



**Fig. 1. Cryo-EM structures of human mPSF in complex with PAS RNA.** (A) Schematic drawing of the human canonical cleavage and polyadenylation 3'-end processing machinery. The mPSF is colored red. (B) Cryo-EM structure of human mPSF in complex with an AAUAAA PAS RNA (PNAS, 2018). (C) Selected 2D class averages from our samples of human mPSF in complex with a PAS RNA oligo, showing different views of the complex. (D) Cryo-EM reconstruction of mPSF in complex with RNA. (E). Cryo-EM reconstruction of mPSF where the RNA is not bound. Most of CPSF30 is disordered, and some EM density is missing in the lower right-hand corner in this view as compared to panel D. In fact, we often have both kinds of particles in the same sample, and 3D heterogeneous refinement can separate them.