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Identification of additional Ser/Thr protein kinases in the genome of *Streptococcus thermophilus* using structural homology detection.

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Introduction

The Ser/Thr/Tyr phosphoproteome of *S. thermophilus* LMD-9 shows the phosphorylation of 106 proteins. When the one of and only Ser/Thr Protein Kinase (STPK) identified in this genome -named **PknB**- is depleted, 96 out of those 106 proteins are still phosphorylated, hence evidencing the presence of at least another STPK¹.

Knowing that the catalytic domain of STPK all shares a similar 3D fold, called **Hanks-type** kinase, we hypothesized that the unidentified kinase(s) should share a similar fold². Thus, we screen the whole genome of *S. thermophilus* LMD-9, predicting the structural profil of each of the 1673 fasta sequences and comparing it with to a STPK of reference.

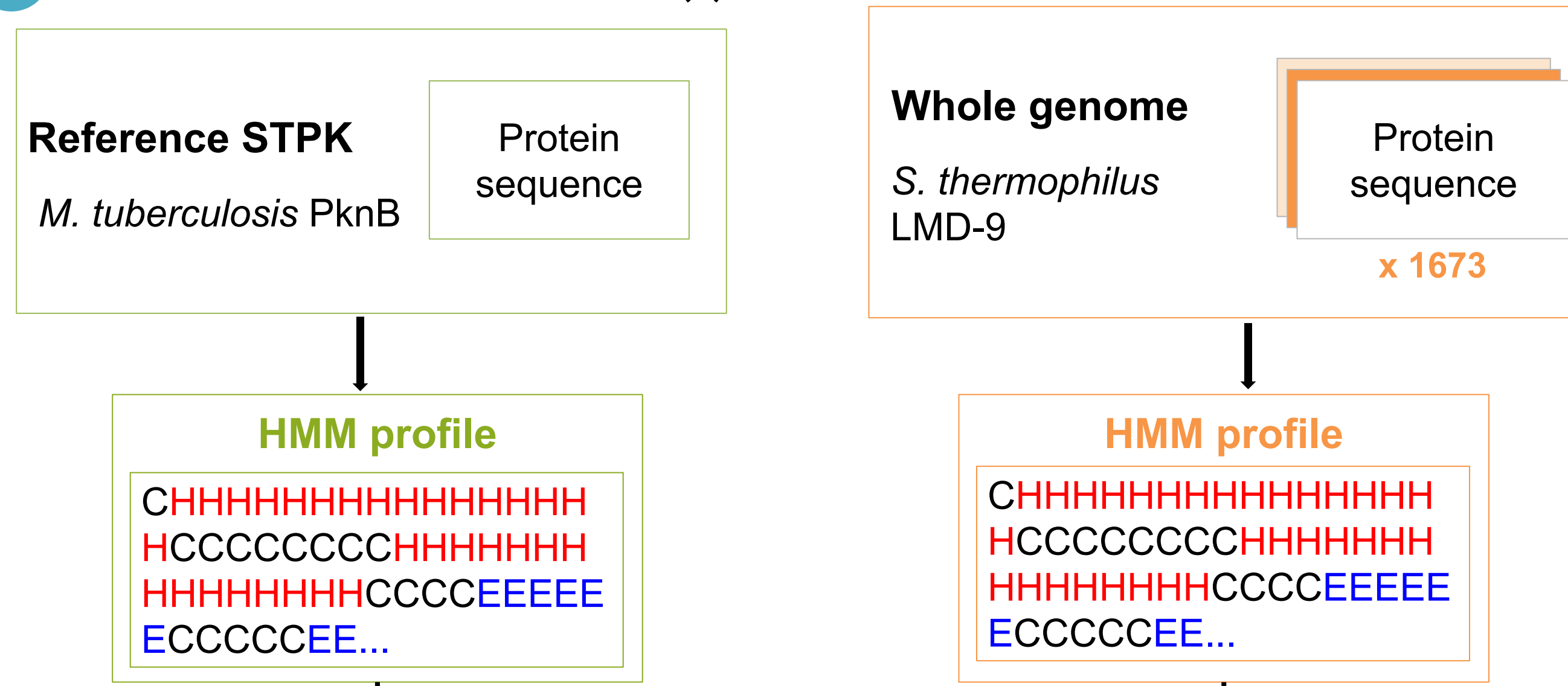
On this basis, our project aims at identifying the missing STP kinase(s).

Objectives

- **Structure/Function analysis** of PknB identified in *S. thermophilus* LMD-9 genome as regard to the solved reference in *Mycobacterium tuberculosis*³.
- **Screening of structural homologues of PknB**, using profile-profile comparison⁴, within the 1673 protein sequences of the *S. thermophilus* LMD-9 genome.
- **Identification and analysis** of the best structural hit(s) once homology modeled⁵.

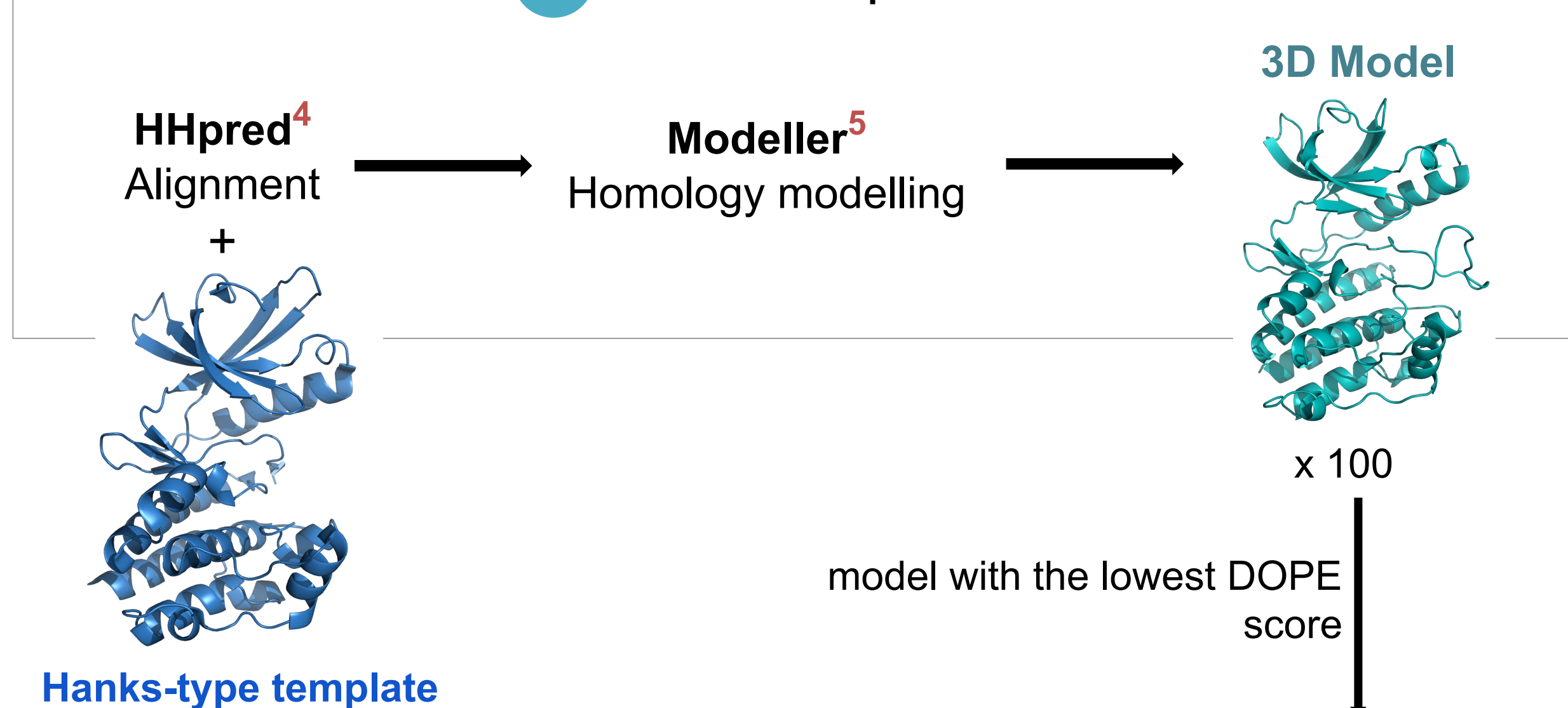
Method: Metafoldscan pipeline

1 Detection of structural hit(s)

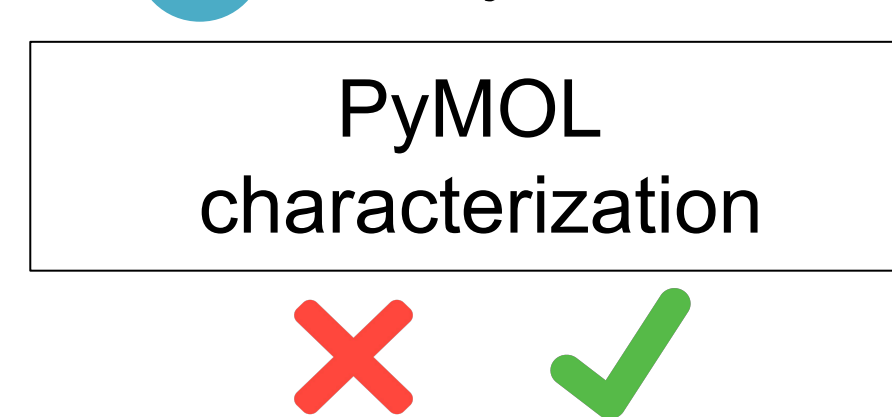


Comparison & Ranking

2 Structure prediction



3 Analysis

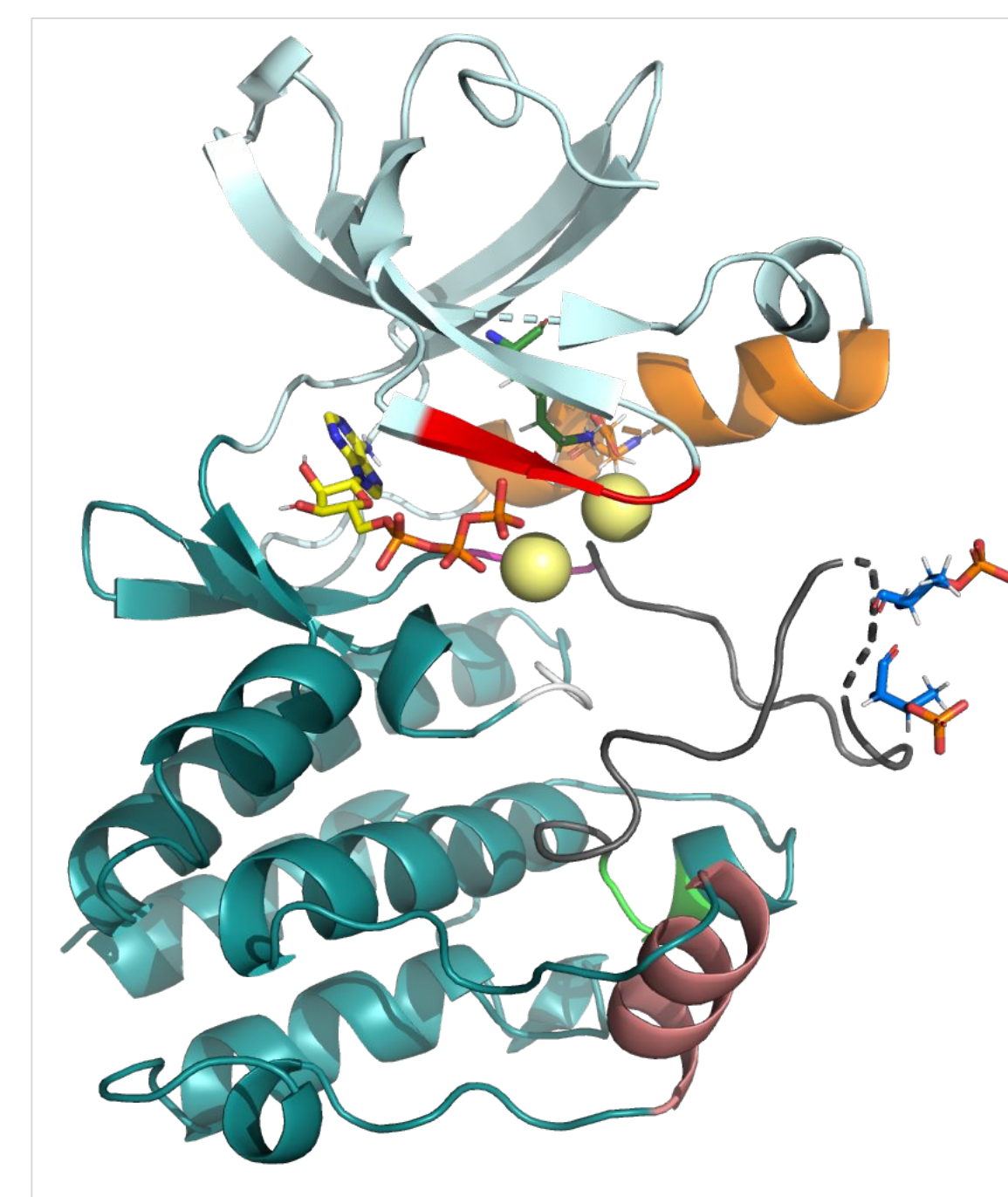


Results: analysis of the structural hits

Structural homologues to the reference **PknB** catalytic domain in *M. tuberculosis*³ (PDBid: 1O6Y - length: 332 amino acids):

Rank	Annotation of the hits	Homology (%)	Identity (%)	Aligned residues
1	Serine/Threonine Protein Kinase PknB	100	40	271
2	Hypothetical protein	99.9	19	251
3	AarF/ABC1/UbiB kinase family protein	99.4	25	138
4	aminoglycoside phosphotransferase	94.2	24	29
5	membrane protein	13.4	43	14

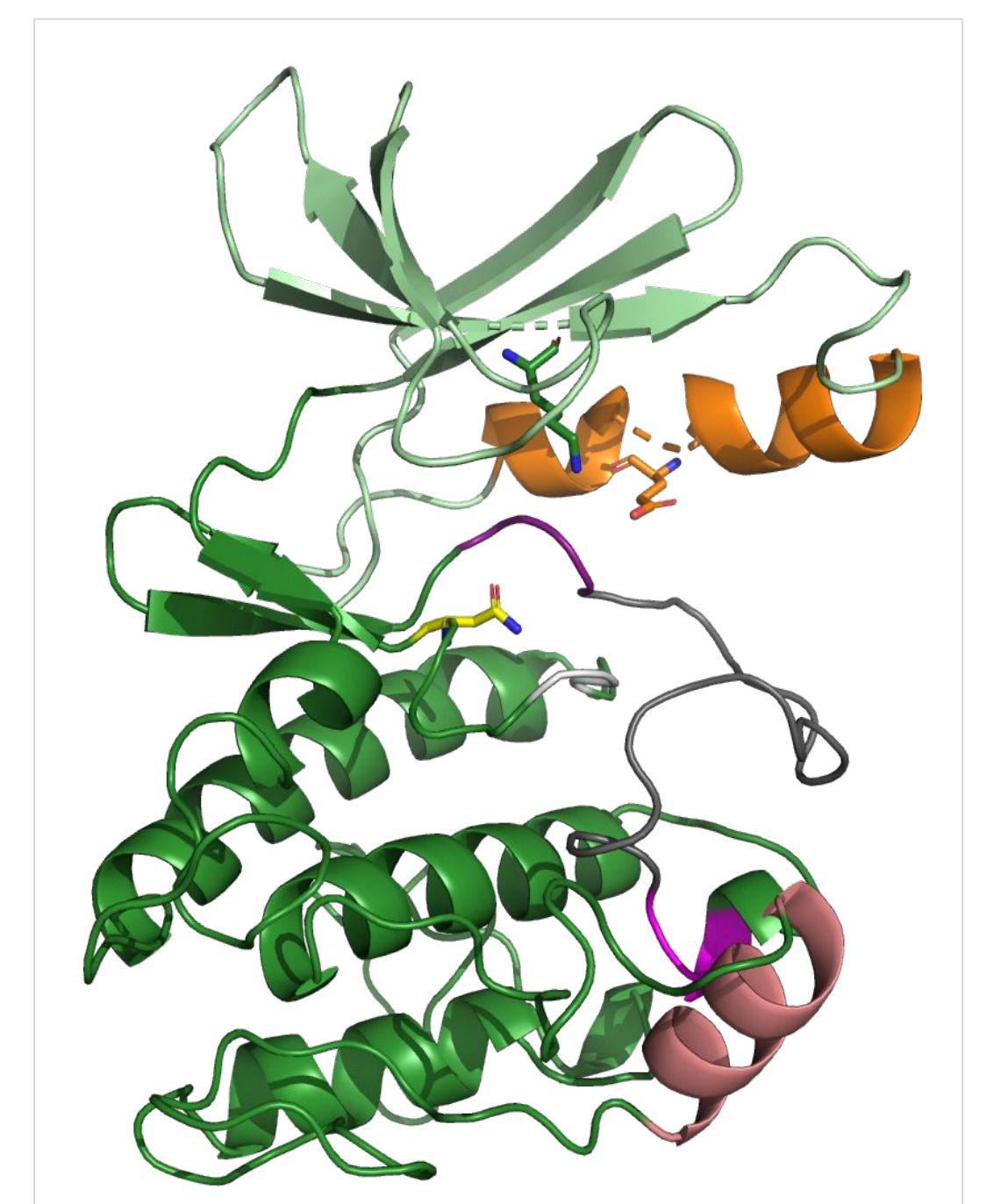
HIT 1 : Ser/Thr Protein Kinase PknB



Hanks-type kinase

- ✓ Structure
- ✓ **Conserved** functional motifs

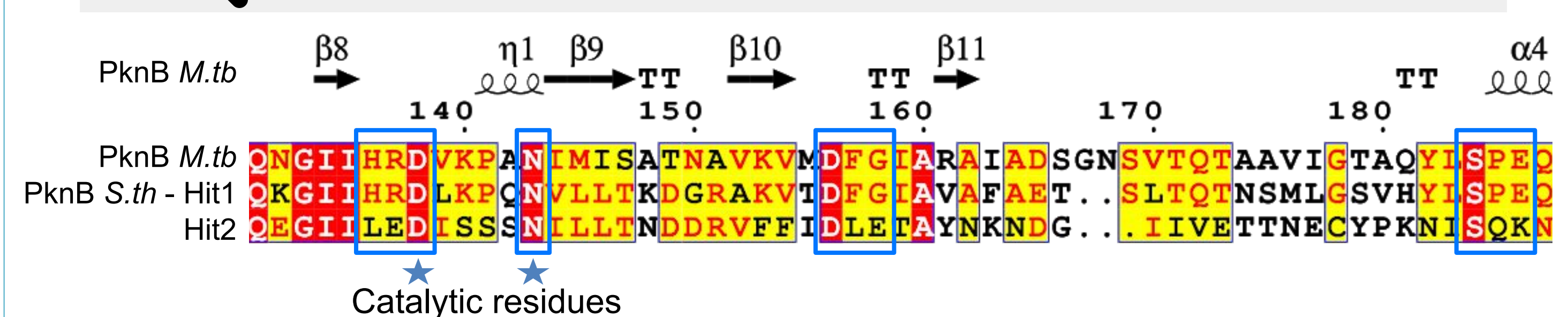
HIT 2 : Hypothetical protein



Pseudokinase ?

- ✓ Structure
- ✓ **Degenerated** functional motifs

ESPrnt alignment between PknB *M. tb* and *S. th* + Hit2



Conclusion & Perspectives

- Structure/Function analysis of *S. thermophilus* LMD-9 PknB.
- Identification of two promising structural hits called Hits 2 & 3.
- Among them, characterization of Hit 2 as a potential pseudokinase.
- Phenotypical experimental validation in progress of Hit 2 and Hit 3.

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