

**CONFORMATIONAL HETEROGENEITY OF HUMAN PANCREATIC GLUCOKINASE  
IN THE ABSENCE AND PRESENCE OF GLUCOSE** *Mioara Larion<sup>1</sup>, Roberto Kopke  
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High-resolution NMR is used to investigate the conformational dynamics of human glucokinase, a 52 kDa monomeric enzyme that displays kinetic cooperativity. <sup>1</sup>H-<sup>15</sup>N TROSY spectra of uniformly labeled glucokinase, collected in the absence and presence of glucose, reveal significant cross-peak overlap and heterogeneous peak intensities that persist over a range of temperatures. <sup>15</sup>N-specific labeling of isoleucines and tryptophans, reporting on backbone and side-chain dynamics respectively, demonstrate that both unliganded and glucose-bound enzymes sample multiple conformations, although glucose stabilizes certain conformations. These results provide the first direct evidence of glucokinase conformational heterogeneity and hence shed light on the molecular basis of kinetic cooperativity.