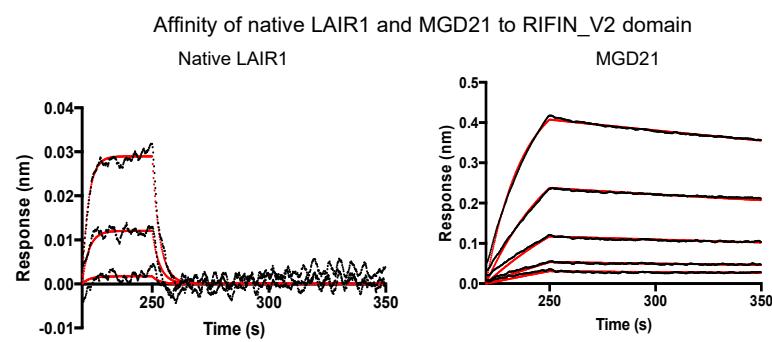
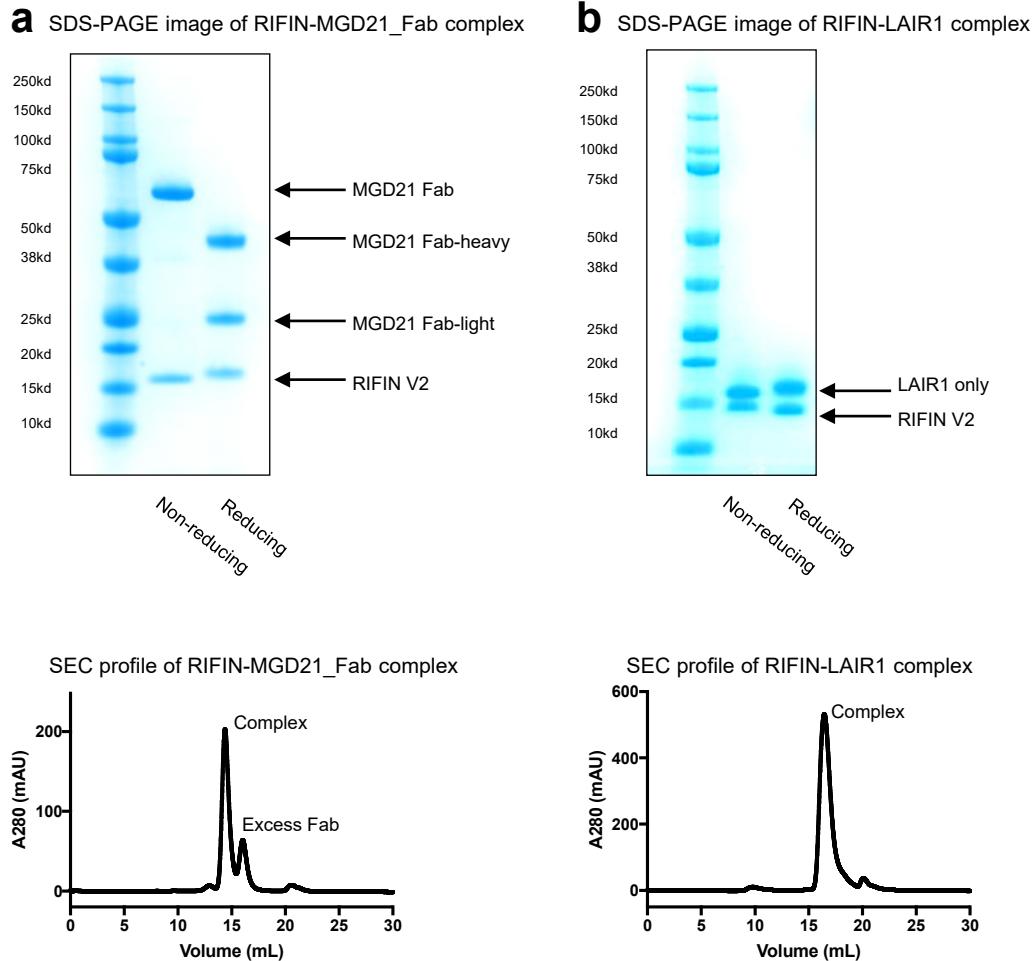


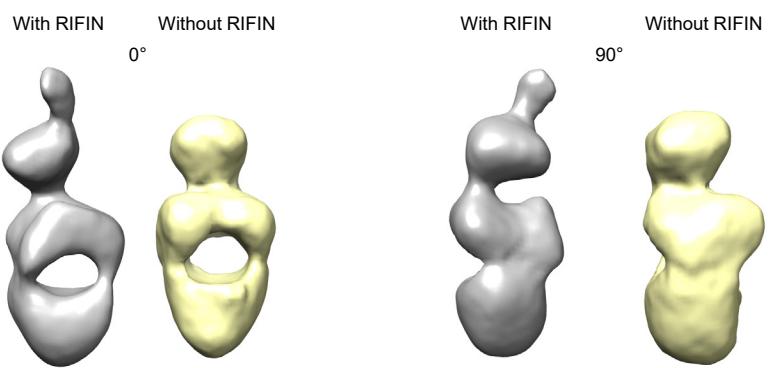
Supplementary Fig. 1 Architectural diversity of LAIR1-inserted antibodies. a, Crystal structure of two type 1 LAIR1-containing antibody Fab domains, including MGC34 and MGD21. **b,** Superimposition of MGD21 Fab structure with PDB ID 5NST. **c, and d,** ns-EM images of type 2 (MGJ5) and type 3 (MGB46) LAIR1-containing antibodies. **e,** Recognition of RIFIN by type 2 LAIR1 inserted antibodies MGJ5 and MGJ5-MGD21 chimera with MGD21-LAIR1 swapped in. nsEM image of MGJ5 chimera with or without RIFIN-V2 domain (PF3D7_1040300) (right panel). The SDS-PAGE runs were repeated at least twice.



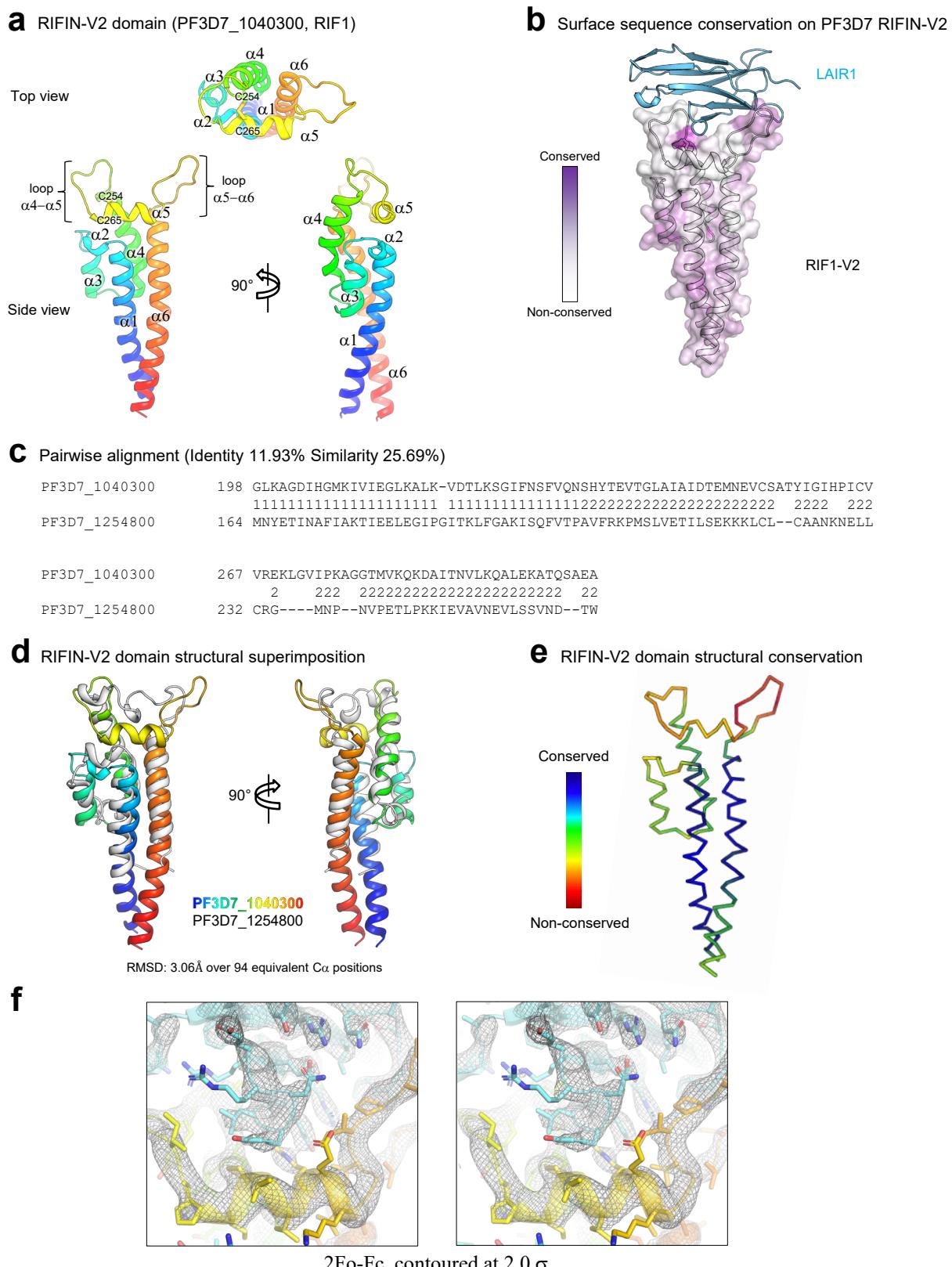
Supplementary Fig. 2 RIFIN-V2 domain mediates LAIR1 binding. Affinity of native and matured LAIR1 to RIFIN (PF3D7_1040300) V2 domain.



Supplementary Fig. 3 Expression and purification of LAIR1 and RIFIN constructs. **a**, Upper panel: SDS-PAGE image of RIFIN-MGD21_Fab (PF3D7_1400600) complex. Lower Panel: SEC profile of RIFIN-MGD21_Fab (PF3D7_1400600) complex. The SDS-PAGE runs were repeated at least twice. **b**, Upper panel: SDS-PAGE image of LAIR1-RIFIN (PF3D7_1040300) complex. Lower Panel: SEC profile of LAIR1-RIFIN (PF3D7_1040300) complex. The SDS-PAGE runs were repeated at least twice.

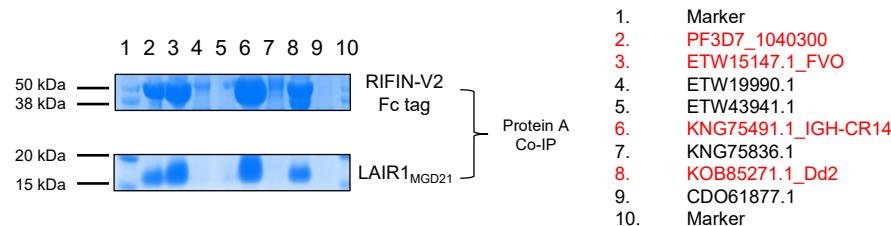


Supplementary Fig. 4 3D reconstruction of nsEM image of MGD21 Fab alone and in complex with RIFIN-V2 (PF3D7_1400600). Maps are superimposed to each other and shown in orthogonal views.



Supplementary Fig. 5 RIFIN-V2 structure and conservation. **a**, Ribbon representation of RIFIN-V2 (PF3D7_1040300, RIF1) structure viewed from two perpendicular angles. **b**, Surface sequence conservation analysis on PF3D7 RIFIN-V2 domain. **c**, Pairwise structural alignment between V2 domain of two RIFINs (PF3D7_1040300 and PF3D7_125480) by FATCAT server. **d**, Structural comparison between V2 domain of two RIFINs (PF3D7_1040300 in rainbow and PF3D7_125480 in white) in orthogonal views. **e**, Structural conservation of RIFIN-V2 domain as assessed by DALI server. **f**, Stereo image of the electron density map (2Fo-Fc, contoured at 2.0 σ) and the structure of the LAIR1-RIFIN binding interface.

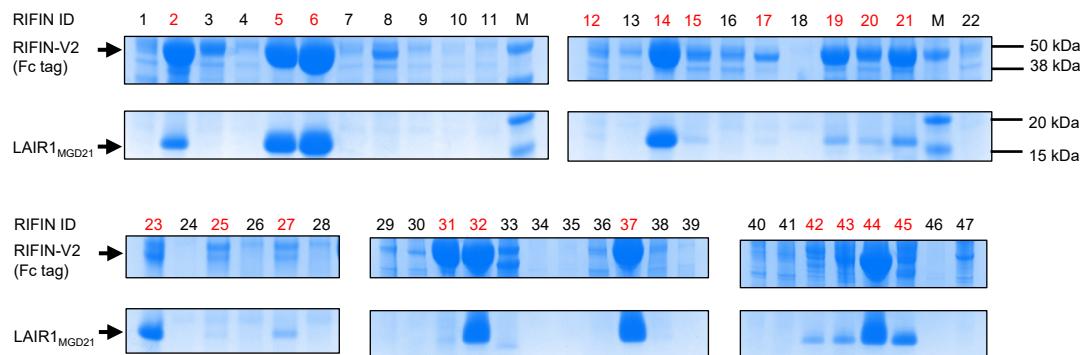
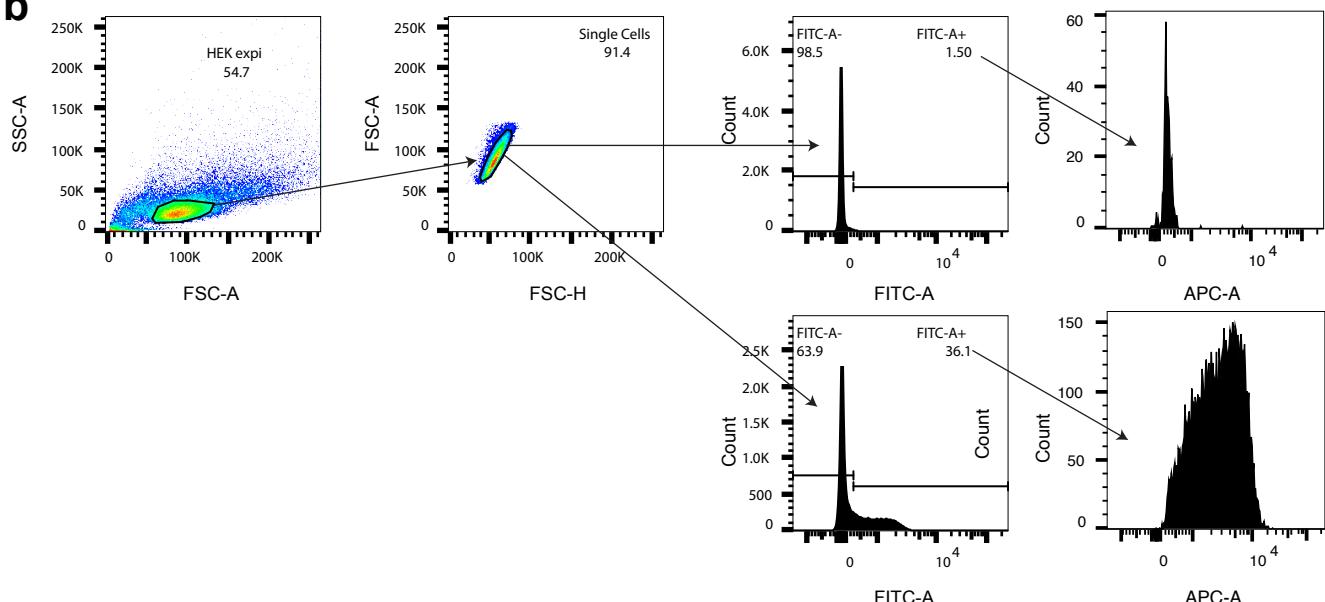
a Co-IP assay by protein-A showing LAIR1-binding by three non-3D7 RIFINs



b

KNG75491.1_IGH-CR14 ETW19990.1 ETW15147.1_FVO PF3D7_1040300 ETW43941.1 CDO61877.1 KOB85271.1_Dd2 KNG75836.1	AAAAQEAIAKGTAAGKIAKGDIHGMEIVIEGLK-VLEVRHLESGIFNSFVNNSHYTEVTKL VTAKELAKAGAAAGLKGADALGMEIVIEGLK-VLEVHTLESQIFNSFVNNSHYTEVTKL AAAMELAKQAGATAGLKGAGNTGHMNVIVIHYLK-GLKVHTLKGSIIFNSFVNNSHYTEVTGL VTAKELAKAGAAAGLKGADIGMKIVIEGLK-ALKVDTLKGSIIFNSFVNNSHYTEVTGL VTAKKLAEEAGAAAGLKGADALGMKIVIKGLK-ALKVDTLKGSIYKTFVTTKRYSEVTGL AAKKAIAIAGLFGKIVGDAKGMEIVIKGLD-VLKADKLIPEIFNSFKNSRHYTEVLDL AAATELAKQAGAAAGLKGADAAGLNVVIGSLKRYLYIDKLNNETPLQSFFTSTSVDVTAI VAAAEAAAMAEGLAEAGIKAGQVAGLAKFIDGFKDFIMDSLNGTQLKSLFTLQNYTNFPNL .::* : * * * .*: * : * .: . * .: . * .: . * .: . * .: . * .: . * .: .
KNG75491.1_IGH-CR14 ETW19990.1 ETW15147.1_FVO PF3D7_1040300 ETW43941.1 CDO61877.1 KOB85271.1_Dd2 KNG75836.1	AIAIDTEMNEVCATSATIG--SQPICALRGKGLVAKPGQSKVEQIDAITKVLKQALEKAT ASVIDTEMNKVCFG----SHPIICALREKGLVAVPGRKMVNQKDAITKVLKQALEKAT VDIINTQMNEVCATSATYIG--THPICVVNRNALGLEAVPGKAKVEQIDVIRRVLNEALEKAT AIAIDTEMNEVCATSATYIG--IHPICVVREKLGVIPKAGGTMVKQKDAITNVVLKQALEKAT VDIIDTEMNKVCSVTYVG--DQSICAVRNALGVIPKPGGTMVNQKDAITNVVTDVFDKAK VDIINTQLNTTCSTGATAHVQNSICVVRETLGVIPKAGGKMVEQKTAITNVLDKALAKAT ANAIDAEADMASCLGSSFG--THTICALRGKGLGLEAVPGGTMVNQKDAITRMINGLVGKAK TRLINEELNKACSVWLTG--SNPICEVRTKLGIVAQAGQKWVEPESIILHVDKIVAESQ . *: :: * .: . ** :* **: . . * * : * : * : : : .
KNG75491.1_IGH-CR14 ETW19990.1 ETW15147.1_FVO PF3D7_1040300 ETW43941.1 CDO61877.1 KOB85271.1_Dd2 KNG75836.1	SSANAKATQVAATKTAALETAQKGAI SSANAKATQVAATKTAALETAQKGAI SSANAKATQVAADKTAEFKIANVGA QSAEALSETTAEDVAKLTAQKTA LSADTEAANVIKATSSKIIAKQT SSANAAAKIAKKEVTAAGKNTGA GTAKAVADSKNAEVVAELTAQKT GAAAGVTKTVTEEATTLTAQKTGV :* : : : : : : : : : : : : :

Supplementary Fig. 6 Identification of additional LAIR1 binding RIFINs from non-3D7 strains. a, Co-immunoprecipitation showing LAIR1-binding by three non-3D7 RIFINs. The SDS-PAGE runs were repeated at least twice. **b**, RIFIN V2 sequence alignment (RIFINs shown by co-immunoprecipitation to be positive for LAIR1 binding labeled in red font).

a**b**

Supplementary Fig. 7 Characterization of RIFIN-LAIR1/LILRB1 interaction. **a**, Coomassie blue-stained SDS-PAGE to assess the co-IP between the LAIR1 domain of MGD21 and various RIFINS. (Related to Fig. 4c with additional Fc-tagged RIFIN-V2 bands shown) Positive LAIR1 binding RIFIN IDs are indicated in red. Lanes marked with “M” are molecular ladders with molecular weights as marked. The SDS-PAGE runs were repeated at least twice. **b**, Gating strategy to determine the percentage of RIFIN positive HEK cells (FITC-A + compartment) and RIFINS that binds to LAIR1 antibodies (APC-A compartment).