Fig. 1

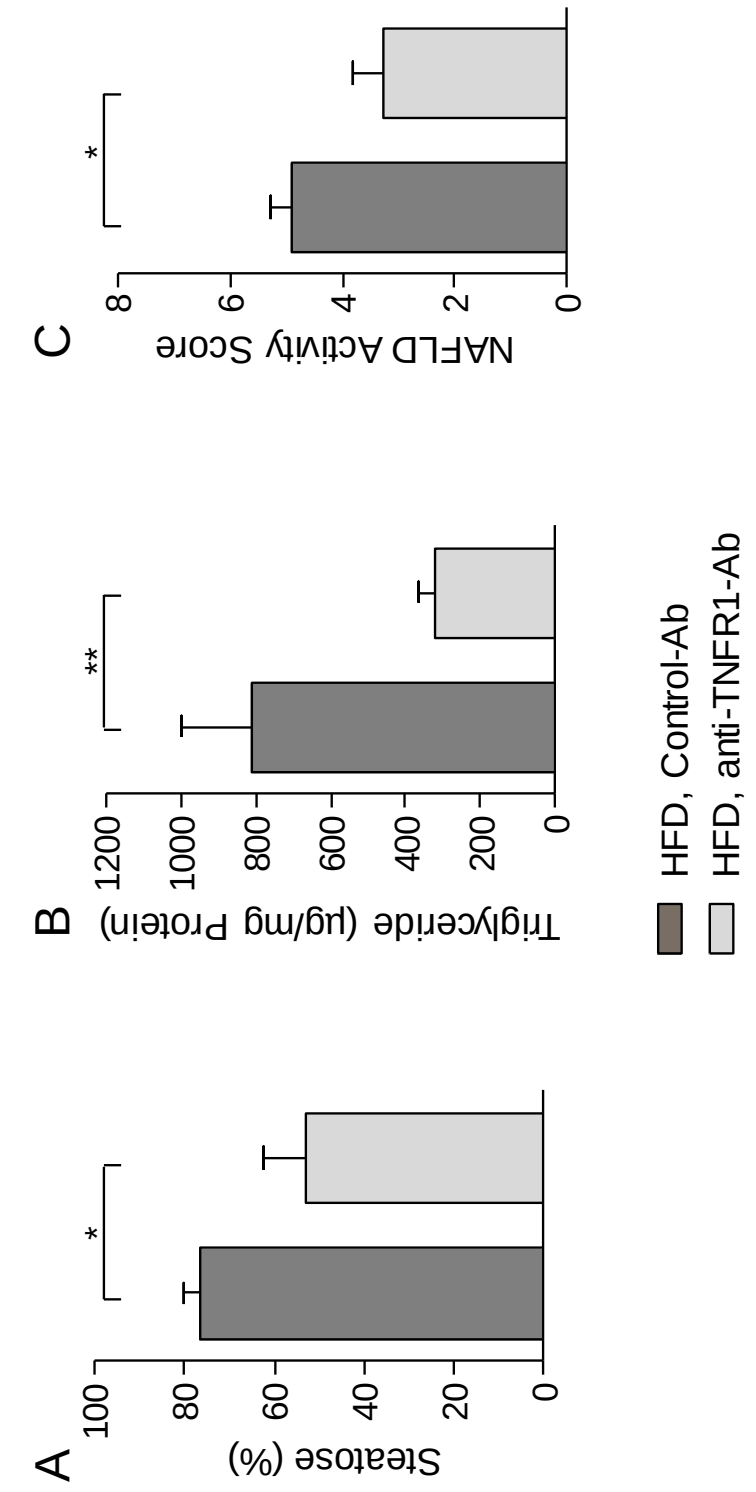

A
Steatose (%)
100
80
60
40
20
0
*
B
Triglyceride (µg/mg Protein)
1200
1000
800
600
400
200
0
**
C
NAFLD Activity Score
8
6
4
2
0
*
HFD, Control-Ab
HFD, anti-TNFR1-Ab

Fig. 2

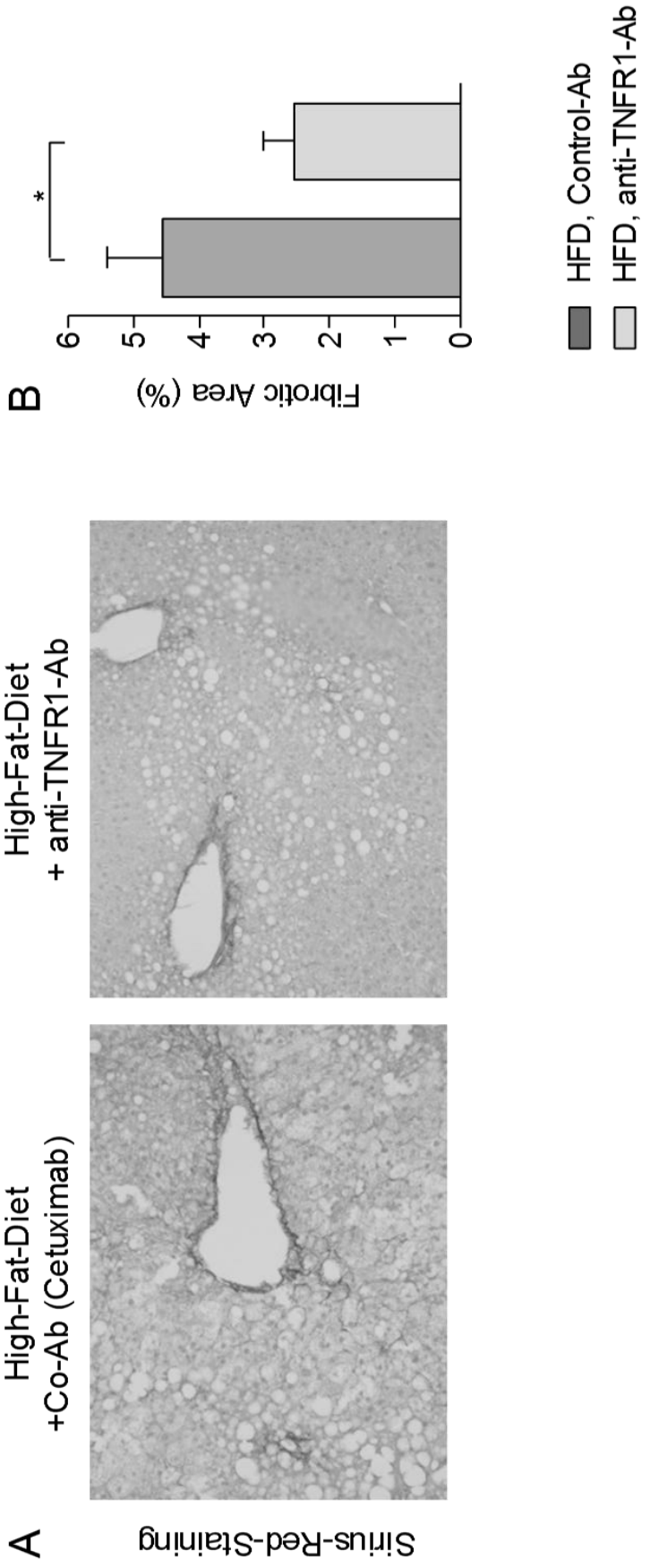

A
Sirius-Red-Staining
High-Fat-Diet
+Co-Ab (Cetuximab)
High-Fat-Diet
+ anti-TNFR1-Ab
B
Fibrotic Area (%)
0
1
2
3
4
5
6
*
HFD, Control-Ab
HFD, anti-TNFR1-Ab

Fig. 3

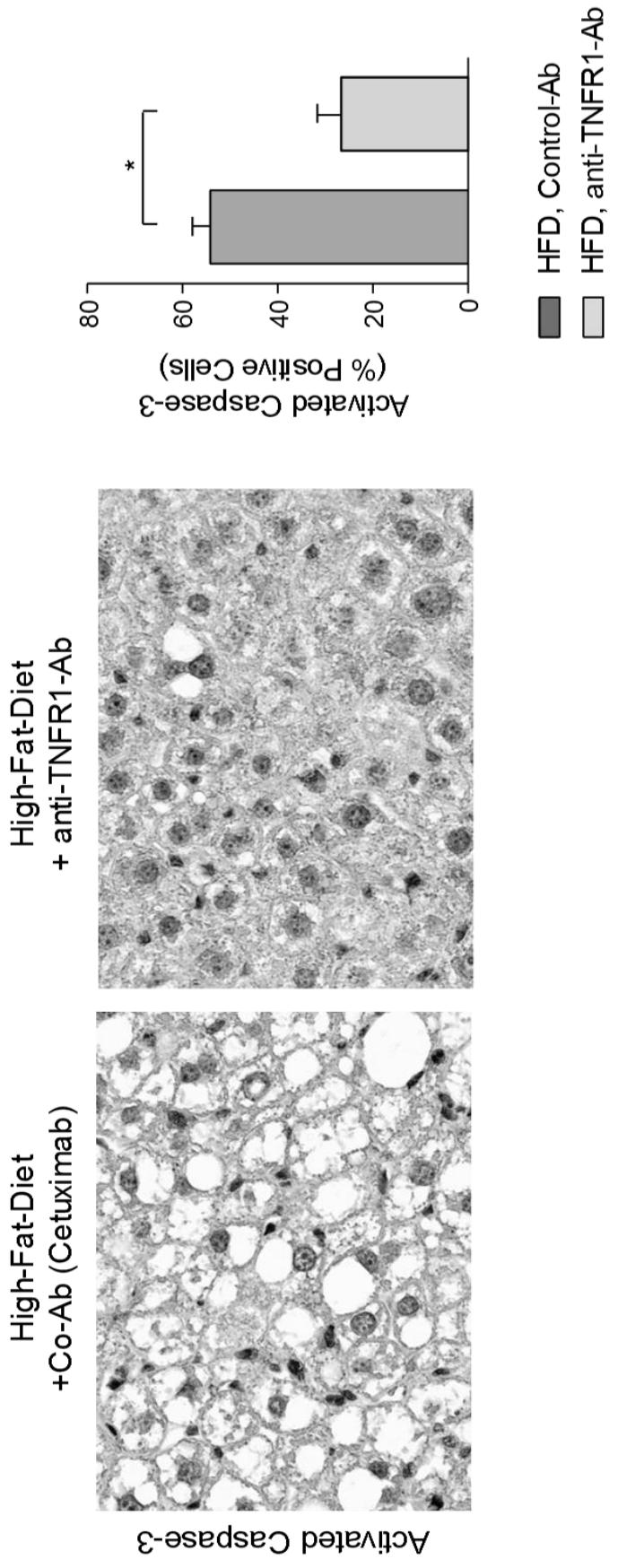

Activated Caspase-3
(% Positive Cells)
0
20
40
60
80
*
HFD, Control-Ab
HFD, anti-TNFR1-Ab
High-Fat-Diet
+Co-Ab (Cetuximab)
High-Fat-Diet
+ anti-TNFR1-Ab
Activated Caspase-3

Fig. 4

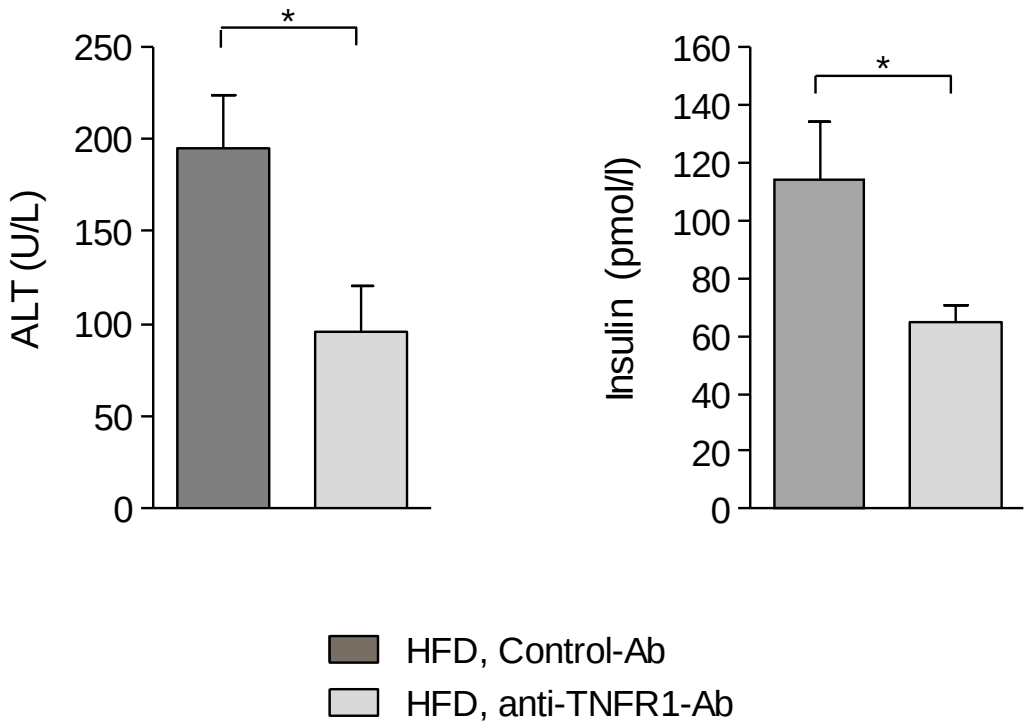

ALT (U/L)
250
200
150
100
50
0
*
Insulin (pmol/l)
160
140
120
100
80
60
40
20
0
*
HFD, Control-Ab
HFD, anti-TNFR1-Ab

Fig. 5:

SEQ ID NO:1:VH-CDR1
DFYIN

SEQ ID NO:2: VH-CDR2
EIXPXXGXAXYNXKFKA
wherein
X at position 3 is any of Y or V;
X at position 5 is any of Y, T, S or G;
X at position 6 is any of S or Q;
X at position 8 is any of H or E;
X at position 10 is any of Y or K;
X at position 13 is any of E or D.

SEQ ID NO:3: VH-CDR3
WDFLDY

SEQ ID NO:4: VL-CDR1
RSSQSLLHSNGNTYLH

SEQ ID NO:5: VL-CDR2
TVSNRFS

SEQ ID NO:6: VL-CDR3
SQXTHVPYT
wherein X at position 3 is any of S or G

SEQ ID NO:7: VH of IgG13.7/ Fab13.7
HVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIVPSQG
EAKYNDKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVTV
SS

SEQ ID NO:8: VL of IgG13.7/ Fab13.7
DVQMTQSPSSLSASVGDRVTITCRSSQSLLHSNGNTYLHWYQQKPGKAPKLLIYTVS
NRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPYTFGGGTKVEIKRTV
AA

SEQ ID NO:9: VH of ATROSAB/ IZI06.1
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIYPYSG
HAYYNEKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVTV
SS

Fig. 5 (continued):

SEQ ID NO:10: VL of ATROSAB/ IZI06.1
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGNTYLHWYLQKPGQSPQLLIYTVSN
RFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPYTFGGGTKVEIKR

SEQ ID NO:11: (Fab13.7 Heavy chain [bold = VH])
HVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIVPSQG
EAKYNDKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC

SEQ ID NO:12: (Fab13.7 Light chain [bold = VL])
DVQMTQSPSSLSASVGDRVTITCRSSQSLLHSNGNTYLHWYQQKPGKAPKLLIYTV
SNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPYTFGGGTKVEIKR
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO:13: ***VL1C (VL13.7-CH2-CH31; VL and CH1 containing chain):***
DVQMTQSPSSLSASVGDRVTITCRSSQSLLHSNGNTYLHWYQQKPGKAPKLLIYTV
SNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPYTFGGGTKVEIKG
TGGGSGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQP
REPSVFPLAPSSKSTSGGTAALGCLVKDYFPSDIAVEWESGALTSGVHTFPAVLQS
SGLYSLSSVVTVPSSSLGTQTYSCSVMHEALHNHYTQKSVEPKSC

VL1C detailed:

SEQ ID NO:14: VL13.7
DVQMTQSPSSLSASVGDRVTITCRSSQSLLHSNGNTYLHWYQQKPGKAPKLLIYTVS
NRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPYTFGGGTKVEIK

SEQ ID NO:15: Linker
GTGGGSG

SEQ ID NO:16: CH2
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAK

SEQ ID NO:17: CH31
GQPREPSVFPLAPSSKSTSGGTAALGCLVKDYFPSDIAVEWESGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYSCSVMHEALHNHYTQKSVEPKSC

SEQ ID NO:18: ***VHkC (VH13.7-CH2-CH3kappa; VH and CLk containing chain*)**:
HVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIVPSQG
EAKYNDKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVT
VSSGTGGGSGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKA
KGQPREPSVFIFPPSDEQLKSGTASVVCLVNNFYPRDIAVEWEVDNALQSGNSQES
VTEQDSKDSTYSLSSTLTLSKADYEKHKVYSCSVMHEALHNHYTQKSFNRGEC

Fig. 5 (continued):

VHkC detailed:

SEQ ID NO:19: VH13.7
HVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIVPSQG
EAKYNDKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVTV
SS

SEQ ID NO:15: Linker
GTGGGSG

SEQ ID NO:16: CH2
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAK

SEQ ID NO:20: CH3k
GQPREPSVFIFPPSDEQLKSGTASVVCLVNNFYPRDIAVEWEVDNALQSGNSQESVT
EQDSKDSTYSLSSTLTLSKADYEKHKVYSCSVMHEALHNHYTQKSFNRGEC

SEQ ID NO:21: ***VL1C (VL13.7-CH2-CH31; VL and CH1 containing chain):***
gatgtgcagatgacccagagccccagcagcctgtctgccagcgtgggcgacagagtgaccatcacctgtcggagcag
ccagagcctgctgcacagcaacggcaacacctacctgcattggtatcagcagaagcccggcaaggcccccaagctg
ctgatctacaccgtgtccaacagattcagcggcgtgccctctagattctccggctctggcagcggcaccgacttcaccctg
accatctctagcctgcagcccgaggacttcgccacctactactgcagccagtccacccacgtgccgtatacctttggcgg
aggcaccaaggtggaaatcaaaggtaccggcggaggatctggccctagcgtgttcctgttcccccccaaagcccaagg
acaccctgatgatctcccggacccccgaagtgacctgcgtggtggtggatgtgtcccacgaggaccctgaagtgaagttt
aattggtacgtggacggcgtggaagtgcataacgccaagaccaagcccagagaggaacagtacaacagcacctac
cgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaagtgcaaggtgtccaacaa
gggcctgcccagcagcatcgagaaaaccatcagcaaggccaagggccagcctcgggaaccctccgtgtttcctctgg
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ccgtggaatgggagtctggcgccctgaccagcggagtgcatacctttccagcagtgctccagagcagcggcctgtaca
gcctgagcagcgtcgtgacagtgcccagctctagcctgggcacccagacctactcttgcagcgtgatgcacgaggccct
gcacaaccactacacccagaaaagcgtggaacccaagagctgc

SEQ ID NO:22: ***VHkC (VH13.7-CH2-CH3kappa; VH and CLk containing chain*):**
cacgtgcagctggtgcagtctggcgccgaagtgaagaaacccggcagcagcgtgaaggtgtcctgcaaggccagcg
gctacaccttcaccgacttctacatcaactgggtgcgccaggctccaggacagggcctggaatggatcggcgagatcgt
gcctagccagggcgaggccaagtacaacgacaagttcaaggccagagtgaccatcaccgccgacaagagcacca
gcaccgcctacatggaactgagcagcctgcggagcgaggacaccgccgtgtactactgcgccagatgggacttcctg
gactactggggccagggcaccaccgtgacagtctcgagcggtaccggcggaggatctggccctagcgtgttcctgttcc
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gaccctgaagtgaagttcaattggtacgtggacggcgtggaagtgcacaacgccaagaccaagcccagagaggaac
agtacaacagcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggcaaagagtacaag
tgcaaggtgtccaacaagggcctgcccagcagcatcgagaaaaccatcagcaaggccaagggccagcctcgggaa
cccagcgtgttcatcttcccaccctccgacgagcagctgaagtctggcacagccagcgtcgtgtgcctcgtgaacaactt
ctaccccagagacattgccgtggaatgggaggtggacaacgccctccagagcggcaacagccaggaaagcgtgac
cgagcaggacagcaaggactccacctacagcctgagcagcaccctgaccctgagcaaggccgactacgagaaac
ataaggtgtacagctgctccgtgatgcacgaggccctgcacaaccactacacccagaagtccttcaaccggggcgagt
gc

Fig. 5 (continued):

SEQ ID NO:23
DFYIN

SEQ ID NO:24
EIYPYSGHAYYNEKFKA

SEQ ID NO:25
WDFLDY

SEQ ID NO:26
RSSQSLLHSNGNTYLH

SEQ ID NO:27
TVSNRFS

SEQ ID NO:28
SQSTHVPYT

SEQ ID NO:29:
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDFYINWVRQAPGQGLEWIGEIYPYSG
HAYYNEKFKARVTITADKSTSTAYMELSSLRSEDTAVYYCARWDFLDYWGQGTTVTV
SS

SEQ ID NO:30:
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGNTYLHWYLQKPGQSPQLLIYTVSN
RFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPYTFGGGTKVEIKR

SEQ ID NO:31: human IgG1 Fc:
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA
KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO:32: huTNFR1 sequence:
MGLSTVPDLLLPLVLLELLVGIYPSGVIGLVPHLGDREKRDSVCPQGKYIHPQNNSICC
TKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCLSCSKCRKEMGQVEIS
SCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCLNGTVHLSCQEKQNTVCTCHA
GFFLRENECVSCSNCKKSLECTKLCLPQIENVKGTEDSGTTVLLPLVIFFGLCLLSLLFI
GLMYRYQRWKSKLYSIVCGKSTPEKEGELEGTTTKPLAPNPSFSPTPGFTPTLGFSP
VPSSTFTSSSTYTPGDCPNFAAPRREVAPPYQGADPILATALASDPIPNPLQKWEDSA
HKPQSLDTDDPATLYAVVENVPPLRWKEFVRRLGLSDHEIDRLELQNGRCLREAQYS
MLATWRRRTPRREATLELLGRVLRDMDLLGCLEDIEEALCGPAALPPAPSLLR

SEQ ID NO:33: IgG1 hinge region:
DKTHTCPPCPAPELLGG

Fig. 6:

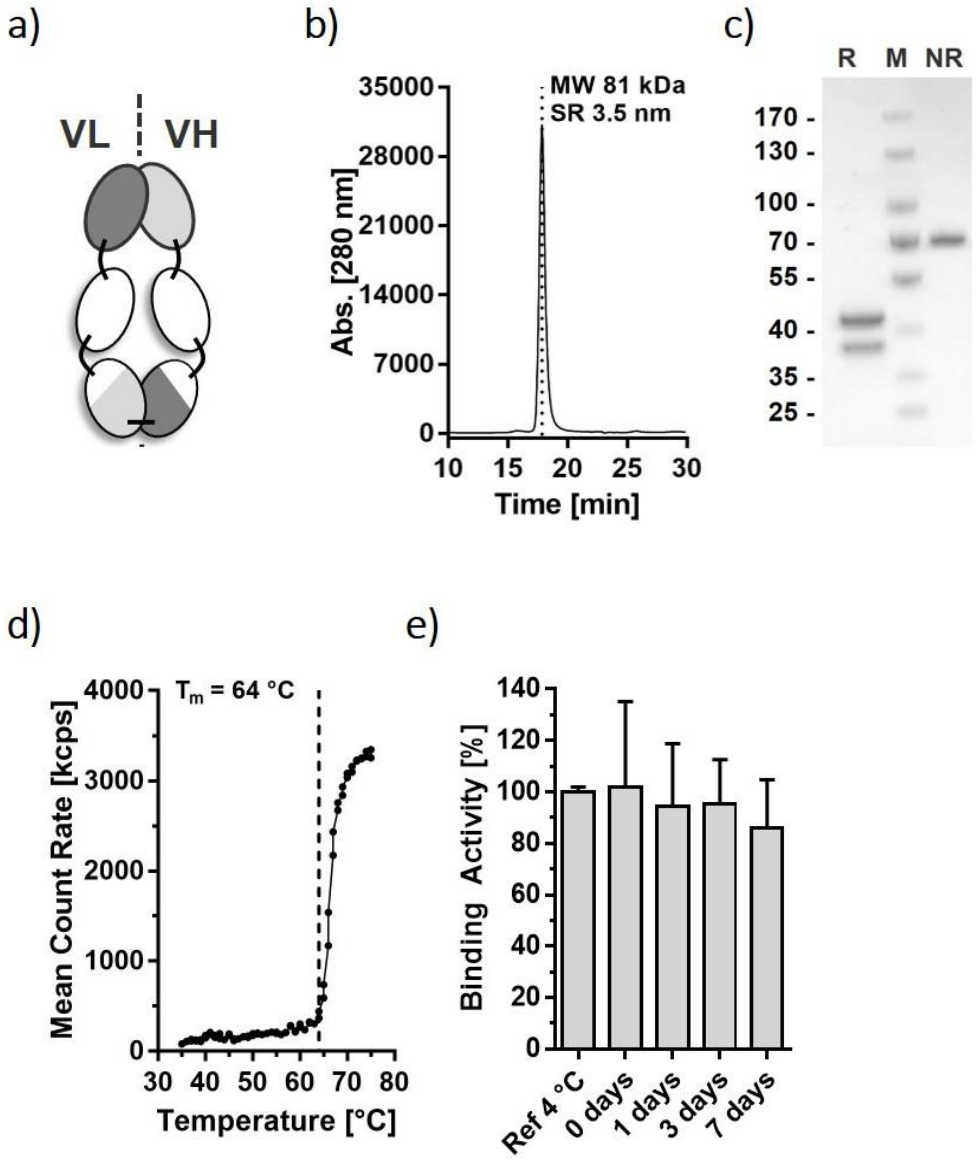

a)
VL
VH
b)
MW 81 kDa
SR 3.5 nm
Abs. [280 nm]
35000
28000
21000
14000
7000
0
10 15 20 25 30
Time [min]
c)
R M NR
170 -
130 -
100 -
70 -
55 -
40 -
35 -
25 -
d)
T_m = 64 °C
Mean Count Rate [kcps]
4000
3000
2000
1000
0
30 40 50 60 70 80
Temperature [°C]
e)
Binding Activity [%]
140
120
100
80
60
40
20
0
Ref 4 °C
0 days
1 days
3 days
7 days

Fig.7:

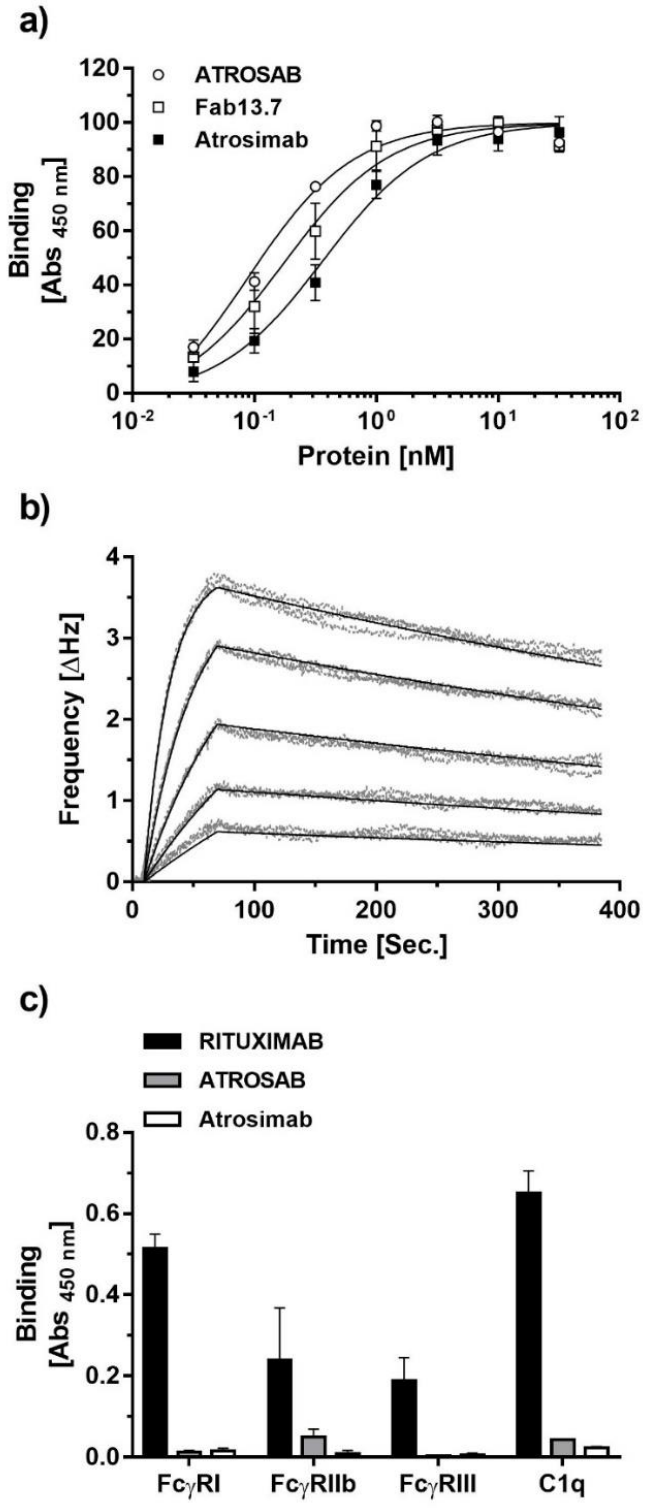

a)
ATROSAB
Fab13.7
Atrosimab
Binding [Abs 450 nm]
Protein [nM]
b)
Frequency [ΔHz]
Time [Sec.]
c)
RITUXIMAB
ATROSAB
Atrosimab
Binding [Abs 450 nm]
FcγRI
FcγRIIb
FcγRIII
C1q

Fig. 8:

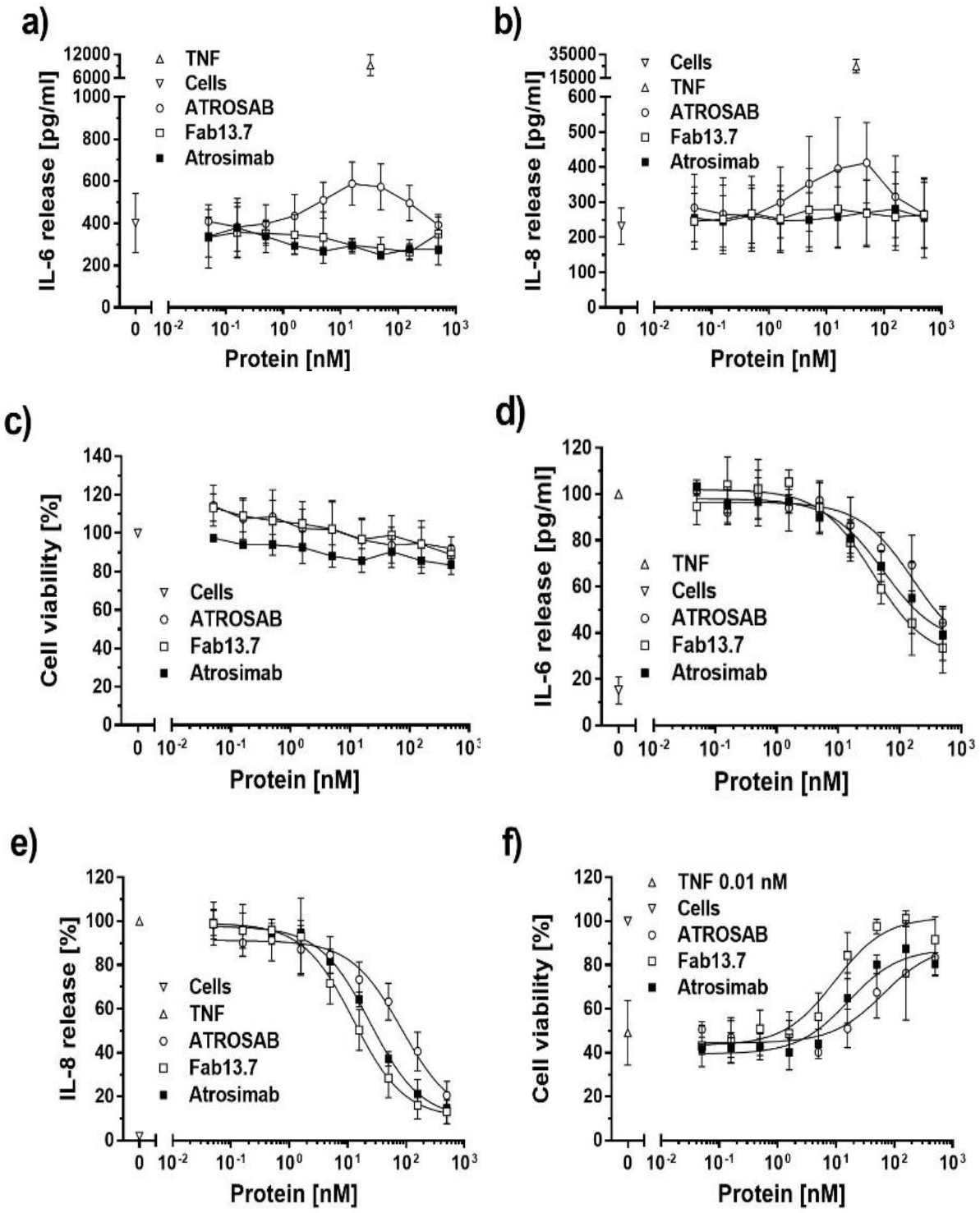

a)
IL-6 release [pg/ml]
TNF
Cells
ATROSAB
Fab13.7
Atrosimab
Protein [nM]
b)
IL-8 release [pg/ml]
Cells
TNF
ATROSAB
Fab13.7
Atrosimab
Protein [nM]
c)
Cell viability [%]
Cells
ATROSAB
Fab13.7
Atrosimab
Protein [nM]
d)
IL-6 release [pg/ml]
TNF
Cells
ATROSAB
Fab13.7
Atrosimab
Protein [nM]
e)
IL-8 release [%]
Cells
TNF
ATROSAB
Fab13.7
Atrosimab
Protein [nM]
f)
Cell viability [%]
TNF 0.01 nM
Cells
ATROSAB
Fab13.7
Atrosimab
Protein [nM]

Fig. 9:

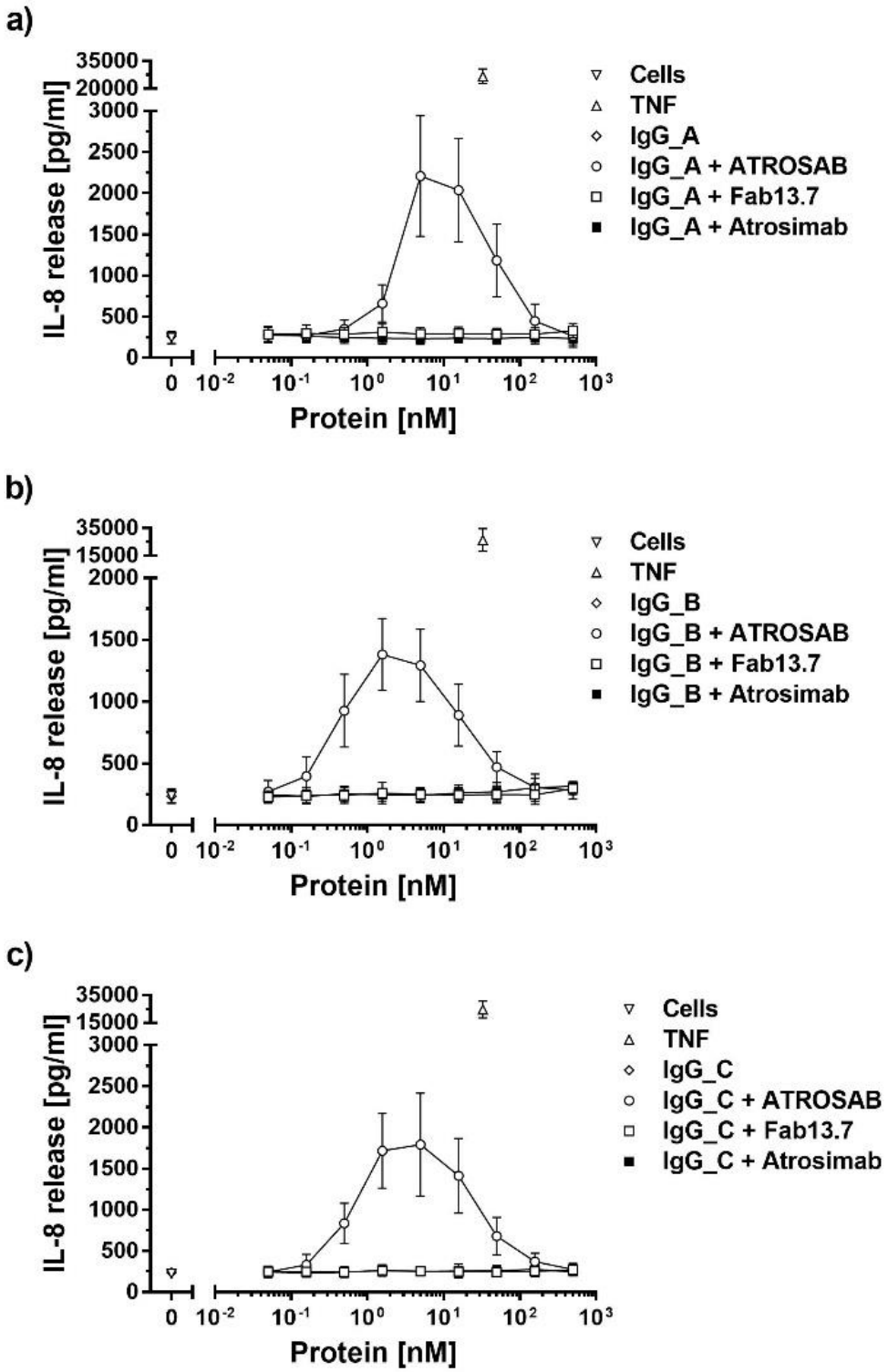
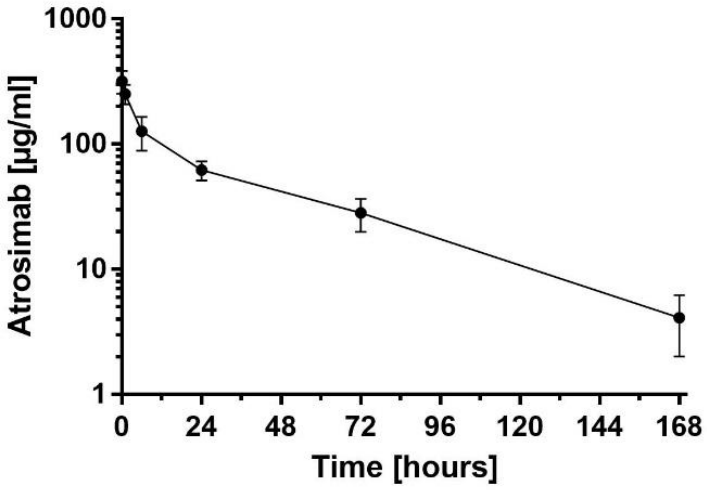

a)
IL-8 release [pg/ml]
Protein [nM]
Cells
TNF
IgG_A
IgG_A + ATROSAB
IgG_A + Fab13.7
IgG_A + Atrosimab
b)
IL-8 release [pg/ml]
Protein [nM]
Cells
TNF
IgG_B
IgG_B + ATROSAB
IgG_B + Fab13.7
IgG_B + Atrosimab
c)
IL-8 release [pg/ml]
Protein [nM]
Cells
TNF
IgG_C
IgG_C + ATROSAB
IgG_C + Fab13.7
IgG_C + Atrosimab

Fig. 10:


1000
100
10
1
Atrosimab [µg/ml]
0
24
48
72
96
120
144
168
Time [hours]