Supplemental Information

Crystal structure of isoflurane bound to integrin LFA-1 supports a unified mechanism of volatile anesthetic action in the immune and central nervous systems

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- **Supplemental Figure 1**
- **Supplemental Table 1**

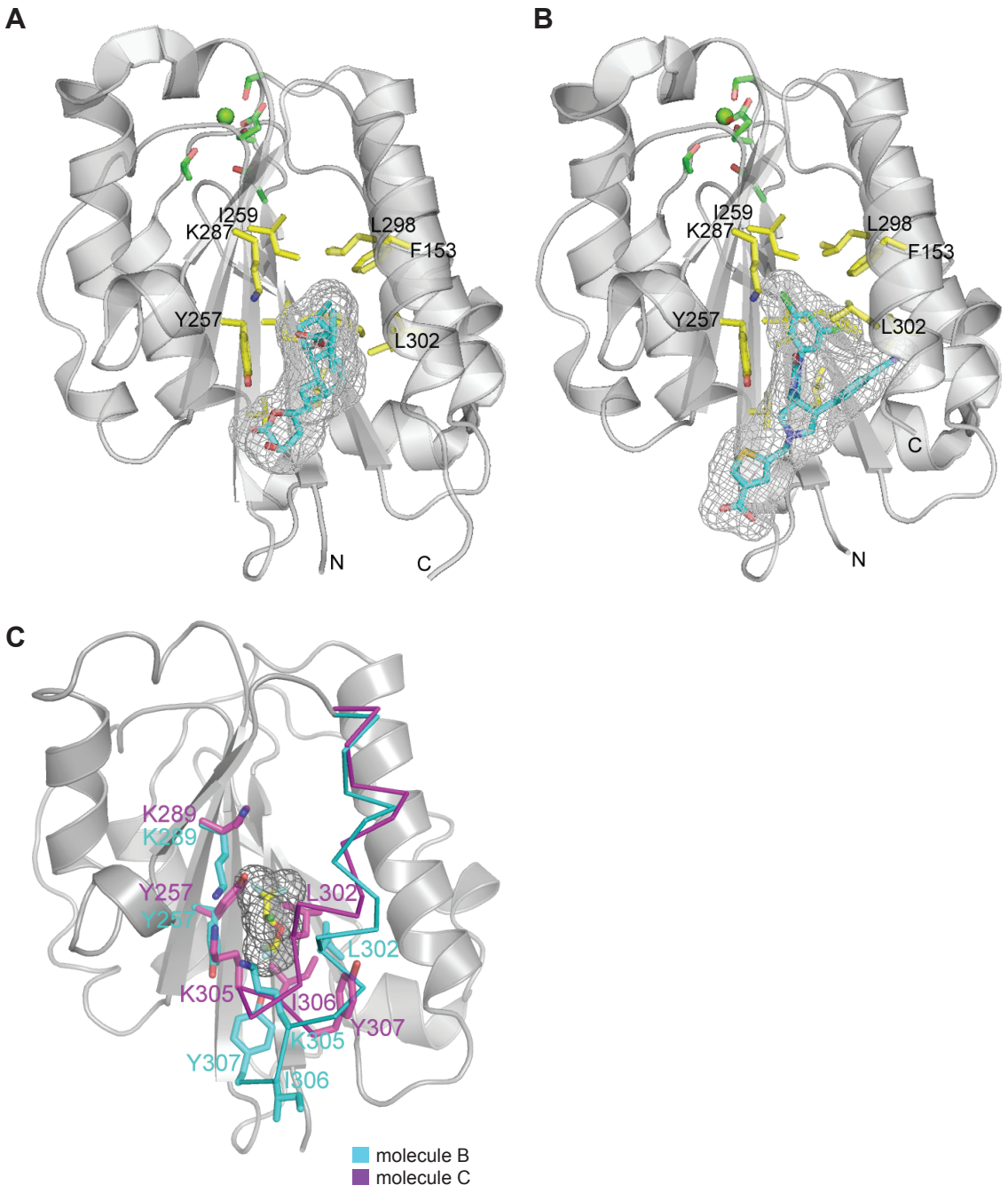

Figure S1. Interactions with I domain by LFA-1 antagonists or isoflurane. (**A&B**) Ribbon diagram display of the I domain in complex with the inhibitor lovastatin (**A**, PDB code 1CQP) and the spirocyclic hydantoin-based compound 8 (**B**, PDB code 2ICA). The side-chains of the antagonist-interacting (yellow) and the MIDAS (green) residues are shown as a stick model with red oxygen and blue nitrogen atoms. The Mg^{2+} ions at the MIDAS are depicted as green spheres. Lovastatin and compound 8 are shown as a stick model with cyan carbon, red oxygen, yellow sulfur, and blue nitrogen, and green chloride atoms. A mesh representation of Van der Waals surface is shown for the antagonists. (**C**) A crystal lattice contact-induced distortion of the C-terminal α7 helix in molecule C excluding isoflurane binding. The superposition of molecules B and C is shown by a gray ribbon diagram except for the C-terminal helix which is shown with cyan (molecule B) and magenta (molecule C) sticks. The side-chains, whose orientations substantially differ in molecules B and C, are shown as a stick model with the same colors as the corresponding α7 helix and red oxygen and blue nitrogen atoms, labeled accordingly. Bound isoflurane in molecules B is depicted as a stick model with carbon (yellow), oxygen (red), chloride (green), and fluorine (sky blue) atoms color-coded. A mesh representation of Van der Waals surface for the bound isoflurane is shown.

Table S1: Data reduction and refinement statistics

PDB code	3F74 (- isoflurane)	3F78 (+ isoflurane)
Space group	$P2_1$	$P2_1$
a (Å)	61.8	62.7
b (Å)	85.6	85.87
c (Å)	63.6	63.97
β (°)	117.93	118.18
Molecule/asymmetric unit	3	3
Wavelength (Å)	0.97931	0.97931
Resolution (Å)	20-1.70	20-1.60
Unique reflections	64731	76838
Completeness (%)	99.9 (99.8)	97.9 (90.4)
R_{sym}[a] (%)	7.0 (57.3)	6.5 (61.6)
I/σ (I)	18.9 (2.1)	22.2 (1.7)
Redundancy	3.9 (3.7)	4.4 (3.3)
Reflections (work/test)	61381/3280	72906/3872
R^b/R_{free} (%)	14.58/17.79	15.28/18.08
Ramachandran plot (favored/allowed/outlier %)	97.2/2.8/0	96.8/3.2/0
Protein/water atoms	4426/708	4458/644
Average B-factor (Å^2)	14.8	22.8[c]
R.m.s.d. from ideal values		
Bond lengths (Å)	0.009	0.008
Bond angles (°)	1.202	1.187

Numbers in parentheses are for the highest resolution shell

[a]$Rsym=\sum_{hkl}|I-\langle I\rangle|/\sum I$, where I is the observed intensity and <I> is the average intensity from observations of symmetry-related reflections. A subset of the data (5%) was excluded from the refinement and used to calculate Rfree.

[b]$R=\sum||Fo|-|Fc||/\sum|Fo|$.

[C]the average B-factor for molecules A, B, and C; the value for only the isoflurane-bound structures (i.e., molecule A and B) is 20.8 Å^2