

GCK PM1 Residues

Applicable for glucose and ATP-binding sites¹⁻⁹

Residue Domain Comment

Glucose binding site (22 residues)¹

Ser151 - Pro153	S	Ser151 makes H-bond interaction with Glc in closed conf.
Thr168 - Lys169	S	Thr168 and Lys169 make H-bond interaction with Glc in closed conf. Lys169 is a general acid catalyst in the catalytic ternary complex.
Asn204 - Thr206	L / CRII	Asn204 and Asp205 make H-bond interaction with Glc in closed conf. Asp205 is part of the catalytic ternary complex (general base catalyst).
Ile225 - Asn231	L	Asn231 makes H-bond interaction with Glc in closed conf ^{2,3} .
Asn254 - Gly258	L	Glu256 makes H-bond interaction with Glc in closed conf ^{2,3} .
Gln287	L	Gln287 makes H-bond interaction with Glc in closed conf.
Glu290	L	Glu290 makes H-bond interaction with Glc in closed conf ^{2,3} .

Mg²⁺- ATP binding site (29 residues)

Asp78 - Arg85	S	Phosphate 1 motif. Asp78 is important for coordinating the Mg ²⁺ ion in ternary complex. Thr82 H-binding to ATP-γ-S in crystal structure 3VEY ⁶ .
Ser151	S	Ser151 is important for coordinating the Mg ²⁺ ion in ternary complex ¹ .
Lys169	S	Lys169 makes H-bond interaction with ATP in closed conf. Lys169 is a general acid catalyst in the catalytic ternary complex ⁷ .
Asp205	L / CRII	Part of the Connect 1 motif. Asp205 makes H-bond interactions with Mg ²⁺ and ATP. Part of the catalytic ternary complex (general base catalyst) ¹ .
Ile225 - Gly229	L	Phosphate 2 motif. Thr228 makes H-bond interaction with ATP and is part of the catalytic scaffold of GK ^{1,8} .
		Gly229: H-binding to AMP-PNP according to crystal structure GK•Glc•AMP-PNP ¹ .
Gly295 - Lys296	L	
Glu331 - Arg333	L	
Ser336	L	H-binding to AMP-PNP according to crystal structures ^{1,4,5} .
Gly410 - His416	L	Adenosine motif. Ser411: H-binding to AMP-PNP according to crystal structures ¹ .

References

1. Petit et al (2011) The active conformation of human glucokinase is not altered by allosteric activators. *Acta Crystallogr D Biol Crystallogr* 67 929-935. PMID: 22101819
2. Molnes et al (2008) Catalytic activation of human glucokinase by substrate binding: residue contacts involved in the binding of D-glucose to the super-open form and conformational transitions. *FEBS J.* May;275(10):2467-81. PMID: 18397317
3. Kamata K, Mitsuya M, Nishimura T, Eiki J-i & Nagata Y (2004) Structural basis for allosteric regulation of the monomeric allosteric enzyme human glucokinase. *Structure* 12, 429-438. PMID: 15016359
4. Mahalingam B, Cuesta-Muñoz A, Davis EA, Matschinsky FM, Harrison RW & Weber IT (1999) Structural model of human glucokinase in complex with glucose and ATP: implications for the mutants that cause hypo- and hyperglycemia. *Diabetes* 48, 1698-1705. PMID: 10480597
5. Gloyn et al in Matschinsky FM, Magnuson MA (eds): *Glucokinase and Glycemic Disease: From Basics to Novel Therapeutics*. Front Diabetes. Basel, Karger, 2004, p.92-109.
6. Liu et al (2012) Insights into mechanism of glucokinase activation: observation of multiple distinct protein conformations. *J Biol Chem.* 287(17):13598-610. PMID: 22298776
7. Zhang J, Li C, Shi T, Chen K, Shen X & Jiang H (2009) Lys169 of human glucokinase is a determinant for glucose phosphorylation: implication for the atomic mechanism of glucokinase catalysis. *PLoS One* 4, e6304. PMID: 19617908
8. Molnes et al (2011) Binding of ATP at the active site of human pancreatic glucokinase – nucleotide-induced conformational changes with possible implications for its kinetic cooperativity. *FEBS J.* Jul;278(13):2372-86. PMID: 21569204
9. Harrison RW & Weber IT (2004) Molecular Models of Human Glucokinase and the Implications for Glycemic Diseases. In *Glucokinase and Glycemic Disease: From Basics to Novel Therapeutics* (Matschinsky FM & Magnuson MA, eds), pp. 135-144. Karger, Basel.