early events of bacterial species requires pressing investigation.

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shown evidence for the horizontal transfer of bacterial type PPK1 and PPK2 encoding sequences to some simple eukaryotes.

Now that we know the distribution of PPK1 and 2 predicted by bioinformatics, it would be important to check on polyphosphate production in a sample of those strains without these enzymes, especially given ignorance of the enzymes involved. The paper by Sanyal et al. (2013) adds urgency to the need to identify those unknown enzymes responsible for synthesizing poly P in the sizeable minority of bacteria that lack both PPK1 and PPK2.

A variety of actin-like molecules is found in eubacteria or archaea, including MreB, FtsA, Mbl, ParM, Alfa, MamK and Ta0583 (Graumann, 2007). We propose that the actin-like Arp proteins with PPK activity first identified by Kornberg’s group (Gómez-García & Kornberg, 2004) and with distant homologues in bacteria (Joseph et al., 2008) may be early PPKs with continued activity in modern bacteria, particularly those that lack PPK1 and PPK2. In view of the crucial role of PPK1 in determining pathogenic responses in M. tuberculosis shown by Sanyal et al. (2013), the possible existence of other, unknown enzymes responsible for the synthesis of poly P in many bacterial species requires pressing investigation.

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