

Supplementary Material

Structure-Based *De Novo* Design for the Discovery of Miniprotein Inhibitors Targeting Oncogenic Mutant BRAF

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Figure S1. Amino acid sequence alignments of 14-3-3 (residues 164-232) with miniproteins (a) 76 and (b) 63. Identical and similar residues are colored in red and green, respectively.

(a)

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14-3-3 164 THPIRLGLALNFSVFYYEILNSPKACQLAKQAFDDAELDTLNEDSYKDSTLIMQLLR
miniprot 1 SIQGGARQCLVSKIKCTVANEWLDRLSLTSKAFMFVLLNEIDMLDIMLEAMGISTEEDR
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14-3-3 224 DNLTLWTSD 232
miniprot 61 EHQTTRRVNY 69
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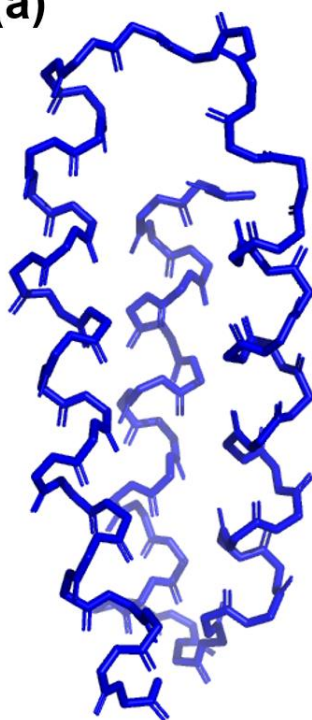
(b)

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14-3-3 164 THPIRLGLALNFSVFYYEILNSPKACQLAKQAFDDAELDTLNEDSYKDSTLIMQLLR
miniprot 1 -SIQGGARQCLVSKIKCTVANEWLDRLSLTSKAFMFVLLNEIDMLDIMLEAMGISTEEDR
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14-3-3 224 DNLTLWTSD- 232
miniprot 60 REHQTTRRVNY 69
```

Figure S2. 3D structural alignments of (a) backbone groups and (b) sidechains of 14-3-3, miniprotein 76, and miniprotein 63. Sidechain atoms of 14-3-3, miniprotein 76, and miniprotein 63 are indicated in green, cyan, and blue, respectively.

(a)



(b)

