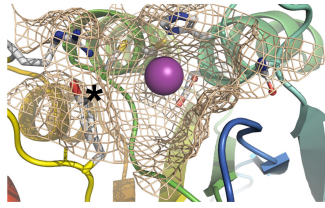
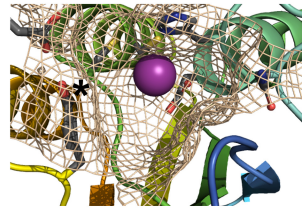


A.

Hs-AID

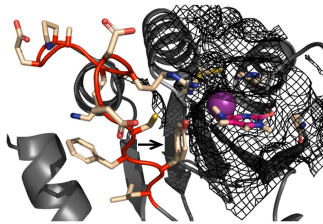


Dr-AID

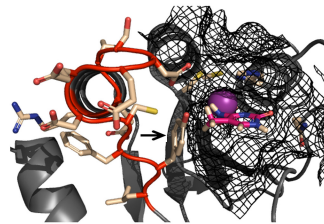
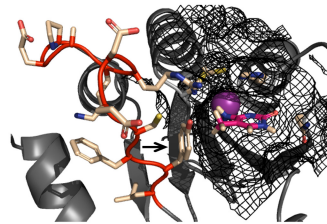
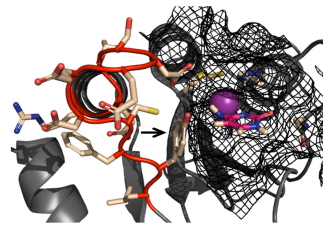


B.

Hs-AID

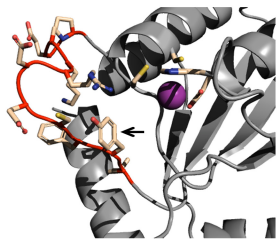


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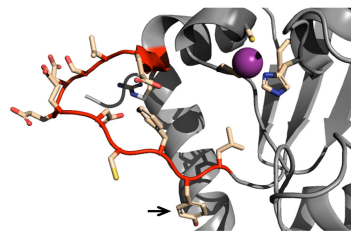
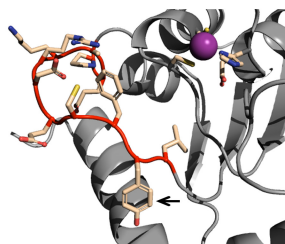
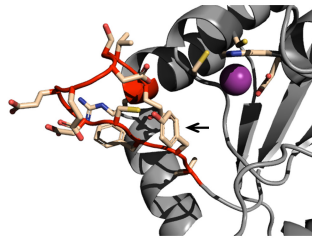


Hs-AID

C.



Dr-AID



Supplementary Figure legends:

Supplementary Figure 1. Comparison of the primary structure of AID from human and four bony fish. Residues are colored according to side-chain. Blue, green and red underlines indicate identical, similar and unlike residues. Arrows denote the borders of the catalytic domain. Sequence alignment based on published sequences of AID (Homo sapiens: AAM95406.1, Danio rerio: NP001008403, Ictalurus punctatus: AAR97544) and based on unpublished sequences (Oryzias latipes and Tetradon nigroviridis).

Supplementary Figure 2. (A) Combination ribbon and mesh model of Hs-AID (left panel) and Dr-AID (right panel), showing the position of Y114 in Hs-AID and its equivalent residue in Dr-AID (Y126) relative to the catalytic pocket. Positions of Y114 and 126 are indicated by *. (B). Combination mesh and ribbon diagram of Hs-AID (left panel) and Dr-AID (right panel) with C (top row) or mC (bottom row) docked into the catalytic pocket, showing proximity to Y114 (Hs-AID) and Y126 (Dr-AID). The backbone of the flexible loop (in Hs-AID: L113-P123, in Dr-AID: L125-R136) containing the tyrosine residue is colored in red. Arrows denote the position of Y114 and 126. (C). Comparison of the relative positions of Y114 in Hs-AID and Y126 in Dr-AID between models based on the X-ray determined structure of APOBEC3G catalytic unit (top row), or its NMR-determined structure (bottom row). Comparison of the top and bottom row reveals a high probability of significant breathing of Y114 and Y126. Arrows denote the position of Y114 and 126.