Structural and Functional Characterization of *Anaplasma phagocytophilum* Guanylate Kinase

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Background

GK

GMP + ATP ⟶ GDP + ADP

- This reaction supports **purine salvage pathways.**
- GK activity ensures a steady supply of GDP and GTP.
- GTP functions both as a nucleotide building block and an energy source.
- ***A. phagocytophilum* solely relies on the salvage pathway for its purine requirements.**
- Since GK are essential for normal cellular function, ApGK could be a potential drug target.
- Lack of progress in anaplasmosis drug development warrants the need for new therapeutic options.

Objective

To identify key structural and functional features of *A. phagocytophilum* guanylate kinase (ApGK).

Evidence of possible dimer of ApGK

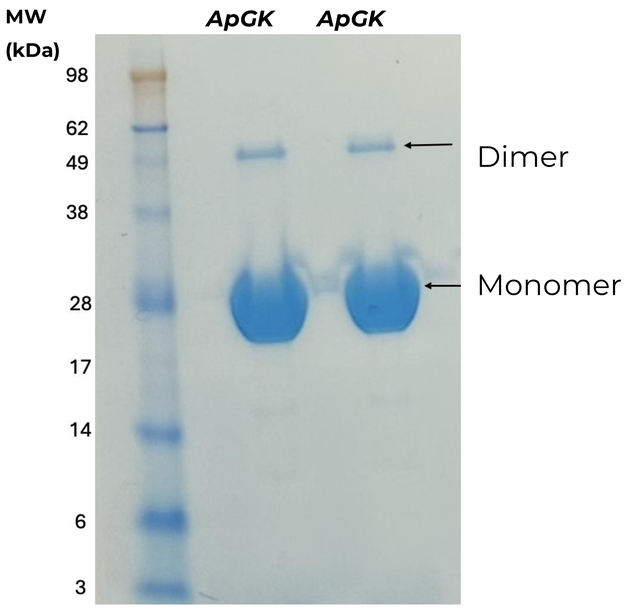

Figure 1. ApGK protein purification shows possible dimers.

ApGK crystal structure shows a typical Guanylate Kinase

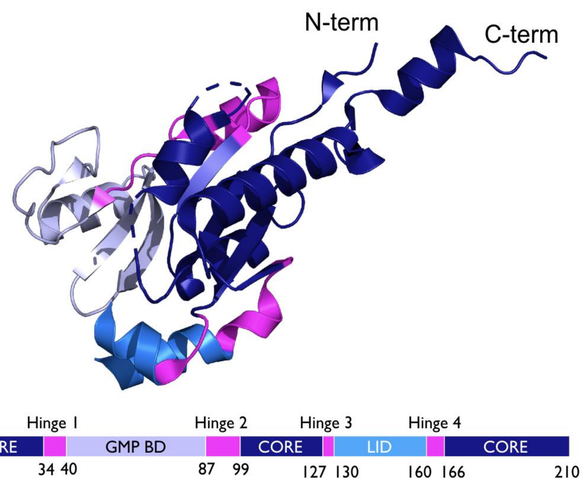

Figure 2. Core structural components present in ApGK.

Structural Analysis of ApGK

ApGK is distinguished from its homologs

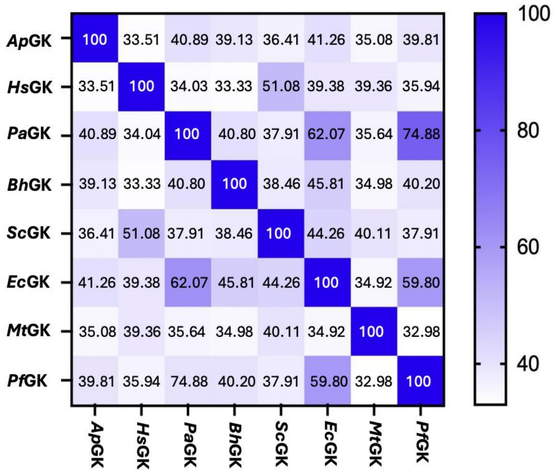

Figure 3. ApGK has 33% similarity with Human GK.

Conolly structure shows dimer

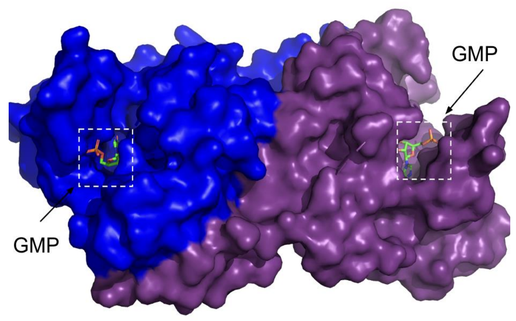

Figure 4. Connolly structure strongly supports the dimer structure.

Differential substrate binding modes for ApGK and Human GK

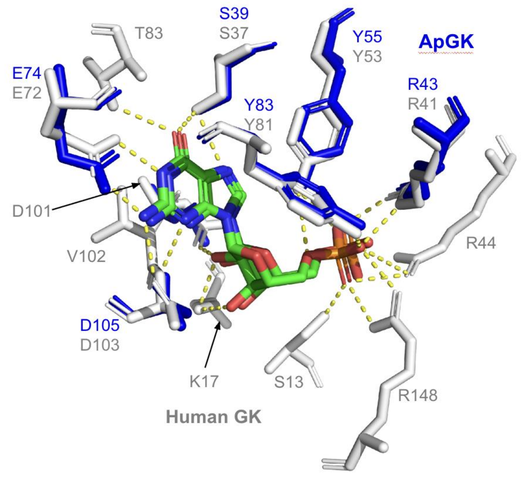

Figure 7. Overlay of residues required for GMP binding in ApGK and Human GK.

ApGK is distinguished from the Human GK

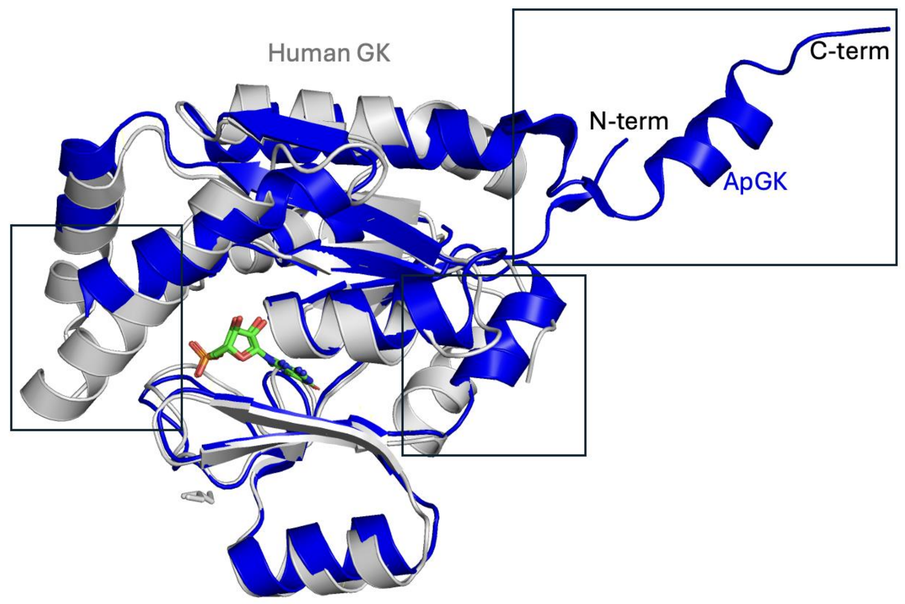

Figure 5. Superimposed image of ApGK (blue) and Human GK (grey).

Nucleotides are highly conserved when bonded to active site

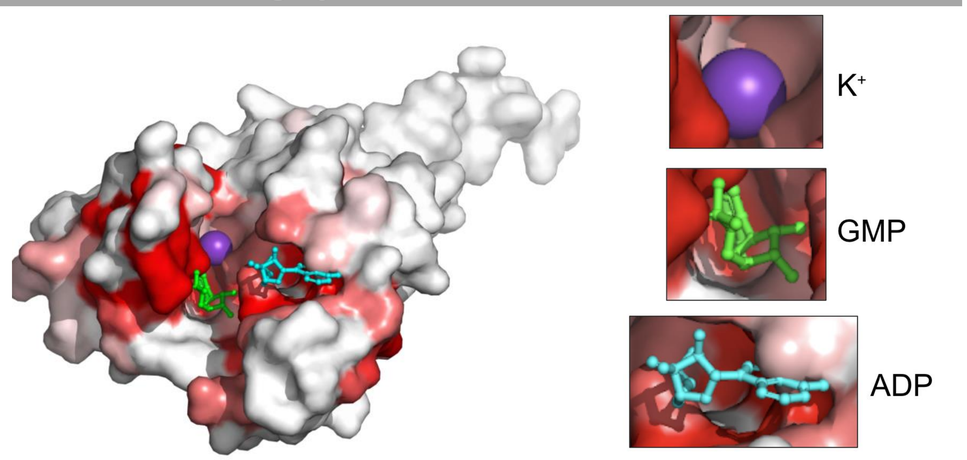

Figure 6. GMP, K^+, and ATP (ADP) binding regions are highly conserved across different guanylate kinase isoforms.

ApGK nucleotide induced conformational changes

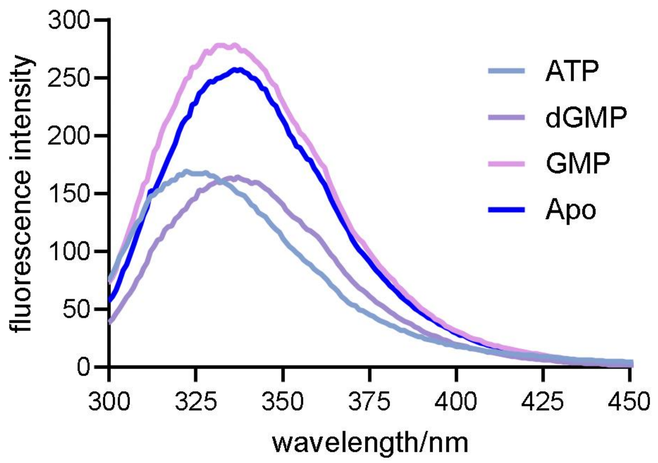

Figure 8. *Nucleotides differentially alter the tertiary structure conformation ApGK.*

Discussion

- ApGK is structurally distinguished from HsGK (figures 3, 5, 7).
- Active site differences support potential drug targeting efforts (figure 7).
- Future experiments could validate ApGK as a future drug target.

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References