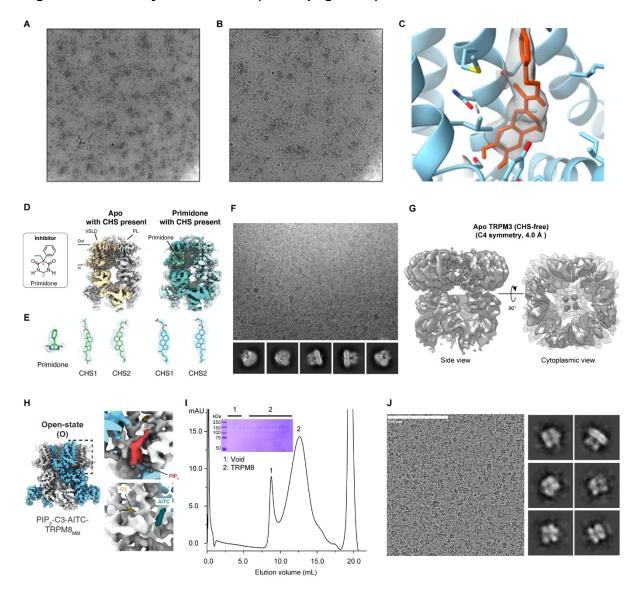
## Figures/Preliminary Data Results (max 1 page PDF)



(A and B) Representative cryo-EM micrographs of TRPV1 WT nanodisc with capsazepine at 48° C. Pixel sizes are 1.2 Å.

- **(C)** Close-up view of capsazepine in the vanilloid pocket of TRPV1 at 48°C. The cryo-EM density is shown at 0.023 thresholding.
- **(D)** Chemical structure of the ligand used for the complex structure with TRPM3 (left), 3D reconstructions of TRPM3 in apo state (middle) and inhibitor-bound state (right).
- (E) Cryo-EM densities for the bound ligands in TRPM3 structures.
- **(F)** Representative raw micrograph (top) and 2D class averages (bottom) of apo TRPM3 in the absence of CHS. Pixel size is 1.22 Å.
- (G) 3D reconstruction of apo TRPM3 in the absence of CHS.
- **(H)** 3D reconstruction of TRPM8 in complex with PIP<sub>2</sub>, C3, and AITC (left), close-up view of the EM densities for PIP<sub>2</sub> (red), C3 (yellow), AITC (teal) from the dashed box in the O state.
- (I) Gel filtration chromatogram and SDS-PAGE image (inset) of TRPM8.
- (J) Representative raw micrograph (left) and 2D class averages (right) of TRPM8 in complex with menthol. Pixel size is 0.93 Å.