The experiments presented above are all consistent with the idea that α5-α2 mutations may function by relieving IST1 autoinhibition and thereby activate IST1 for membrane binding and assembly. However, IST1 autoinhibition and activation has not been documented, and we note that there are alternative possible explanations for the data because the IST1 α5-α2 mutations all block CHMP1B binding (which could explain the loss of abscission functions) and it is possible that the mutations simply reduce protein solubility by inducing IST1 to sample a non-native protein conformation (which could explain the repartitioning of these mutants into the membrane-bound/insoluble fraction). Hence, our experiments support the idea that IST1 can be activated by disruption of the α5-α2 interface, but do not prove this model.


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