Benoît Grellier, Fabrice Le Pogam, Marc Vitorino, Jean-Philippe Starck, Michel Geist, Vanessa Duong, Hélène Haegel, Thierry Menguy, Jean-Yves Bonnefoy, Jean-Baptiste Marchand, and Philippe Ancian

3D modeling and characterization of the human CD115 monoclonal antibody H27K15 epitope and design of a chimeric CD115 target

2013; mAbs 6(2)

http://dx.doi.org/10.4161/mabs.27736

Supplemental Legends

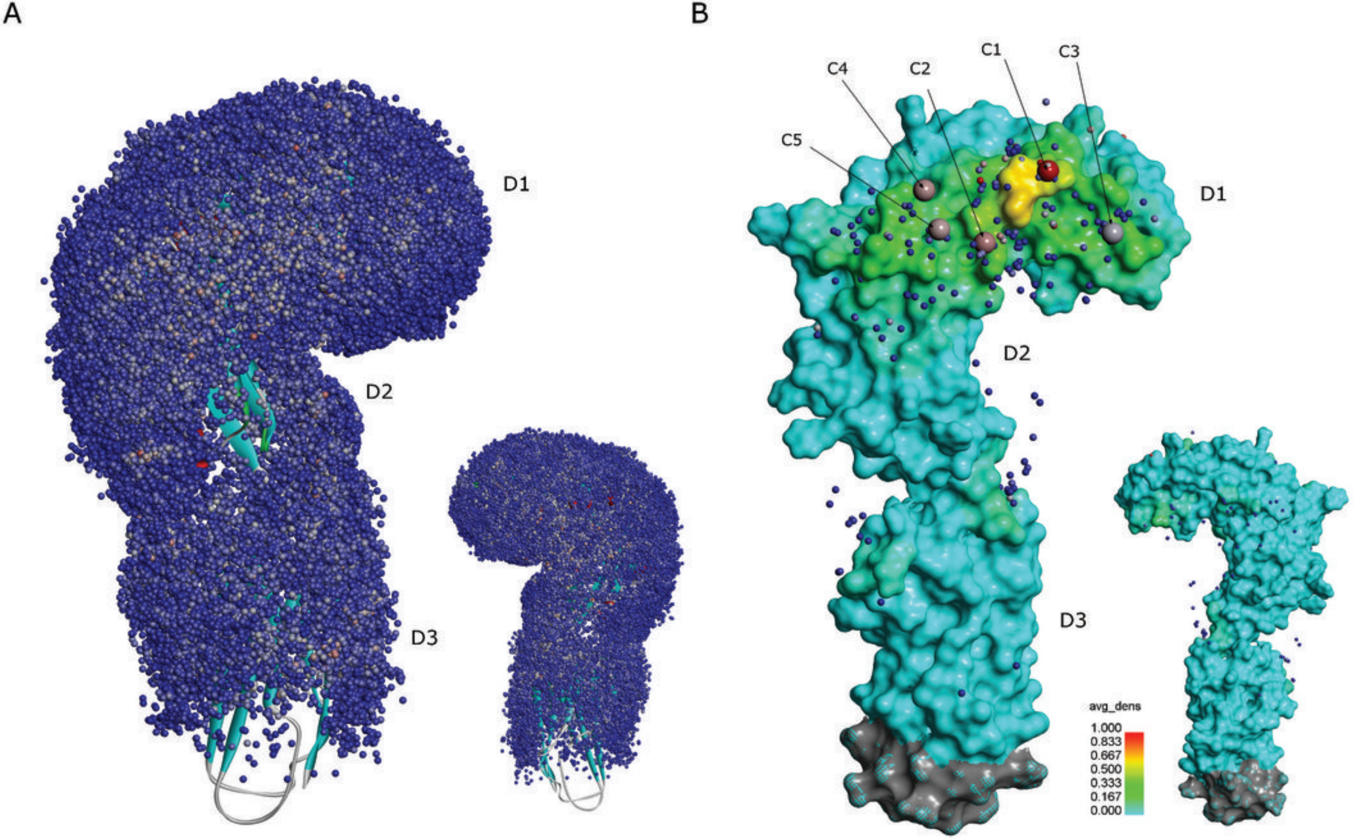
Supplementary Figure 1. Docking results between hCD115$_{D1\text{-}D3}$ crystal structure and H27K15 4m model. **A**: localization of the 54,000 poses assessed for docking analysis. The C-terminal region of the CD115 D3 domain was excluded from the analysis. **B**: the average density colored surface was calculated with Discovery Studio from the best 2,000 ZRANK poses. The top 200 poses used for spatial clustering are shown as small spheres; centers from the 5 clusters with the highest density of poses are shown as large spheres (C1 to C5); domain excluded from analysis is indicated in gray. Small panels, reverse views. Views were generated with Discovery Studio v3.5.

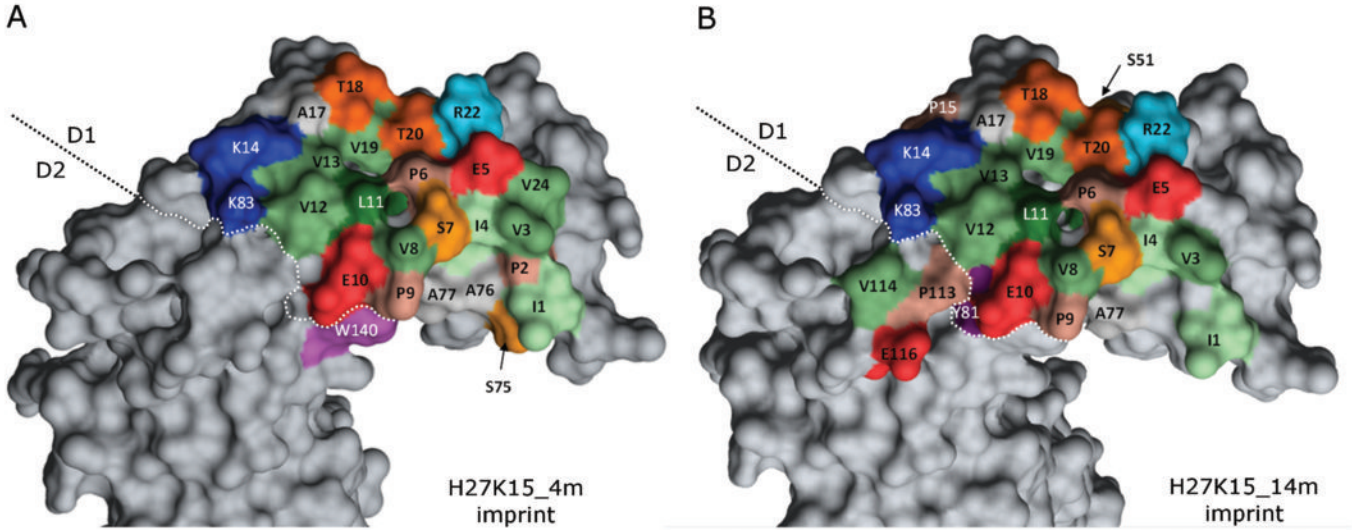
Supplementary Figure 2. Predicted epitope surface of H27K15 after docking on hCD115 model. D1/D2 delimitation is drawn in dotted line. Interacting residues of hCD115 are indicated, colored by amino acids. Panel **A**, 4m epitope; Panel **B**, 14m epitope.

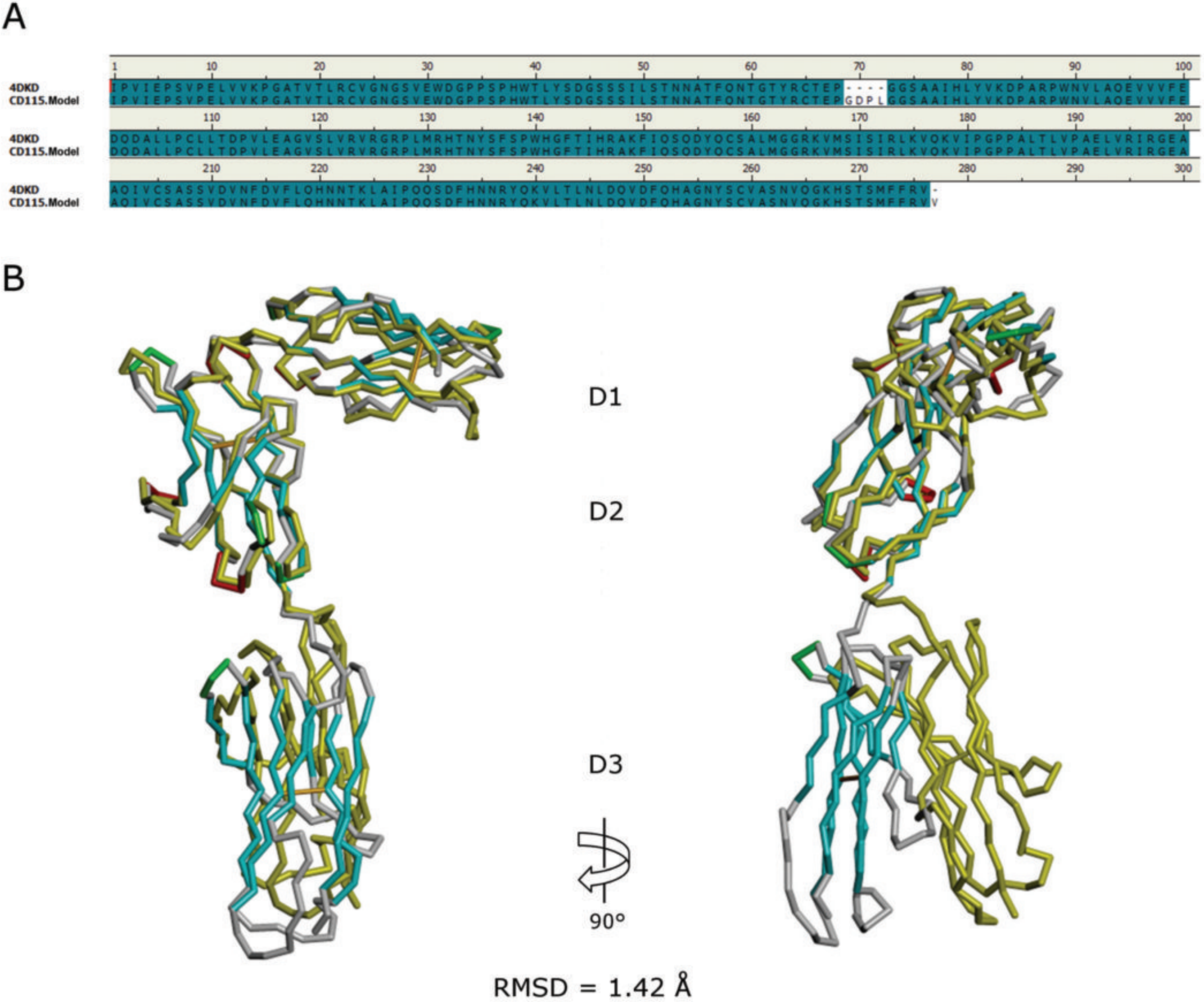
Supplementary Figure 3. Structural alignment of hCD115 model and crystal. **A**, sequence alignment; the gap illustrates the unresolved loop in the crystal. **B**, structural alignment of D1-D2 main chains. RMSD refers to D1-D2 only.

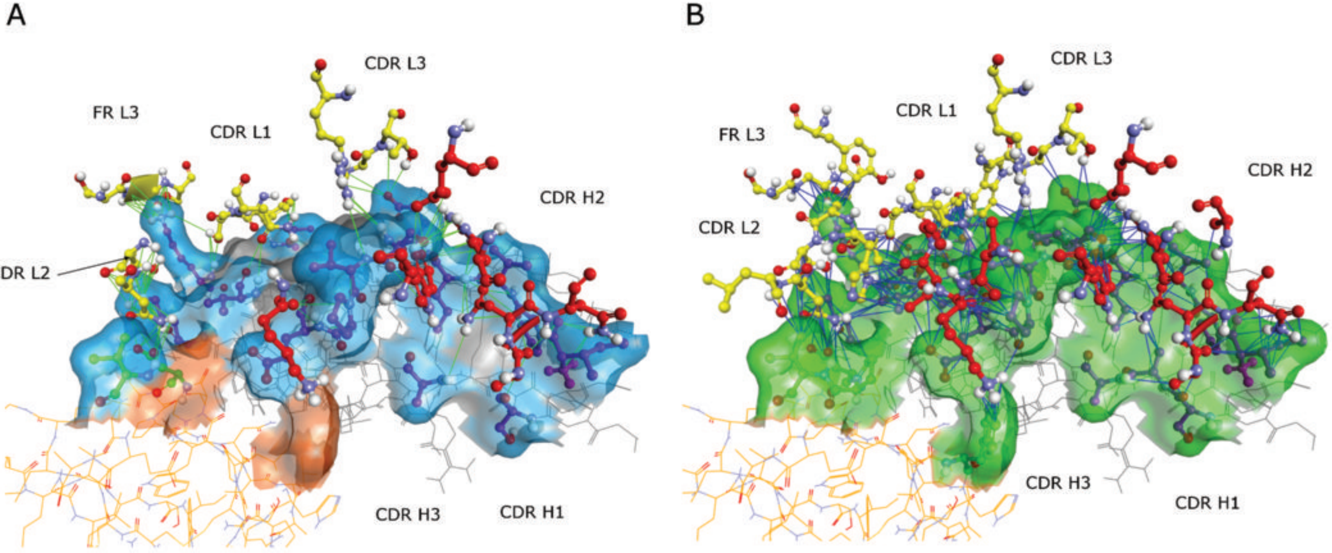
Supplementary Figure 4. H27K15/hCD115 interface according to (**A**) polar and (**B**) Van der Waals interactions. Grey, D1 domain; orange, D2 domain; blue, polar interacting residues; green, residues involved in Van der Waals interactions; yellow, light chain; red, heavy chain.

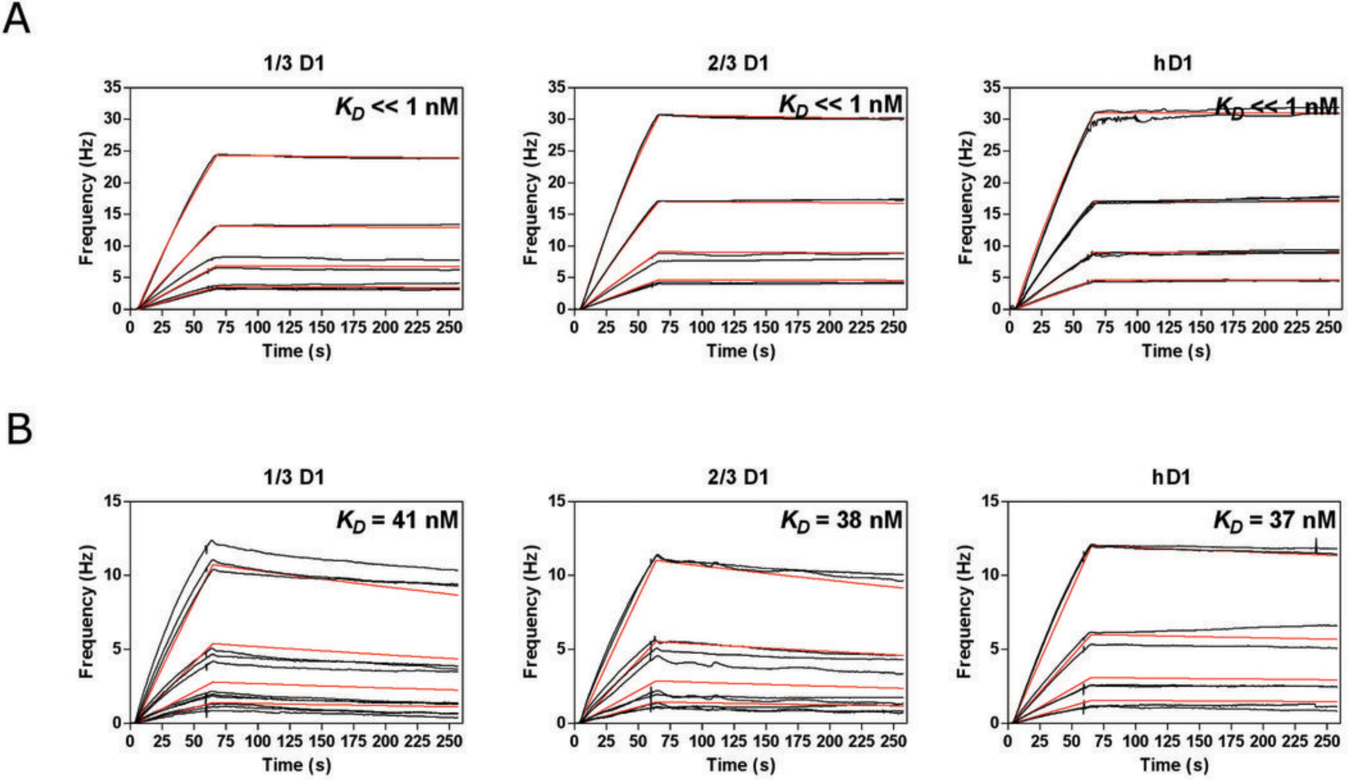
Supplementary Figure 5. Quartz Crystal Microbalance association and dissociation profiles of the mouse ligands mCSF-1 **(A)** or mIL-34 **(B)** with the immobilized chimeric $CD115_{D1\text{-}D5}$ constructs 1/3 D1, 2/3D1 and hD1. Raw data (black); model fitting (red). Kinetics parameters deduced from these curves are reported in Table IV.


A
D1
D2
D3
B
C4
C2
C1
C3
C5
D1
D2
D3
avg_dens
1.000
0.833
0.667
0.500
0.333
0.167
0.000


A
T18
A17
R22
D1
D2
K14
V19
T20
V13
P6
E5
V24
K83
V12
L11
S7
I4
V3
V8
P2
E10
P9
A77
A76
I1
W140
S75
H27K15_4m
imprint
B
S51
P15
T18
A17
R22
D1
D2
K14
V19
T20
V13
P6
E5
K83
L11
V12
S7
I4
V3
V8
V114
P113
E10
Y81
P9
A77
I1
E116
H27K15_14m
imprint


A
1
10
20
30
40
50
60
70
80
90
100
4DKD IPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNTGTYRCTEP----GGSAAIHLYVKDPARPWNVLAQEVVVFE
CD115.Model IPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNTGTYRCTEPGDPLGGSAAIHLYVKDPARPWNVLAQEVVVFE
110
120
130
140
150
160
170
180
190
200
4DKD DQDALLPCLLTDPVLEAGVSLVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAELVRIRGEA
CD115.Model DQDALLPCLLTDPVLEAGVSLVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAELVRIRGEA
210
220
230
240
250
260
270
280
290
300
4DKD AQIVCSASSVDVNFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQHAGNYSCVASNVQGKHSTSMFFRV-
CD115.Model AQIVCSASSVDVNFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQHAGNYSCVASNVQGKHSTSMFFRVV
B
D1
D2
D3
90°
RMSD = 1.42 Å


A
CDR L3
FR L3
CDR L1
CDR H2
CDR L2
CDR H3
CDR H1
B
CDR L3
CDR L1
FR L3
CDR H2
CDR L2
CDR H3
CDR H1


A
1/3 D1
K_D << 1 nM
2/3 D1
K_D << 1 nM
hD1
K_D << 1 nM
Frequency (Hz)
0 5 10 15 20 25 30 35
Time (s)
0 25 50 75 100 125 150 175 200 225 250
B
1/3 D1
K_D = 41 nM
2/3 D1
K_D = 38 nM
hD1
K_D = 37 nM
Frequency (Hz)
0 5 10 15
Time (s)
0 25 50 75 100 125 150 175 200 225 250