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# Identification of additional Serine/Threonine 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 STPK<sup>1</sup>. 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 fold<sup>2</sup>. 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.

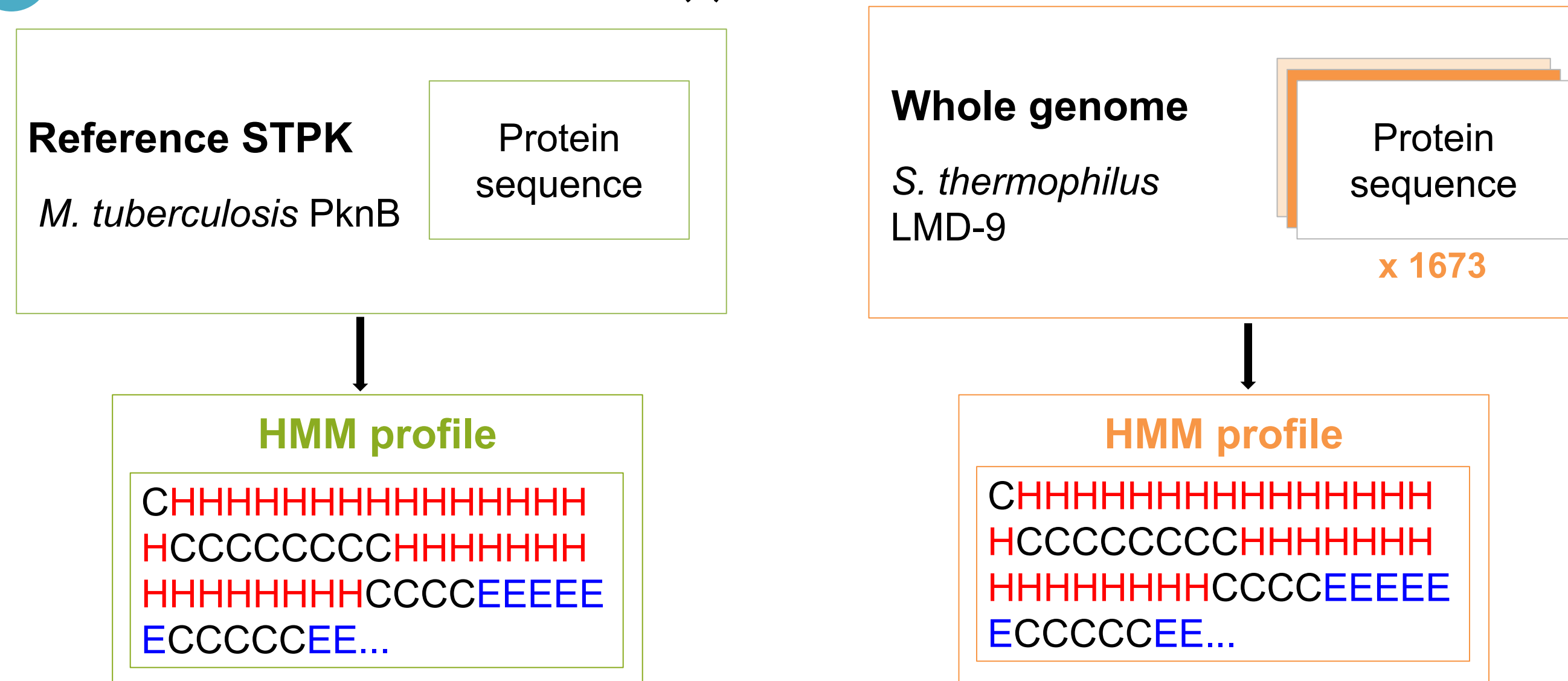
On this basis, our project aims at identifying the missing STP kinase(s).

## Objectives

- **Structure/Function analysis** of PknB identified in *S. thermophilus* LMD-9 genome as regard to the solved reference in *Mycobacterium tuberculosis*<sup>3</sup>.
- **Screening of structural homologues of PknB**, using profile-profile comparison<sup>4</sup>, within the 1673 protein sequences of the *S. thermophilus* LMD-9 genome.
- **Identification and analysis** of the best structural hit(s) once homology modeled<sup>5</sup>.

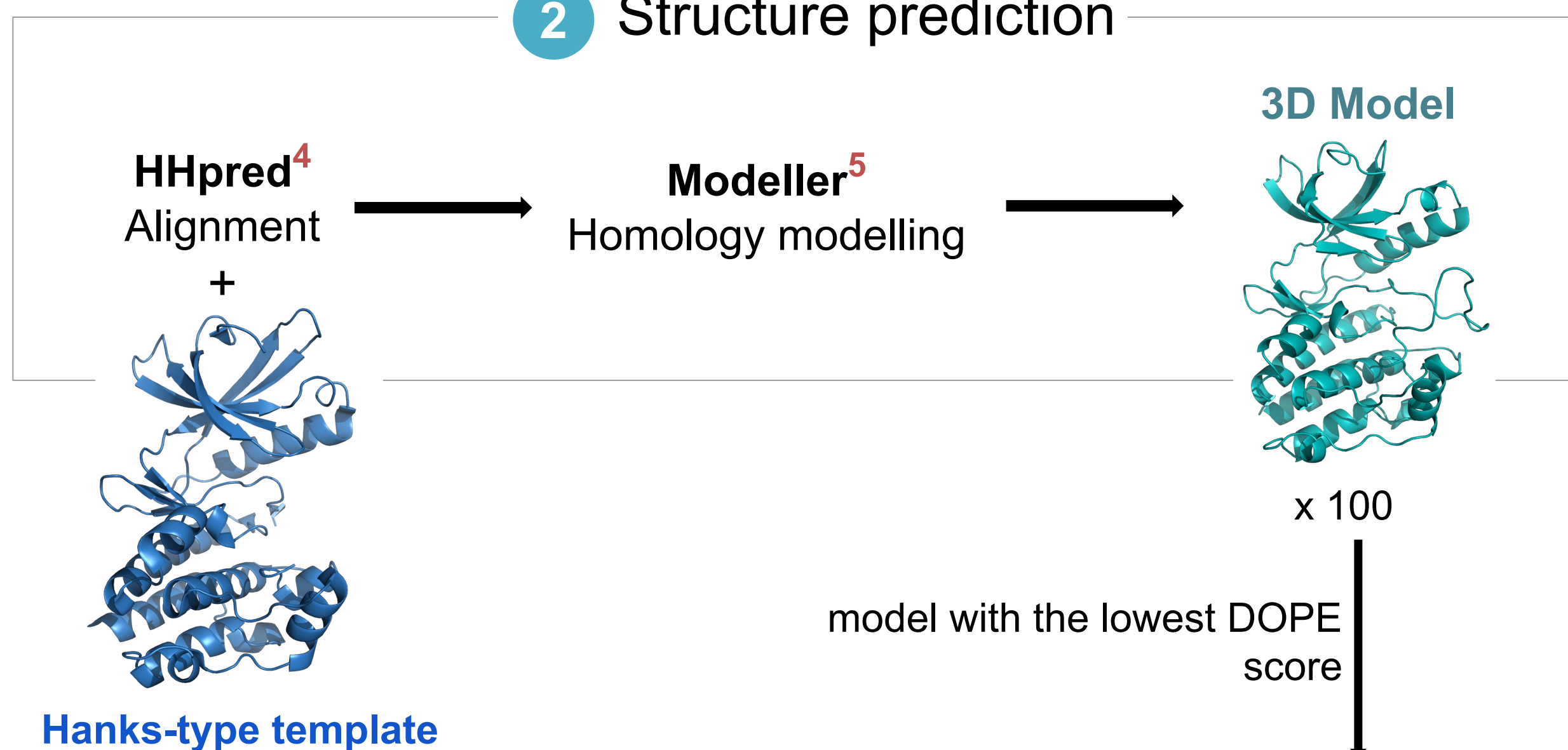
## Method: Metafoldscan pipeline

### 1 Detection of structural hit(s)

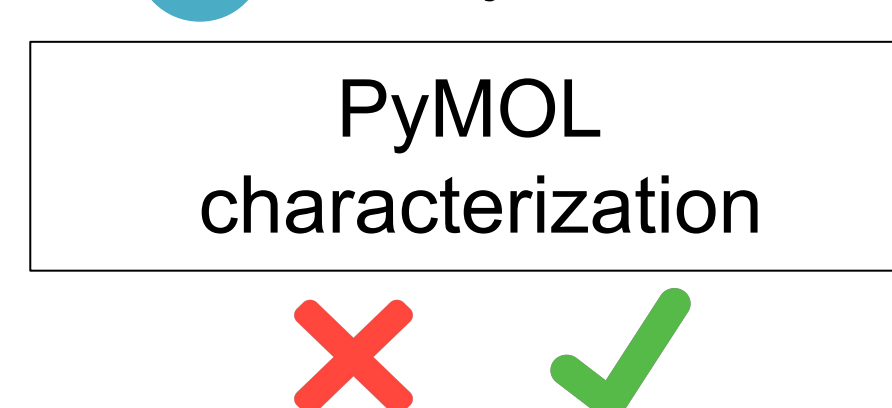


### Comparison & Ranking

### 2 Structure prediction



### 3 Analysis

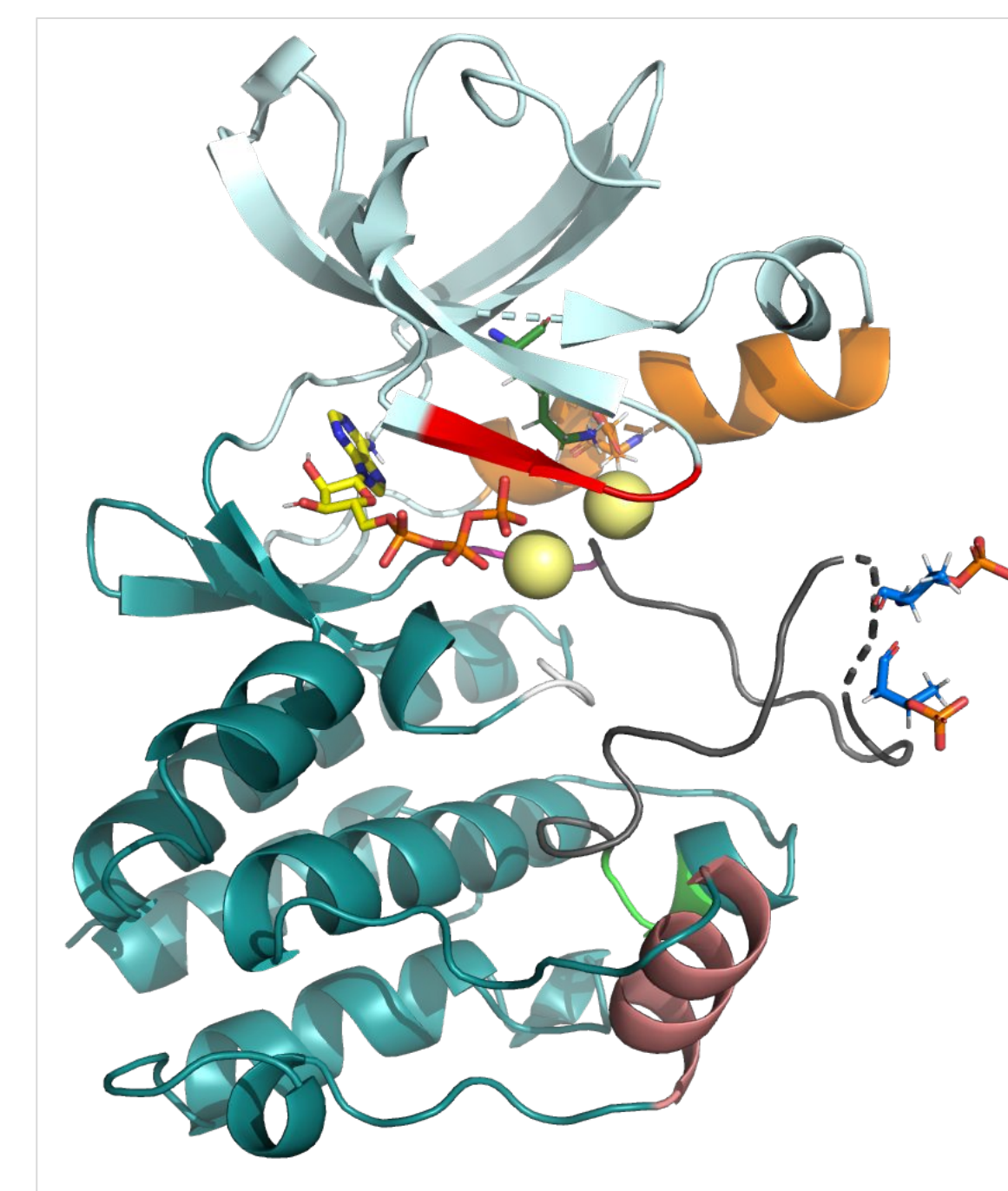


## Results: analysis of the structural hits

→ Structural homologues to the reference **PknB** catalytic domain in *M. tuberculosis*<sup>3</sup> (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               |

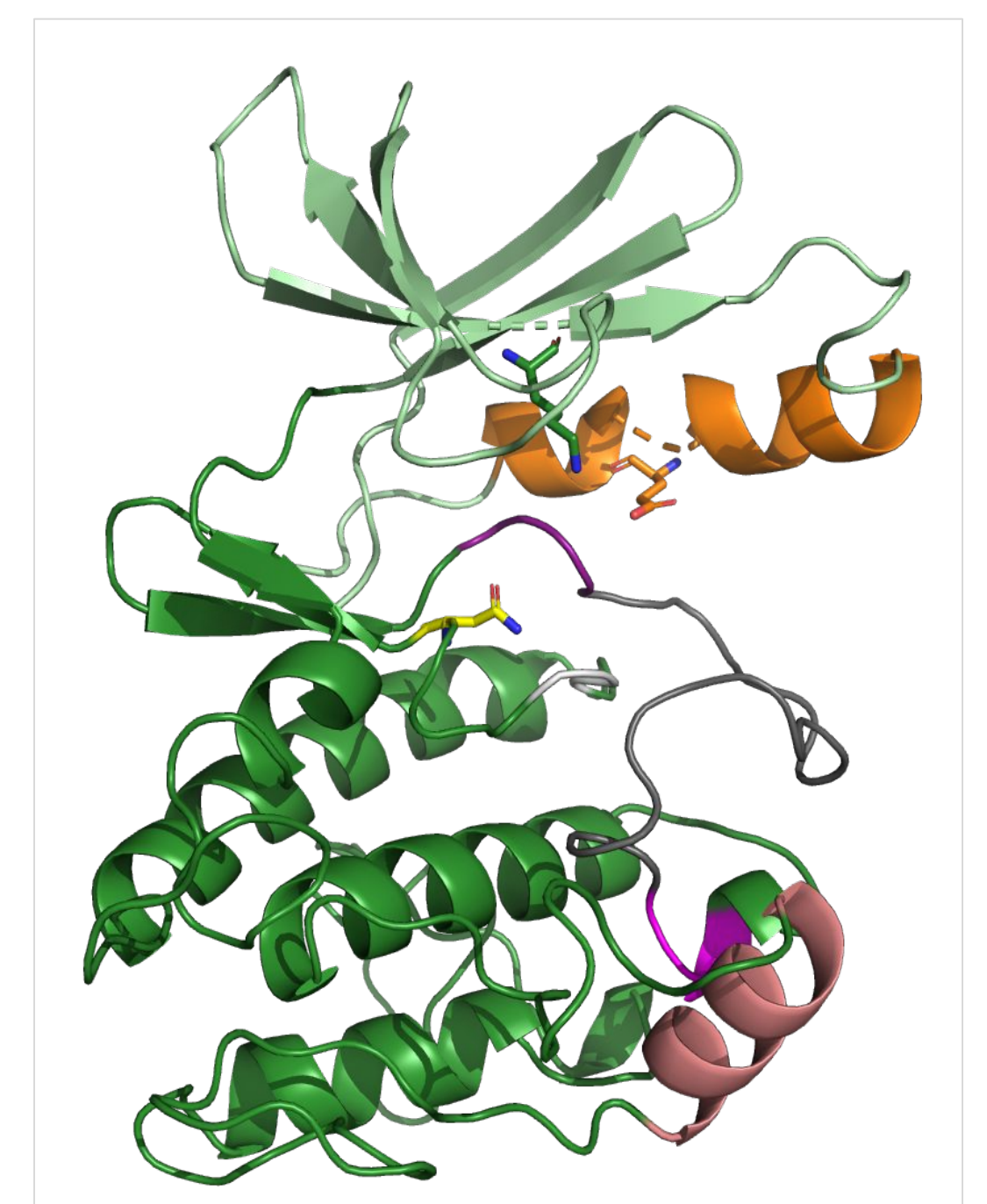
### HIT 1 : Ser/Thr Protein Kinase PknB



Hanks-type kinase

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

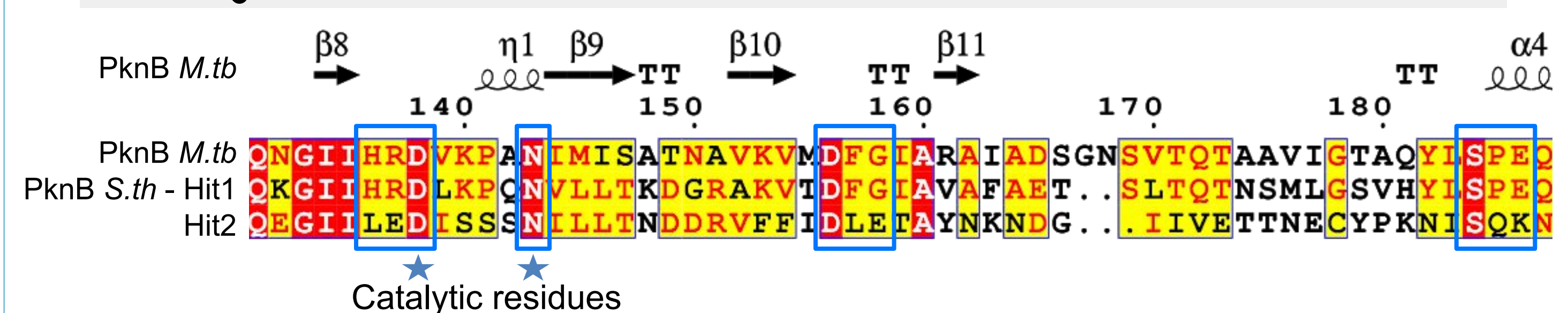
### HIT 2 : Hypothetical protein



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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