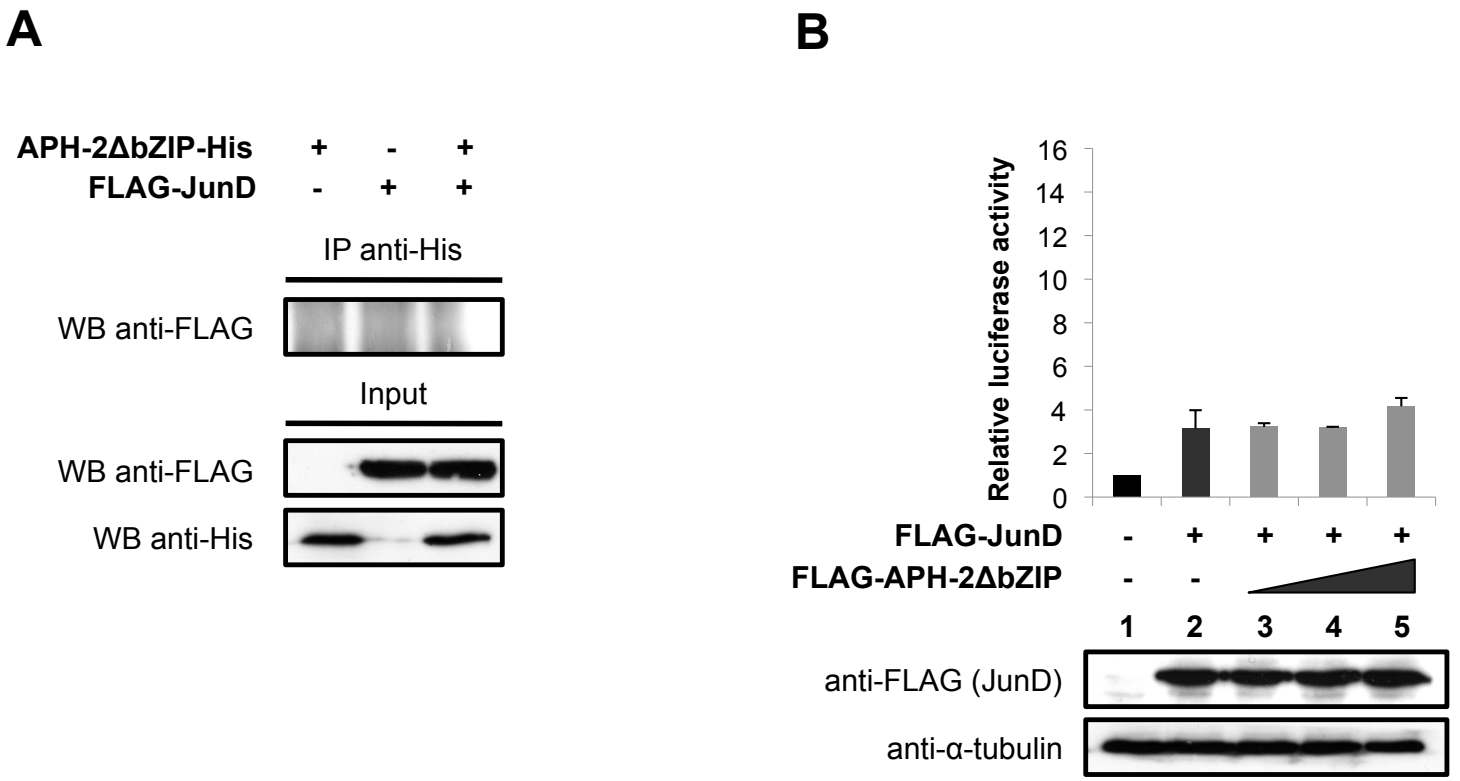**Additional File 2**