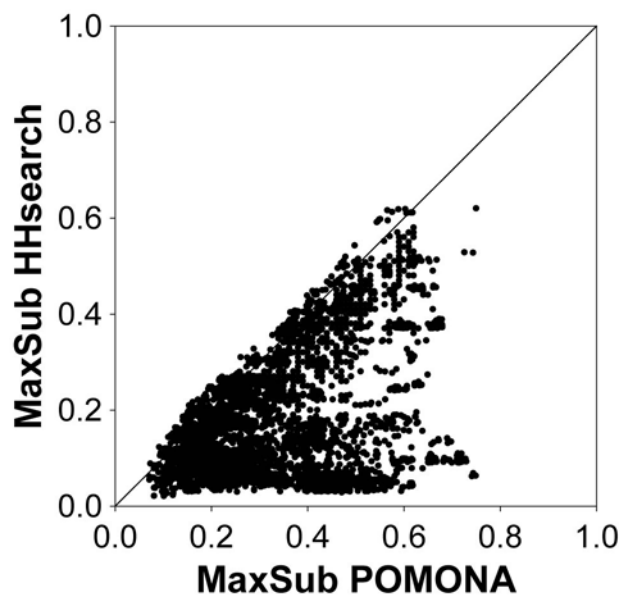


Supplementary Figure 1

Quality of protein structure alignments obtained by various methods.

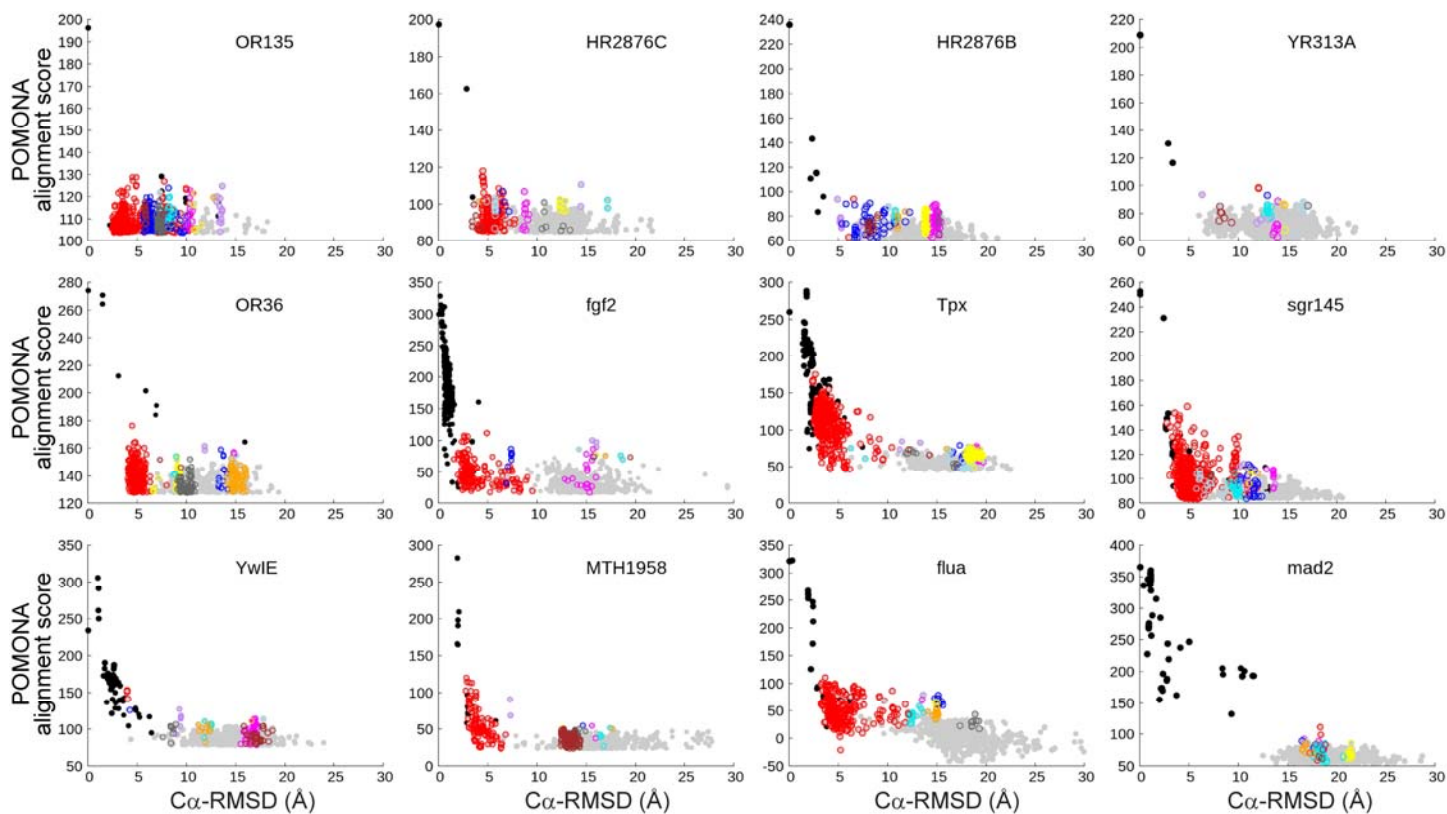
Structural quality is represented by the MaxSub score, with alignments identified by POMONA in red and by the sequence alignment method HHsearch in black, while the DALI-based structure alignment method (blue) shows the best possible alignments available in the PDB. Results are shown for each of the test proteins in **Table 1**, using a PDB from which all proteins with $\geq 20\%$ sequence identity were removed. DALI and HHsearch results correspond to default thresholds of $Z > 2$ and $\text{Prob} < 10\%$, respectively, used by these programs to identify homologs. Positive POMONA alignments are taken from the first 10 clusters (solid red bars) within the top 1,000 alignments (solid + transparent red) selected on the basis of highest H_{\square} score (equation (10)).



Supplementary Figure 2

Comparison of alignment quality obtained by sequence searching (HHsearch) and chemical shift-based alignment (POMONA).

MaxSub score of alignments obtained by HHsearch versus those obtained by POMONA (using a <20% sequence identity cutoff for both). The HHSearch alignments correspond to a setting of Prob \geq 10%.



Supplementary Figure 3

Results of POMONA alignment for the 12 test proteins not shown in **Figure 1**.

For each protein, the database proteins with the top 1,000 POMONA alignment scores are shown as a function of C^α r.m.s. deviation relative to the experimental structures, with the C^α r.m.s. deviation restricted to the aligned parts in the target protein. Gray and black dots correspond to database proteins with a sequence identities of $<20\%$ and $\geq 20\%$, respectively. For the database hits with 20% sequence identity to the query protein, the ten clusters containing the highest alignment scores are colored according to the cluster number (red, purple, blue, magenta, light blue, yellow, cyan, orange, dark gray and brown for clusters 1–10, respectively). No NOEs were used.