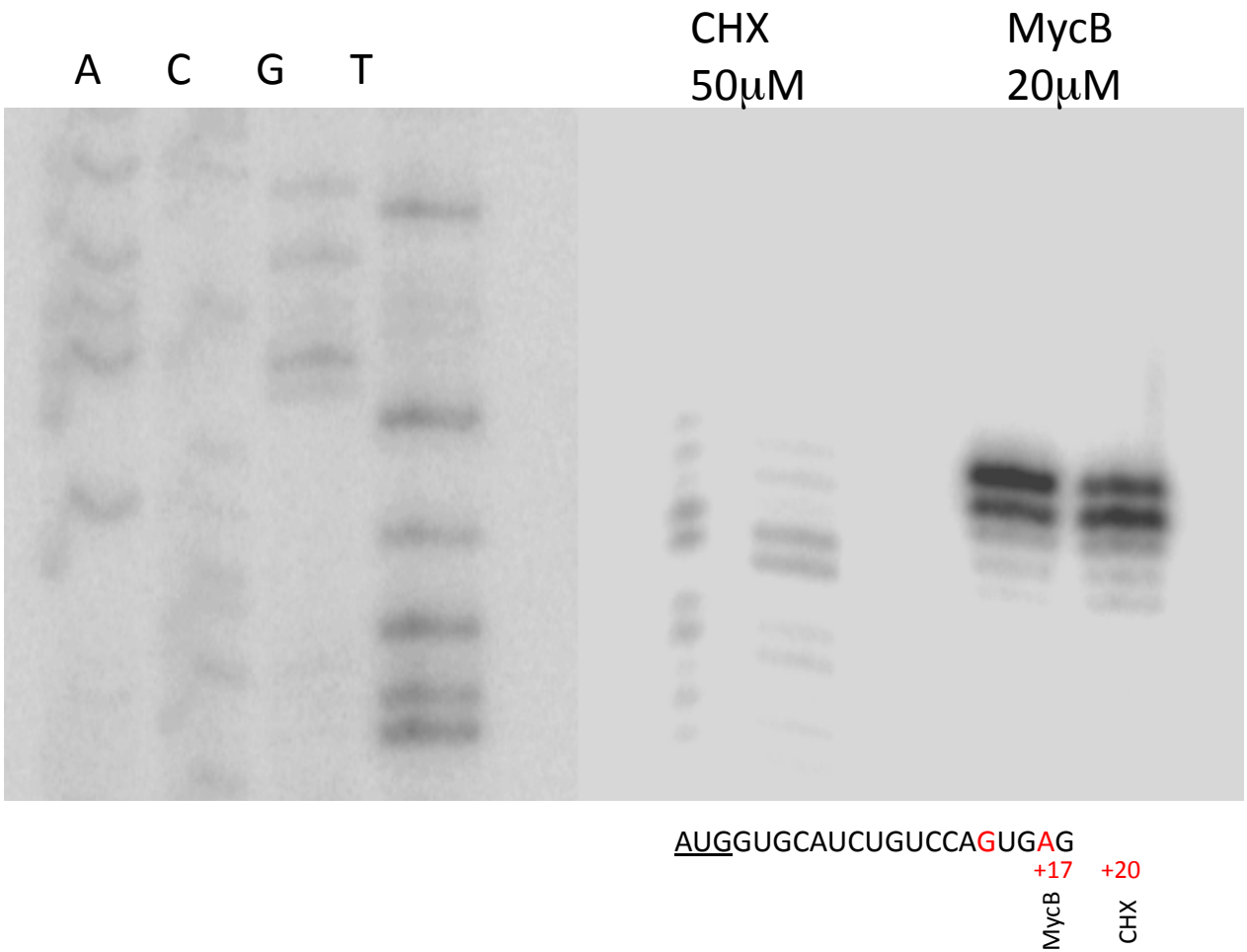
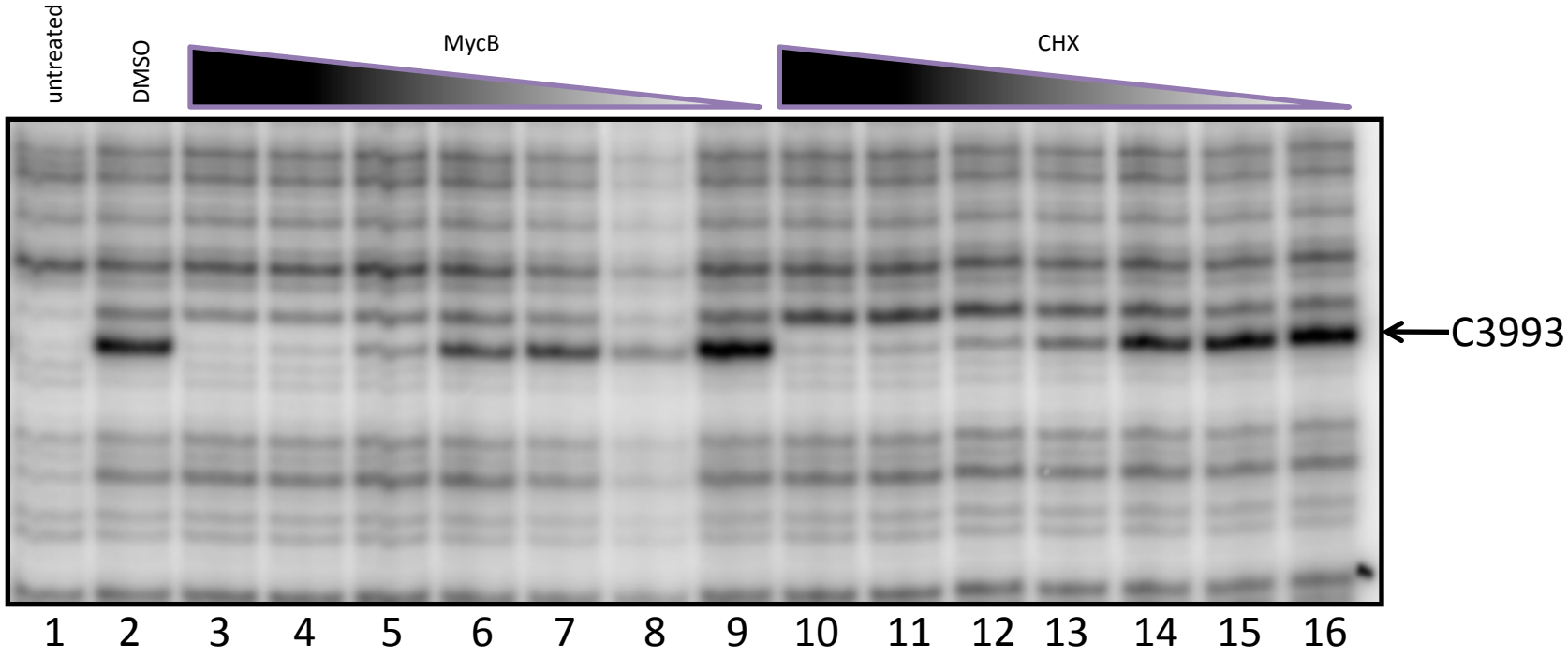
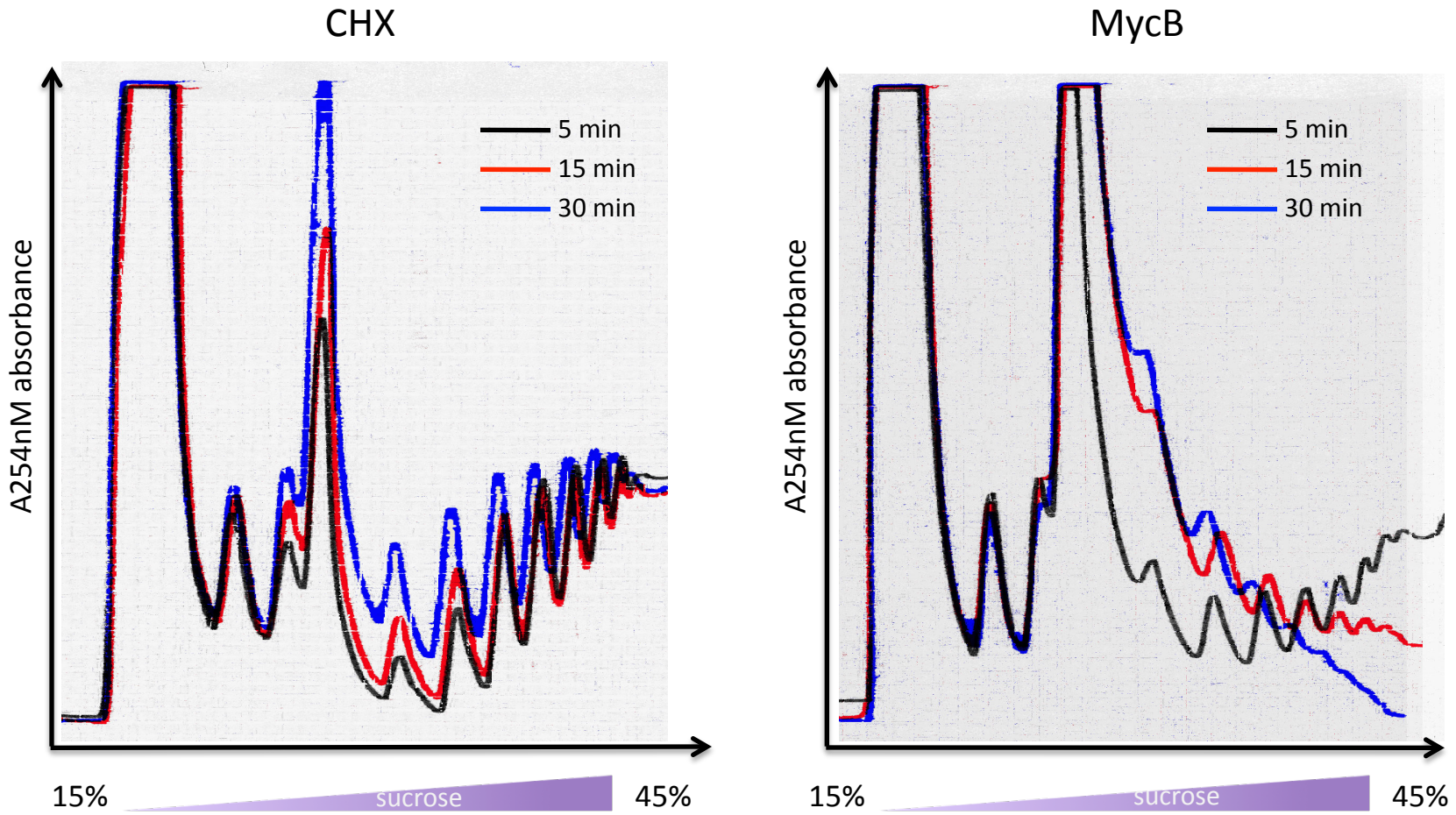


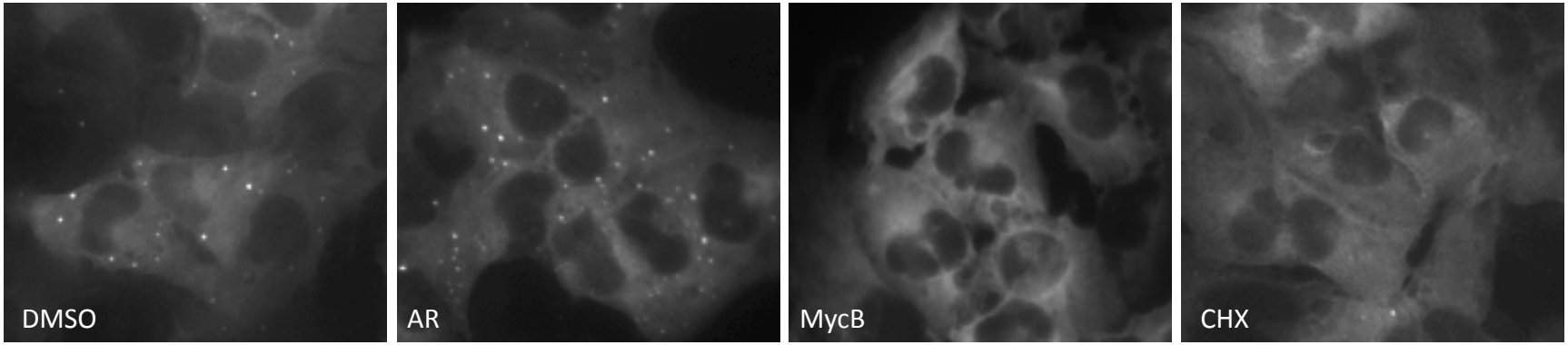
Supplemental Fig. 1. 80S fractions of lysates treated with the indicated compounds were collected and utilized in toeprinting assays by primer extension. The sequencing reactions were performed with full length β-globin and separated in the far left four lanes.



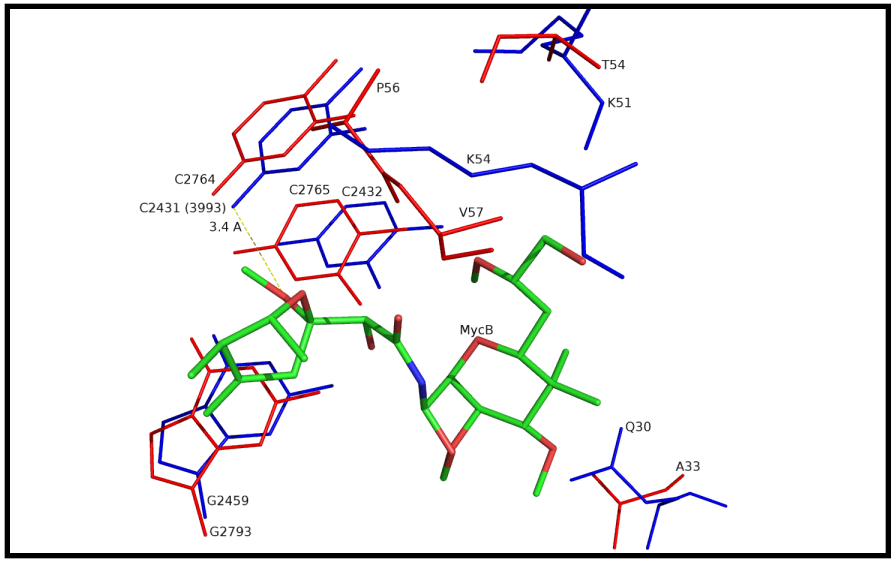
Supplemental Fig. 2. An example of a footprinting gel for K_d measurement for MycB and CHX. Concentration of CHX from lane 3-9: 500, 250, 100, 25, 5, 0.5, 0.05 μM; Concentration of MycB from lane 10-16: 10, 2, 0.5, 0.25, 0.1, 0.05, 0.01 μM.



Supplemental Fig. 3. HEK293T cells were treated with 100μg/ml CHX or 500 nM MycB for 5, 15 or 30 min and harvested with TMK100 buffer. After brief centrifugation, supernatants were loaded onto sucrose gradient for ultracentrifuge. The polysome profile was measured through the absorbance of 254nM.



Supplemental Fig. 4. Processing bodies were disturbed in U2OS cells stably expressing RFP-Dcp1α in the presence of different compounds as indicated. The images were taken with an Axioskop microscope .



Supplemental Fig. 5. Interaction of MycB (in green) with the *H. marismortui* ribosome (PDB ID: 3I55, blue). For comparison, the archaeal ribosome has been superimposed with *S. cerevisiae* ribosome (PDB ID: 3O58, red): A methyl group has been added onto the O-17 of MycA (original structure) to turn the structure into MycB. The numberings correspond to *H. marismortui* ribosome (blue) and *S. cerevisiae* (red) respectively. Note the potential H-bonding interaction between the 6-OMe group of MycB and N4-C2431. This is the conserved cytidine corresponding to C3993 in the eukaryotic ribosome for which we have shown chemical footprinting evidence). A remarkably close alignment is seen between the conserved nucleotide residues (23S of archaea — 25S of yeast): G2459—G2793, C2431 (C3993)—C2764, and C2432—C2765. In the overlay, amino acid residues A33, P56–V57, and T54 emanating from yeast ribosomal protein L42, take the place of Q30, K54, and K51 respectively belonging to the ribosomal protein L44E of *H. marismortui*.