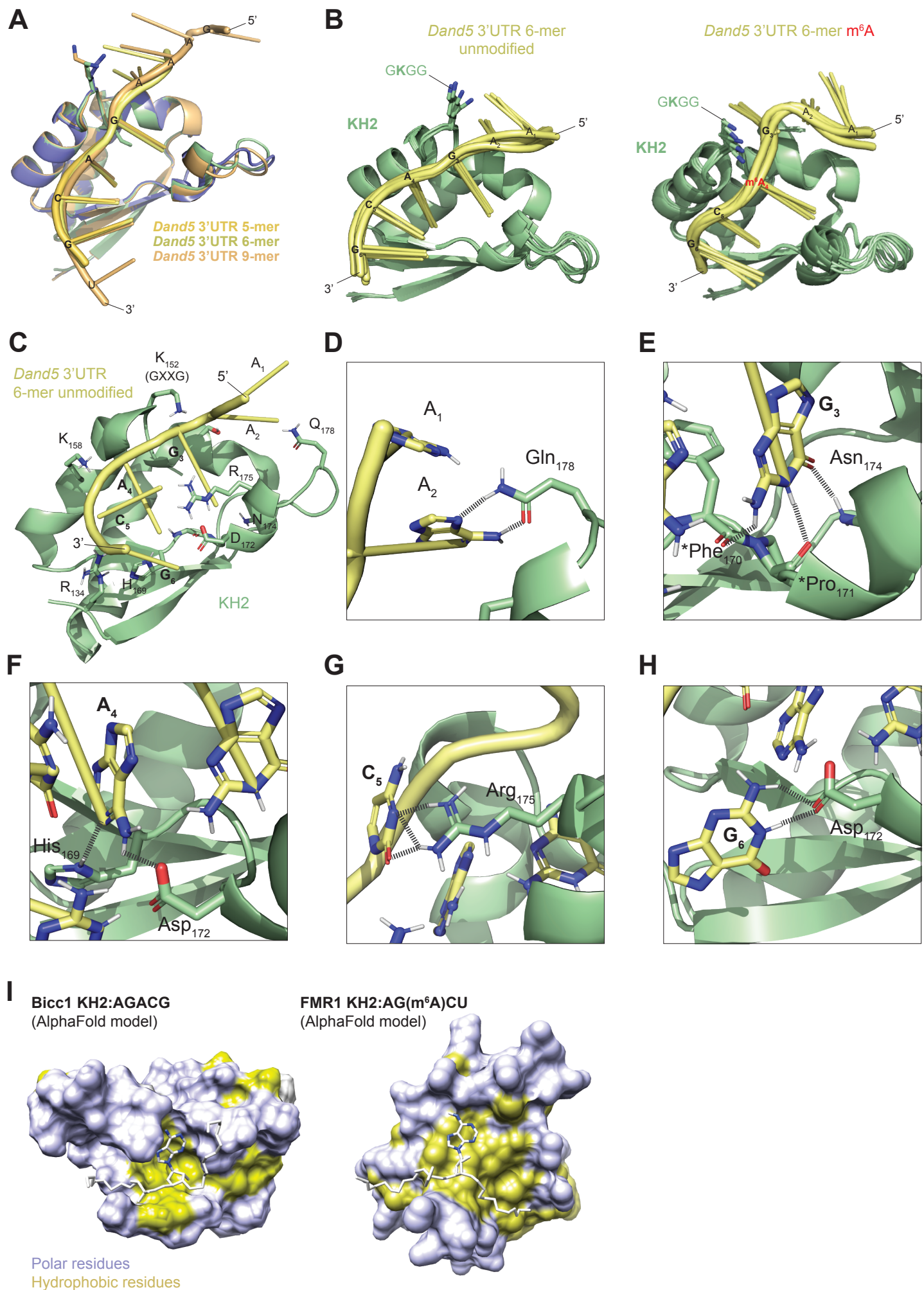


# Supplemental\_Fig\_S2



**Supplemental\_Fig\_S2. Modeling of complexes between Bicc1 KH2 domain and GACG motif-containing RNAs using AlphaFold3.** **(A)** Superimposition of 3D models generated with the AlphaFold3 algorithm between the mouse Bicc1 KH2 domain and cognate RNAs of variable length, i.e. 5-mer, 6-mer and 9-mer. All RNA ligands derive from the *Dand5* 3'UTR and contain the GACG motif. **(B)** Superimposition of the 5 best AlphaFold models of the KH2 domain bound to the RNA hexamer sequence (left) or its m<sup>6</sup>A-methylated (right). The side chain of the residue Lys152 belonging to the GXXG motif is shown. **(C)** AlphaFold structure model of the KH2 domain bound to the RNA hexamer sequence AAGACG after 5 ps of MD simulation. Side chains of amino acids involved in electrostatic contacts with phosphate backbone or nucleobases are highlighted. **(D-H)** Predicted H-bonds (distance < 4Å) between nucleobases and KH2 amino acid side chains and main chains (\*). **(I)** Comparison between the KH2 domain of Bicc1 bound to the AGACG motif and the KH2 domain of human FMR1 bound to the methylated AGm<sup>6</sup>ACU motif. The 3D model of FMR1 bound to its cognate RNA was generated using AlphaFold3. Surface representation highlights the shape of the RNA binding cleft, with polar and hydrophobic surfaces in purple and yellow, respectively. The RNA backbone is depicted in white, and the aromatic ring of the adenosine targeted by the m<sup>6</sup>A machinery is shown for clarity.