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The High-Resolution Structure of a Processive Exopolyphosphatase with a Novel Regulatory GTPase Fold.

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The *E. coli* Ppx exopolyphosphatase degrades long-chain polyphosphates in a highly processive reaction & hydrolyzes the terminal 5' phosphate of guanosine 5' triphosphate 3' diphosphate (pppGpp). The structure of Ppx has been determined to 1.9Å resolution by X-ray crystallography. Remarkably, 29 sulfate ions are found bound to the Ppx dimer, & they occupy sites where the polyP chain is likely to bind. An aqueduct that passes through the enzyme provides a physical basis for the enzyme's high processivity. The amino-terminal region containing the polyPase active site is a member of the ASKHA (Acetate and Sugar Kinases, Hsp70, Actin) phosphotransferases. A Domain III six-helix claw homologous to the catalytic core of eukaryotic cyclic nucleotide phosphodiesterases is probably the pppGppase. PolyPase activity regulation by pppGpp hydrolysis is reminiscent of the regulation of biochemical reactions by G proteins & other GTPases. Recent enzymological studies of mutant Ppx proteins provide additional insight into the regulation of the bacterial stringent response to nutrient deprivation. A new genus of 3-dimensional protein animation, which illustrates the path of the polyP chain, will be presented.

