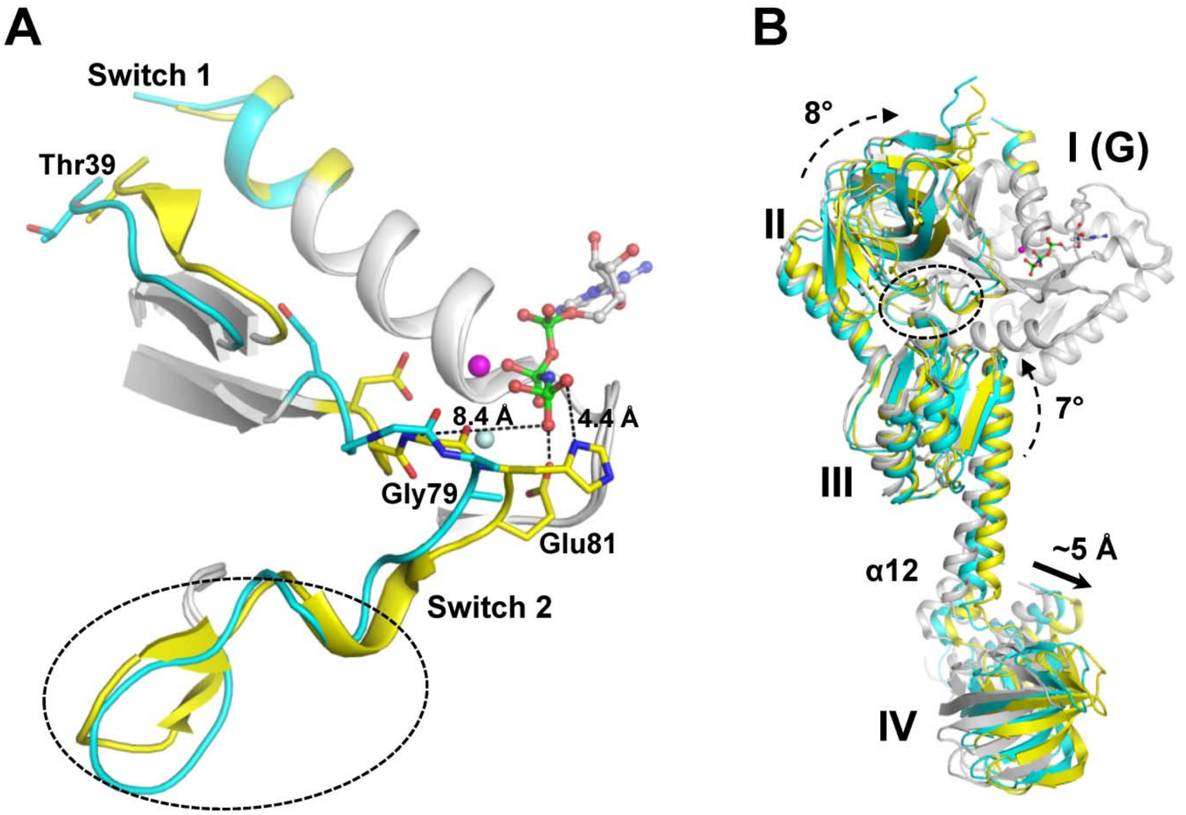

Figure S8. The articulated lever model for eIF5B/IF2 activation (Roll-Mecak et al, 2000; Roll-Mecak et al, 2001). **A)** Superposition of switch 1 and switch 2 from GDP- (cyan) and GDPNP-bound (yellow) aIF5B from *M. thermoautotrophicum* (PDB: 1G7S, 1G7T). The structural transition from the GDP-bound state to the GDPNP-bound form is limited to the N-terminal half of switch 2, which moves ~2 Å towards the nucleotide binding pocket, while switch 1 remains unaltered. Neither Thr39 in the G2 motif nor Gly79 in G3 form a direct contact to the γ-phosphate; the only potential interaction occurs between Glu81 and the γ-phosphate. The region of switch 2 forming the contacts to domain III (dashed circle) remains virtually unchanged. Compare also to Fig. S4. **B)** The GDPNP-induced shift in switch 2 is thought to cause a concerted rearrangement of domains II and III (dashed arrows), resulting in a ~5 Å shift of domain IV (arrow). The interaction interface between switch 2 and domains II and III (dashed circle) remains nearly unchanged. The switch regions are colored as in A); domains II-IV are colored grey for apo aIF5B (PDB: 1G7R), cyan for aIF5B·GDP and yellow for aIF5B·GDPNP. Compare also to Fig. S2A.