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PROTEIN SEQUENCE MOTIFS

The yeast open reading frame encoding a dual specificity phosphatase

The vaccinia virus encodes a phosphatase (VH1) which shows amino acid sequence similarity to the protein tyrosine phosphatases (PTPases). The VH1 phosphatase can dephosphorylate proteins that have phospho-Ser, -Thr or -Tyr residues, a feature which distinguishes this catalyst from other PTPases¹. In the fission yeast *Schizosaccharomyces pombe*, the *cdc25* protein is required to dephosphorylate a specific Tyr residue (Tyr15) in p34^{cdc2}. The dephosphorylation leads to activation of p34^{cdc2}/cyclin B and the onset of mitosis. Sequence similarity between VH1 and *cdc25* suggested a catalytic mechanism by which the *cdc25* gene product would dephosphorylate p34^{cdc2} (Refs 2, 3).

Many viral genes have cellular counterparts that play important roles in signal transduction (e.g. *myc*, *src*). We have found that the viral-encoded VH1 phosphatase has sequence identity with a protein encoded by an open reading frame (ORF) located 3' to the *Saccharomyces cerevisiae* *DAL1* gene, which encodes allantoinase and is located on chromosome IX (Ref. 4). Figure 1 shows the alignment of the protein encoded by the yeast ORF with VH1. The degrees of amino acid identity between the two proteins is 30%. Due to the 30% sequence identity between the yeast ORF and VH1, we have referred to the yeast gene as *YVH1* (for yeast VH1). To demonstrate that the 364-amino acid yeast protein was a phosphatase, the yeast gene

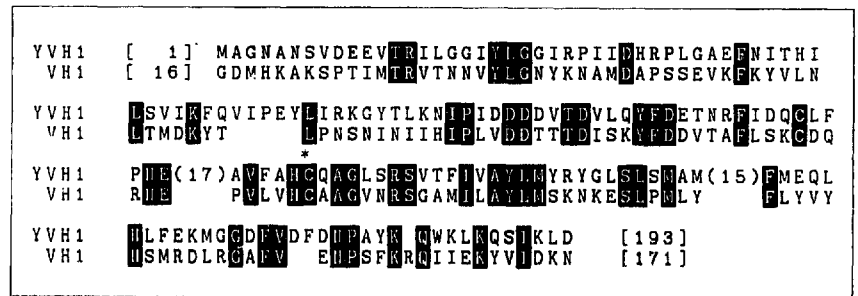


Figure 1

Sequence comparison between the *S. cerevisiae* *YVH1* gene product and the vaccinia virus VH1 protein phosphatase. Letters in black correspond to identical amino acids. *Denotes the Cys residue necessary for catalysis.

was cloned into a glutathione *S*-transferase vector-expression system and the recombinant fusion protein was purified by affinity chromatography. The yeast fusion protein was active toward ³²P-labeled Ser and Tyr residues in phosphoproteins. In addition, a number of residues known to be important in the catalytic mechanisms of the PTPases are conserved in *YVH1*. These include the invariant His-Cys sequence located at the active site of the PTPases, as well as several highly conserved basic residues thought to be important for substrate binding⁵.

Although the function of the vaccinia phosphatase is unknown, it would presumably have rather dramatic effects upon Ser, Thr and Tyr phosphate content in cells infected with the virus. Understanding the role of *YVH1* in cellular regulation should be possible by use of yeast genetics. In addition, the possibility that the *YVH1* function in yeast will also provide clues to the pathogenic role of VH1

in viral infection and/or replication should not be overlooked. Finally, it is likely that higher eukaryotes will also have homologs to the *YVH1* gene.

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