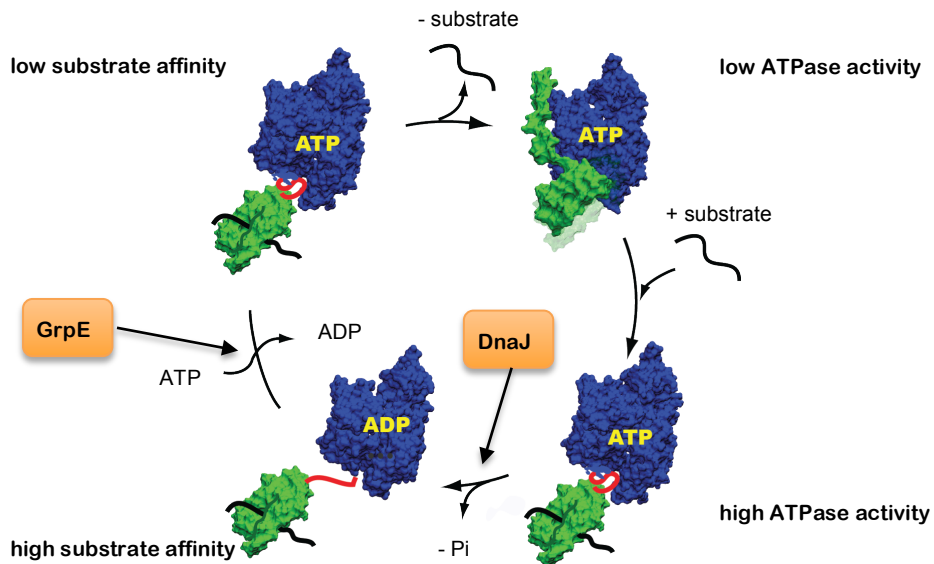


# The allosteric landscape of Hsp70 molecular chaperones

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Hsp70 chaperones are essential to cellular homeostasis and response to stress. Hsp70 chaperones bind extended hydrophobic segments of partially folded proteins and release them in an ATP-dependent manner (shown below is the allosteric cycle of the *E. coli* Hsp70, DnaK).



A major puzzle is how allosteric signals are communicated from one domain to the other. We will describe NMR results showing how signals propagate from the ATP-binding site of DnaK through the nucleotide-binding domain (NBD) to the interdomain linker, and how these conformational signals communicate with the substrate-binding domain (SBD). We will also discuss roles for the poorly understood C-terminal sequences of Hsp70s. We found that the very C-terminal disordered region helps substrate refolding and cellular survival upon stress. The helical subdomain immediately before this region stabilizes the long helical lid that covers the substrate-binding site. We are extending this work to human Hsp70s with a goal of designing inhibitors.