Type A SDF-1 binding nucleic acids

Name	nt.	Sequence: 5′-3′	Comp.
192-A10-001	38	**GCUGUG**AAAGCAACAUGUCAA-UGAAAGGUAGC**CGCAGC**	
192-G10	38	**GCUGUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CACAGC**	<
192-F10	38	**GCUGUG**AAAGUAACACGUCAA-UGAAAGGUAAC**CGCAGC**	<
192-B11	38	**GCUGUG**AAAGUAACACGUCAA-UGAAAGGUAAC**CACAGC**	=
192-C9	38	**GCUGUA**AAAGUAACAUGUCAA-UGAAAGGUAAC**UACAGC**	<
192-E10	38	**GCUGUA**AAAGUAACAAGUCAA-UGAAAGGUAAC**UACAGC**	<
192-C10	38	**GCUGUG**AAAGUAACAAGUCAA-UGAAAGGUAAC**CACAGC**	=
192-D11	38	**GCAGUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CACAGC**	<
192-G11	38	**GCUGUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CACUGC**	<
192-H11	38	**GCUAUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CAUAGC**	<
192-D10	38	**GCUGCG**AAAGCGACAUGUCAA-UGAAAGGUAGC**CGCAGC**	<<
192-E9	38	**GCUGUG**AAAGCAACAUGUCAA-UGAAAGGUAGC**CACAGC**	<<
192-H9	38	**GCUGUG**AAAGUAACAUGUCAA-UGAAAGGUAGC**CGCAGC**	<<
191-A6	39	**AGCGUG**AAAGUAACACGUAAAAUGAAAGGUAAC**CACGCU**	<
Type A Formula-1	26	AAAGYRACAHGUMAAXUGAAAGGUARC	
Type A Formula-2	26	AAAGYRACAHGUMAA-UGAAAGGUARC	
Type A Formula-3	27	AAAGYRACAHGUMAAAUGAAAGGUARC	
Type A Formula-4	26	AAAGYAACAHGUCAA-UGAAAGGUARC	
Type A Formula-5-5′		RSHRYR	
Type A Formula-5-3′		YRYDSY	

terminal nucleotides that may hybridize to each other (bold)

nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides **variable position^**

Fig. 1

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001

=:= equal binding affinity as 192-A10-001; <:= weaker binding affinity than 192-A1-001

<<:= much weaker binding affinity than 192-A10-001

Fig. 1 continued

Derivatives of Type A SDF Binding Nucleic Acid 192-A10-001

Name	nt.	Sequence: 5′-3′	Comp.	PD: K_D [nM]	Biacore: K_D [nM]	TAX IC_{50} [nM]
192-A10-001	38	**GCUGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCAGC**		1.5	1.0	0.1 - 0.2
192-A10-002	36	**CUGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCAG**	=			=
192-A10-003	34	**UGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCA**	<			<
192-A10-004	32	**GUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGC**	<<			<<
192-A10-005	30	**UG**AAAGCAACAUGUCAAUGAAAGGUAGC**CG**	<<			<<
192-A10-006	28	**G**AAAGCAACAUGUCAAUGAAAGGUAGC**C**	<<<			
192-A10-007	26	AAAGCAACAUGUCAAUGAAAGGUAGC	i.a.			

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 192-A10-001

</<</<<:= weaker **(<),** much weaker **(<<)** or very much weaker **(<<<)** binding affinity than 192-A1-001

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-A10-001

PD.:= Clones were tested as aptamers in a pull-down binding assay

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 2A

Derivatives of Type A SDF Binding Nucleic Acid192-A10-001

Name	nt.	Sequence: 5′-3′	Comp.	PD: K_D [nM]	Biacore: K_D [nM]	TAX IC_{50} [nM]
192-A10-001	38	**GCUGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCAGC**		1.5	1.0	0.1 - 0.2
192-A10-002	36	**CUGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCAG**	=			=
192-A10-008	36	**GCGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCGC**	=	1.5	1.4	=
192-A10-015	36	**GCGCG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCGC**	<	4.6		
192-A10-014	34	**GCGG**AAAGCAACAUGUCAAUGAAAGGUAGC**CCGC**	<	8.0		=
192-A10-016	34	**CGUG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGCG**	<			
192-A10-017	34	**GCGC**AAAGCAACAUGUCAAUGAAAGGUAGC**GUGC**	i.a.			
192-A10-018	34	**GUGC**AAAGCAACAUGUCAAUGAAAGGUAGC**GCGC**	<<<			
192-A10-019	34	**CGCG**AAAGCAACAUGUCAAUGAAAGGUAGC**CGUG**	<<			
192-A10-020	34	**GGGC**AAAGCAACAUGUCAAUGAAAGGUAGC**GCCC**	<<*			
192-A10-021	34	**GGCC**AAAGCAACAUGUCAAUGAAAGGUAGC**GGCC**	<<*			
192-A10-022	34	**GCCC**AAAGCAACAUGUCAAUGAAAGGUAGC**GGGC**	<<*			
192-A10-023	34	**CCCC**AAAGCAACAUGUCAAUGAAAGGUAGC**GGGG**	<<*			

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 192-A10-001/ -008

</<</<<:= weaker **(<)**, much weaker **(<<)** or very much weaker **(<<<)** binding affinity than 192-A1-001/ -008

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001 (* = except from 192-A10-020, -021, -022, and –023 which were tested vs. 193-A10-008 that has the identical binding affinity to SDF-1 as 192-A10-001)

PD.:= Clones were tested as aptamers in a pull-down binding assay

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 2B

Type B SDF-1 binding nucleic acids

Name	nt.	Sequence: 5′-3′	Comp.
193-C2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UACGCU**	+
193-G2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**UACGCU**	+
193-F2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAAUGGCUGAUCCUAGUCAGG**UGCGCU**	+
193-G1-002	45	**GCGAG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UGCGC**	<<
193-D2-002	45	**GCGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UGCGC**	<
193-A1-002	45	**GCAUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UGCCC**	<<<
193-D3-002	45	**GCGUG**GUGUGAUCUAGAUGUAAUGGCUGAUCCUAGUCAGG**GACGC**	<
193-B3-002	45	**GCGUG**GUGUGAUCUAGAUGUAGAGGCUGAUCCUAGUCAGG**UACGC**	<<
193-H3-002	45	**GCGUG**GUGUGAUCUAGAUGUAAAGGCUGAUCCUAGUCAGG**UACGC**	<
193-E3-002	45	**GCGUG**GUGUGAUCUAGAUGUAGUGGCUGUUCCUAGUCAGG**UAUGC**	<<
193-D1-002	45	**GCGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUUAGG**UACGC**	<<<
Type B Formula-1	35	GUGUGAUCUAGAUGUADWGGCUGWUCCUAGUYAGG	
Type B Formula-2	35	GUGUGAUCUAGAUGUADUGGCUGAUCCUAGUCAGG	
Type B Formula-3-5′		X_1GCRWG	
Type B Formula-3-3′		KRYSCX_4	

terminal nucleotides that may hybridize to each other (bold)

nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides **variable position**

Comp.:= Clones C2, G2, and F2 were tested as aptamers in a competition binding assay vs. 192-A10-001; all other clones were tested as aptamers in a competition binding assay vs. 193-G2-012 that has the identical binding affinity to SDF-1 as 193-G2-001 (see Fig. 4B)

+:= better binding affinity than 192-A10-001

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 193-G2-001/ -012

X_1 = 'A' or absent X_4 = 'U' or absent

Fig. 3

Derivatives of Type B SDF Binding Nucleic Acids 193-C2/G2-001

Name	nt.	Sequence: 5′-3′	Comp.	PD K_D [nM]	Biacore K_D [nM]
193-G2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**UACGCU**		0.3	0.5
193-C2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UACGCU**	=		0.6
193-C2-002	45	**GCGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UACGC**	=		0.8
193-C2-003	43	**CGUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UACG**	<		
193-C2-004	41	**GUG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UAC**	<<		
193-C2-005	39	**UG**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**UA**	<<<		
193-C2-006	37	**G**GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG**U**	<<<		
193-C2-007	35	GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG	i.a.		

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 193-G2-001

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 193-G2-001

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-G2-001

PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 4A

Derivatives of Type B SDF Binding Nucleic Acid193-C2/G2-001

Name	nt.	Sequence: 5′-3′	Comp.	PD K_D [nM]	Biacore K_D [nM]
193-G2-001	47	**AGCGUG**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**UACGCU**		0.3	0.5
193-G2-012	45	**GCGUG**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**UACGC**	=	0.3	
193-G2-013	45	**GCGCG**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**CGCGC**	<<	5.3	
193-G2-014	43	**GCGC**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**GCGC**	<<	4.7	
193-G2-015	43	**GGGC**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**GCCC**	<<*	4.5	
193-G2-016	43	**GGCC**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**GGCC**	<<*	4.2	
193-G2-017	43	**GCCC**GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG**GGGC**	<<*	4.2	

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 193-G2-001/ -012

</<</<<<:= weaker **(<)**, much weaker **(<<)** or very much weaker **(<<<)** binding affinity than 193-G2-001 and 193-G2-012, respectively

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-G2-001 (* = except from 193-G2-015, -016, -017 which were tested in a competition binding assay vs. 193-G2-012 that has the identical binding affinity to SDF-1 as 193-G2-001)

PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 4B

Type C SDF-1 binding nucleic acids

Name	nt.	Sequence: 5′-3′	Comp.
197-B2	39	**GUGCUGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCAGCAC**	<
191-D5-001	39	**AGCGUGGCGA**GGUUAGGGCUAGAAGUCGG**UCGACACGCU**	<
197-H1	39	**GUGUUGCGGA**GGUUAGGGCUAGAAGUCGG**UCAGCAGCAC**	<
190-D3	48	**CGUGCGGCCUAAGA**GGUUAGGGCUUAAAGUCGG**UCUUUGGCCAACACG**	<<
190-A3-001	48	**CGUG**CGCUUGAGAUAGGGGUUAGGGCUUAAAGUCGGCUGAUUCU**CACG**	<
190-A3-001*	48	CGUGCGCU**UGAGA**UAGGGGUUAGGGCUUAAAGUCGGCUGAU**UCUCA**CG	<
190-A2	48	**CGUGAUUGG**UGA**GG**GGUUAGGGCUUGAAGUCGG**CC**UUGU**CCAGUCACG**	<<
191-A5	39	**AGCGUG**AA**GG**GGUUAGGGCUCGAAGUCGG**CU**GA**CACGCU**	<<
197-H3	39	**GUGCUGCGGG**GGUUAGGGCUCGAAGUCGG**CCCGCAGCAC**	<
197-B1	39	**GUGUU**CCC**GG**GGUUAGGGCUUGAAGUCGG**CCGG**C**AGCAC**	<<
197-E3	39	**GUGUUGCAGG**GGUUAGGGCUUGAAGUCGG**CCUGCAGCAC**	<
197-H2	39	**GUGCUGCGGG**GGUUAGGGCUCAAAGUCGG**CCUGCAGCAC**	<<
197-D1	38	**GUGCUG**C**CGG**GGUUAGGGCUAA-AGUCGG**CCG**A**CAGCAC**	<<
197-D2	39	**GUGCUGUGGG**GGUCAGGGCUAGAAGUCGG**CCUGCAGCAC**	<<
Type C Formula-1	19	GGUYAGGGCUHRXAGUCGG	
Type C Formula-2	18	GGUYAGGGCUHRAAGUCGG	
Type C Formula-3	19	GGUYAGGGCUHR-AGUCGG	
Type C Formula-4	19	GGUUAGGGCUHGAAGUCGG	

terminal nucleotides that may hybridize to each other (bold) nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides **variable position** Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001

=:= equal binding affinity as 192-A10; <:= weaker binding affinity than 192-A10 <<:= much weaker binding affinity than 192-A10

*:= alternative hybridization

Fig. 5

Derivatives of Type C SDF Binding Nucleic Acid 190-A3-001

Name	nt.	Sequence: 5′-3′	Comp.
190-A3-001	48	**CGUG**CGCUUGAGAUAGG GGUUAGGGCUUAAAGUCGG CUGAUUCU**CACG**	
190-A3-001*	48	CGUGCGCU**UGAGA**UA**GG** GGUUAGGGCUUAAAGUCGG **CU**GAU**UCUCA**CG	
190-A3-003	38	**UGAGA**UA**GG** GGUUAGGGCUUAAAGUCGG CUGAU**UCUCA**	=
190-A3-004	36	**GAGA**UA**GG** GGUUAGGGCUUAAAGUCGG **CU**GAU**UCUC**	=
190-A3-007	29	**GG** GGUUAGGGCUUAAAGUCGG **CU**GAUUCU	<<<

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 190-A3-001

</<</<<<:= weaker **(<)**, much weaker **(<<)** or very much weaker **(<<<)** binding affinity than 190-A3-001

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 190-A3-001

*:= alternative hybridization of the terminal nucleotides

Fig. 6

9/50

Derivatives of Type C SDF Binding Nucleic Acid 191-D5-001

Name	nt.	Sequence: 5′-3′	Comp. vs. 191-D5-001	Comp. vs. 191-D5-007	Biacore K_D [nM]
191-D5-001	39	**AGCGUGGCGA**GGUUAGGGCUAGAAGUCGG**UCGACACGCU**		<	0.73
191-D5-002	37	**GCGUGGCGA**GGUUAGGGCUAGAAGUCGG**UCGACACGC**	=		
191-D5-003	35	**CGUGGCGA**GGUUAGGGCUAGAAGUCGG**UCGACACG**	=		
191-D5-004	33	**CG-GGCGA**GGUUAGGGCUAGAAGUCGG**UCGAC-CG**	<		
191-D5-005	33	**CG-GGCGA**GGUUAGGGCUAGAAGUCGG**UCGCC-CG**	=		
191-D5-006	31	**CG--GCGA**GGUUAGGGCUAGAAGUCGG**UCGC--CG**	=		
191-D5-007	29	**CG--G-GA**GGUUAGGGCUAGAAGUCGG**UC-C--CG**	+		0.75
191-D5-010	27	**G--G-GA**GGUUAGGGCUAGAAGUCGG**UC-C--C**		<	

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 191-D5-001/ -007

</<</<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 191-D5-001/ -007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 191-D5-001 or 191-D5-007 whereas both clones have the identical binding affinity to SDF-1 as 191-D5-001

10/50

Fig. 7A

Derivatives of Type C SDF Binding Nucleic Acid 191-D5-001

Name	nt.	Sequence: 5′-3′	Comp. vs. 191-D5-007
191-D5-007	29	**CG--G-GA**GGUUAGGGCUAGAAGUCGG**UC-C--CG**	
191-D5-010	27	**G--G-GA**GGUUAGGGCUAGAAGUCGG**UC-C--C**	<
191-D5-017	27	**CCGC**GGUUAGGGCUAGAAGUCGG**GCGG**	<
191-D5-029	27	**CCCG**GGUUAGGGCUAGAAGUCGG**CGGG**	<
191-D5-024	27	**GGCG**GGUUAGGGCUAGAAGUCGG**CGCC**	<
191-D5-017-29a	29	**CCCGC**GGUUAGGGCUAGAAGUCGG**GCGGG**	<
191-D5-017-29b	29	**GCCGC**GGUUAGGGCUAGAAGUCGG**GCGGC**	<
191-D5-019-29a	29	**CCCCG**GGUUAGGGCUAGAAGUCGG**CGGGG**	<
191-D5-024-29a	29	**CGGCG**GGUUAGGGCUAGAAGUCGG**CGCCG**	=
191-D5-024-29b	29	**GGGCG**GGUUAGGGCUAGAAGUCGG**CGCCC**	=

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 191-D5-007

</<</<<:= weaker **(<)**, much weaker **(<<)** or very much weaker **(<<<)** binding affinity than 191-D5-007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 191-D5-007

Fig. 7B

Derivatives of Type C SDF Binding Nucleic Acid197-B2

Name	nt.	Sequence: 5′-3′	Comp.vs. 197-B2	Comp. vs. 191-D5-007	Biacore K_D [nM]	TAX IC_{50}[nM]
197-B2	39	**GUGCUGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCAGCAC**		=	0.9	0.1-0.2
197-B2-001	37	**UGCUGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCAGCA**	=		1.1	
197-B2-002	35	**GCUGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCAGC**	=			
197-B2-003	33	**CUGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCAG**	=			
197-B2-004	31	**UGCGGG**GGUUAGGGCUAGAAGUCGG**CCUGCA**	=			
197-B2-005	29	**GCGGG**GGUUAGGGCUAGAAGUCGG**CCUGC**	=			
197-B2-006	29	**GCCGG**GGUUAGGGCUAGAAGUCGG**CCGGC**	=	=		0.1-0.2
197-B2-006-31a	31	**GGCCGG**GGUUAGGGCUAGAAGUCGG**CCGGCC**		=		
197-B2-006-31b	31	**CGCCGG**GGUUAGGGCUAGAAGUCGG**CCGGCG**		=		

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **=:=** equal binding affinity as 197-B2 or 191-D5-007

</<</<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than as 197-B2 or 191-D5-007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 197-B2 or 191-D5-007 whereas both clones have the identical binding affinity to SDF-1

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 8

Further SDF-1 Binding Nucleic Acids

Name	nt.	Sequence: 5′-3′	PD K_D [nM]
194-A2-001	48	**CGUGG**UCCGUUGUGUCAGGUCUAUUCGCCCCGGUGCAGGGCAU**CCGCG**	12.0
196-B12-003	49	GCAGUGUGACGCGGACGUGAUAGGACAGAGCUGAUCCCGCUCAGGUGAG	7.6
196-B12-004	49	CAACAGCAGUGUGACGCGGACGUGAUAGGACAGAGCUGAUCCCGCUCAG	5.3

terminal nucleotides at the 5′- and the 3′-end that may hybridize to each other (bold) **nt.:=** nucleotides

PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 9

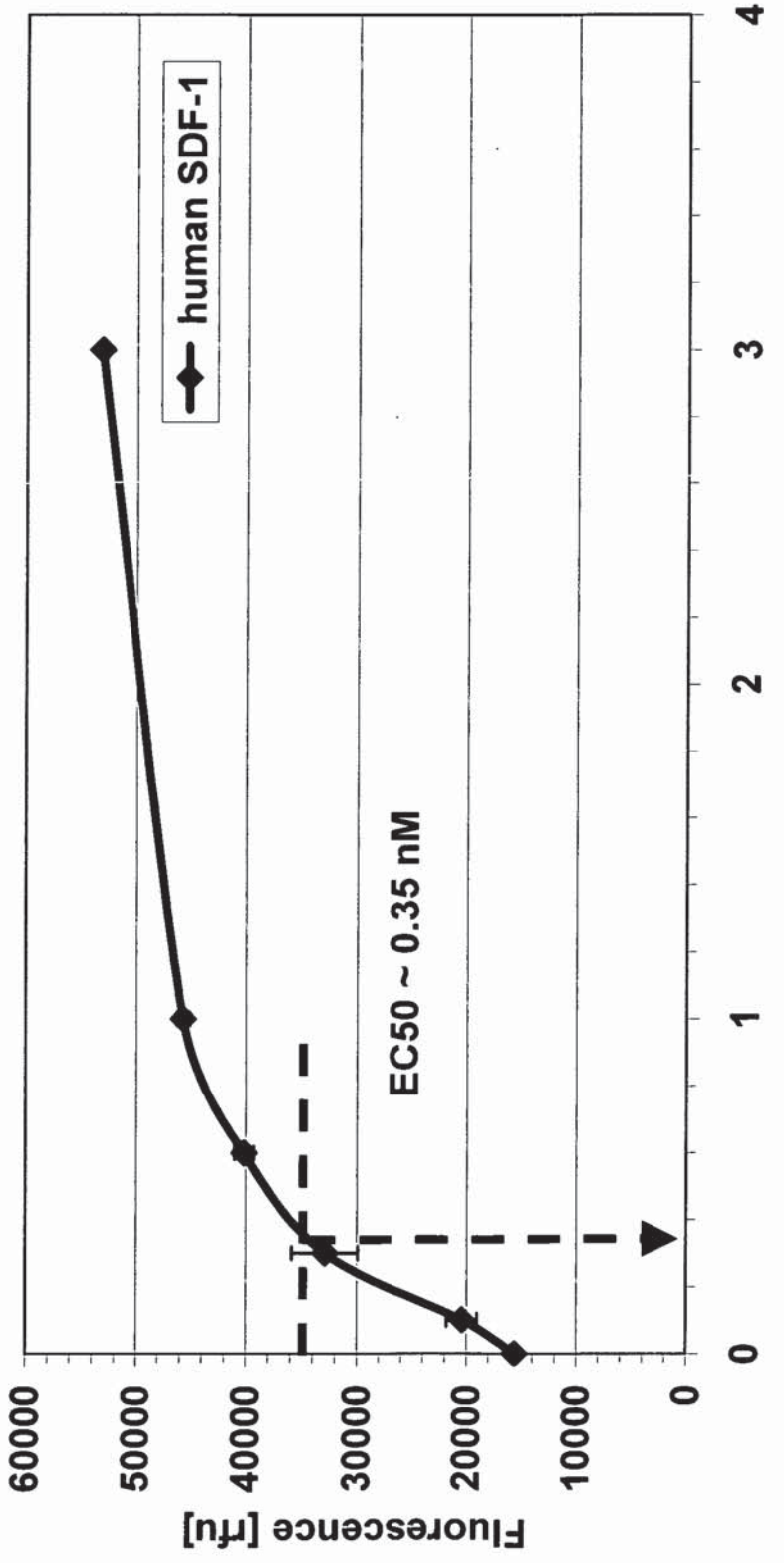

human SDF-1
EC50 ~ 0.35 nM
Fluorescence [rfu]
human SDF-1 [nM]
0
10000
20000
30000
40000
50000
60000
0
1
2
3
4

Fig. 10

binding to biotinylated human D-SDF1 [%]
70
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF1 [nM]
192-A10-001 (KD = 1.5 nM)

Fig. 11

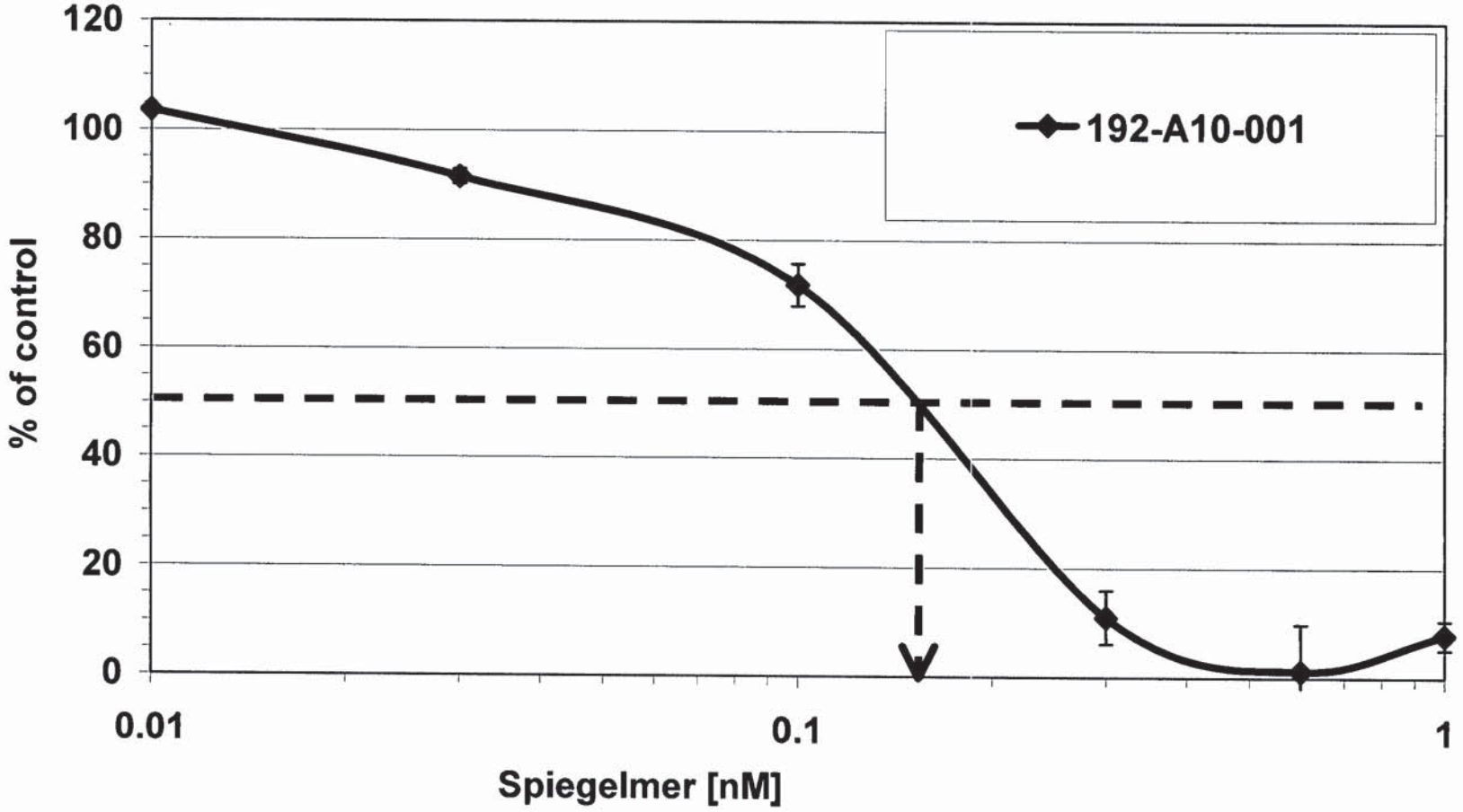

120
100
80
60
40
20
0
% of control
192-A10-001
0.01
0.1
1
Spiegelmer [nM]

Fig. 12

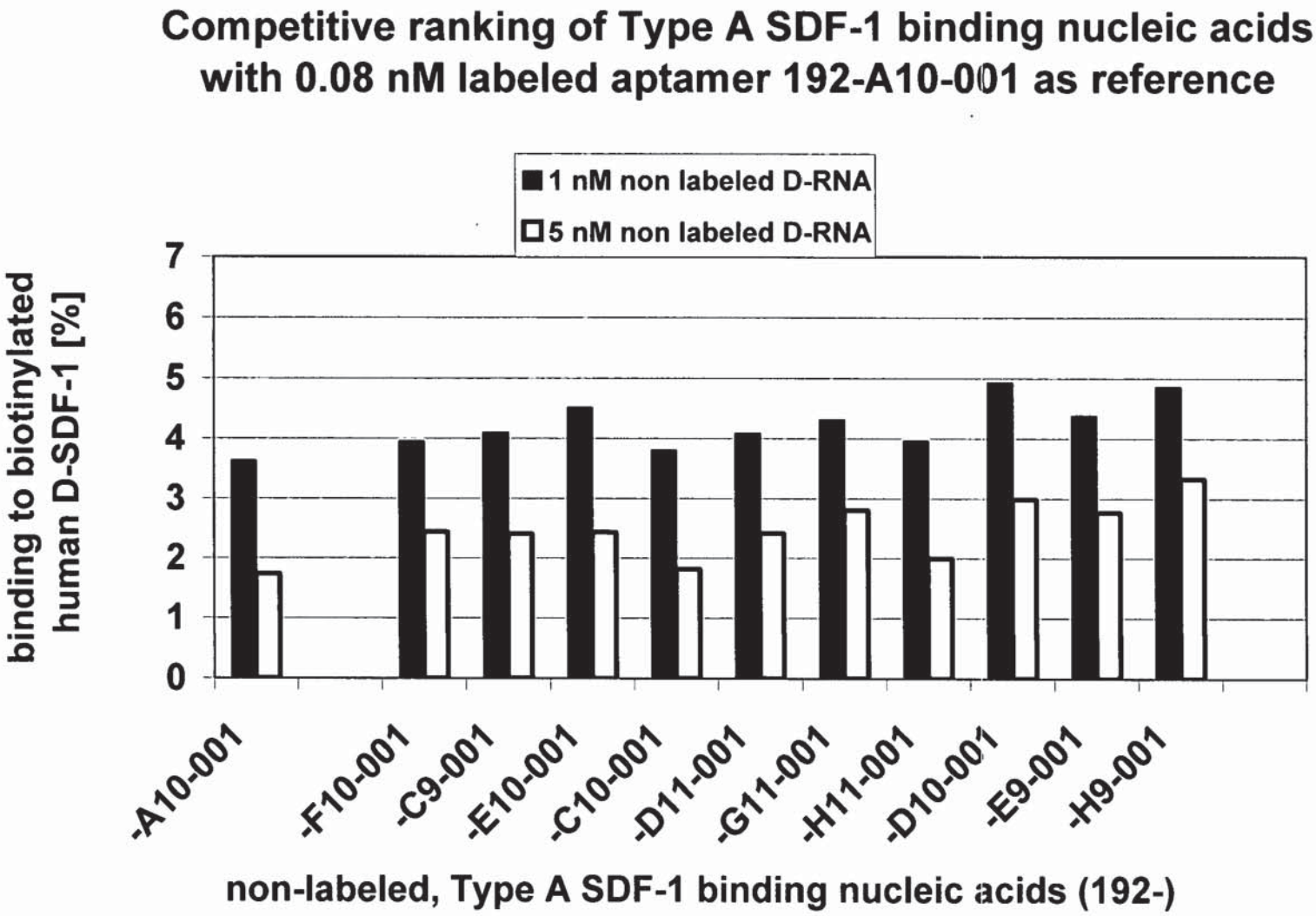
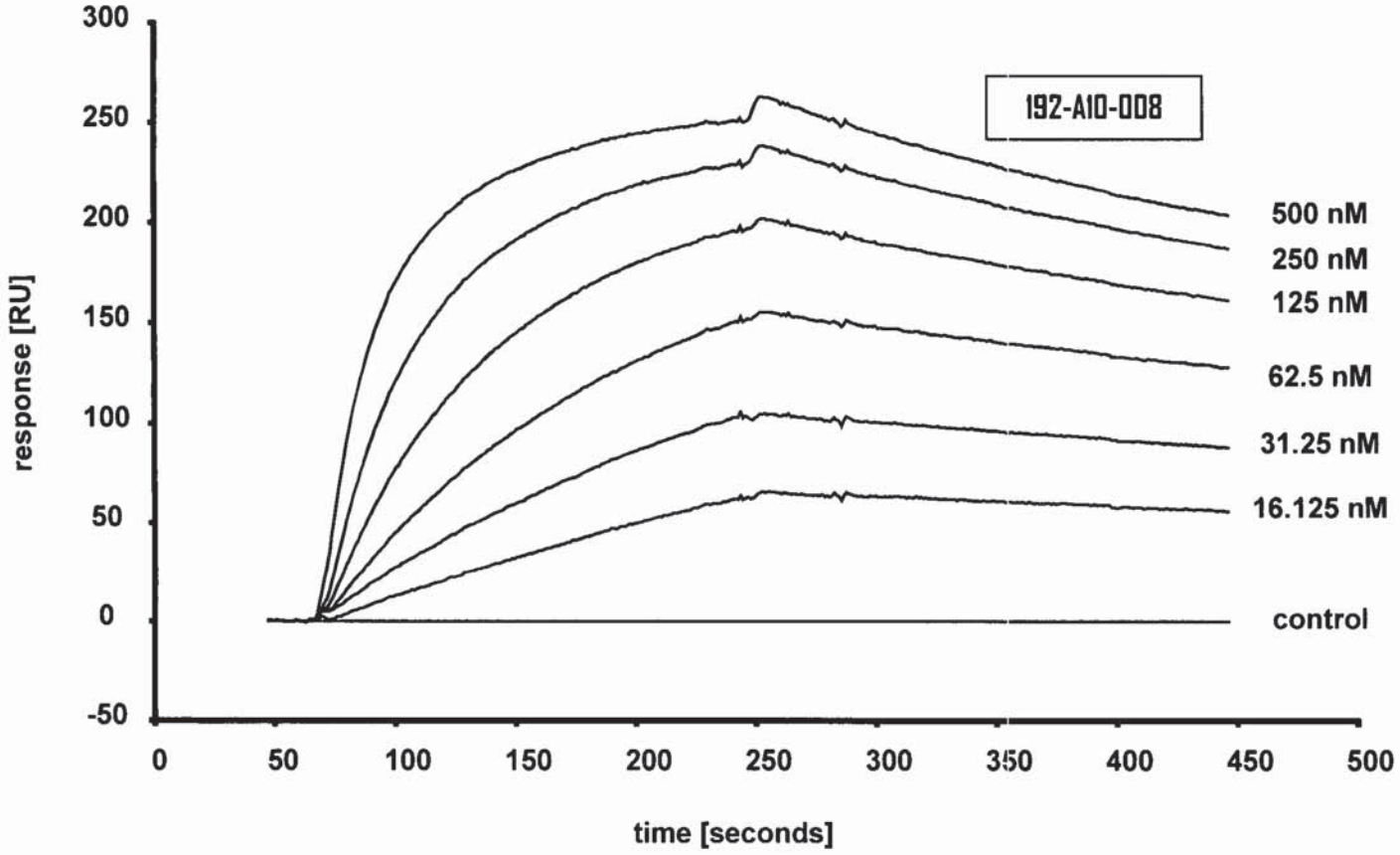

Competitive ranking of Type A SDF-1 binding nucleic acids
with 0.08 nM labeled aptamer 192-A10-001 as reference
1 nM non labeled D-RNA
5 nM non labeled D-RNA
binding to biotinylated
human D-SDF-1 [%]
0
1
2
3
4
5
6
7
-A10-001
-F10-001
-C9-001
-E10-001
-C10-001
-D11-001
-G11-001
-H11-001
-D10-001
-E9-001
-H9-001
non-labeled, Type A SDF-1 binding nucleic acids (192-)

Fig. 13

binding to biotinylated human D-SDF1 [%]
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF1 [nM]
192-A10-008 (KD = 1.5 nM)

Fig. 14



Spiegelmer	k_a [$M^{-1} x s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
192-A10-008	3.83×10^5	5.35×10^{-4}	1.40

Fig. 15

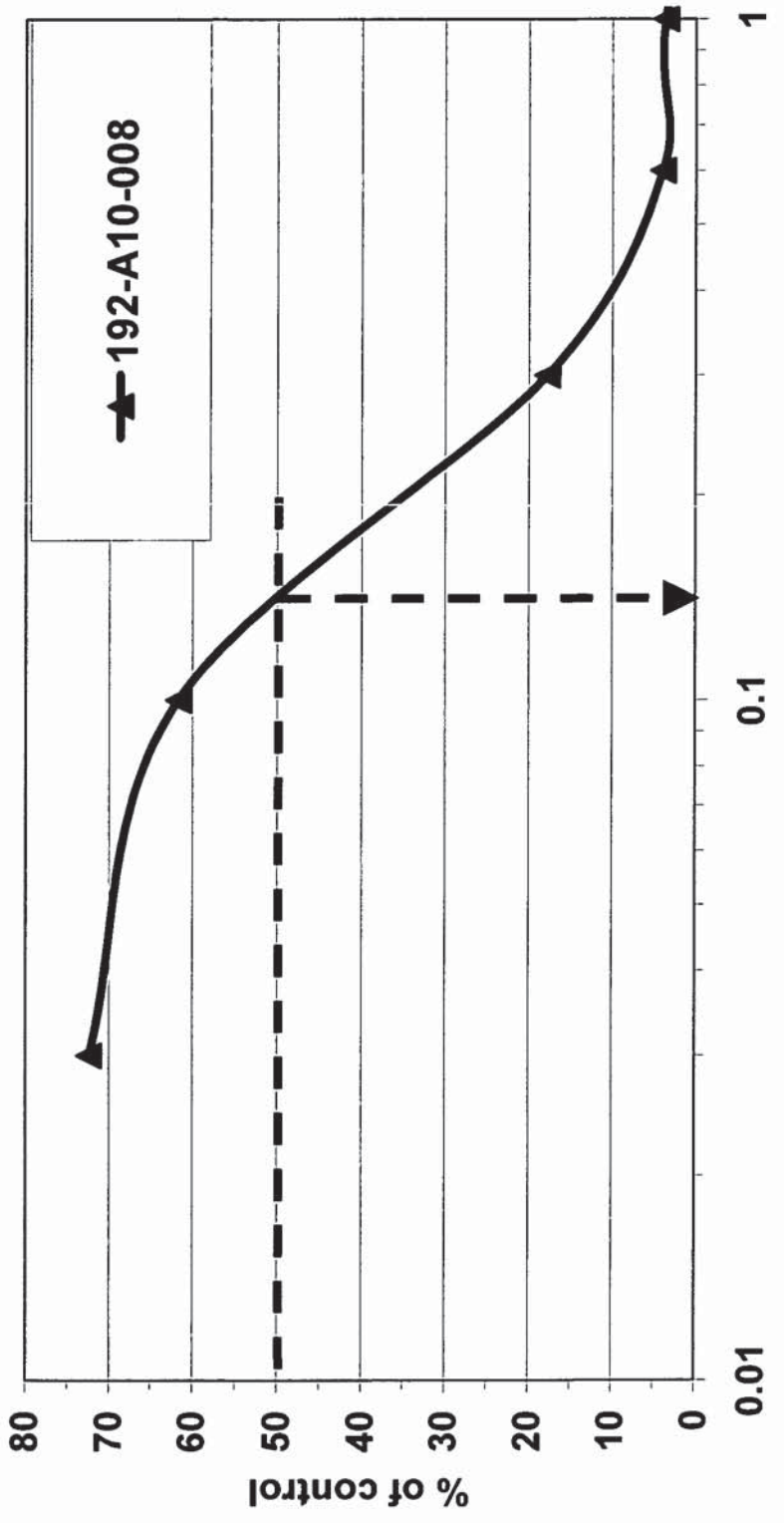
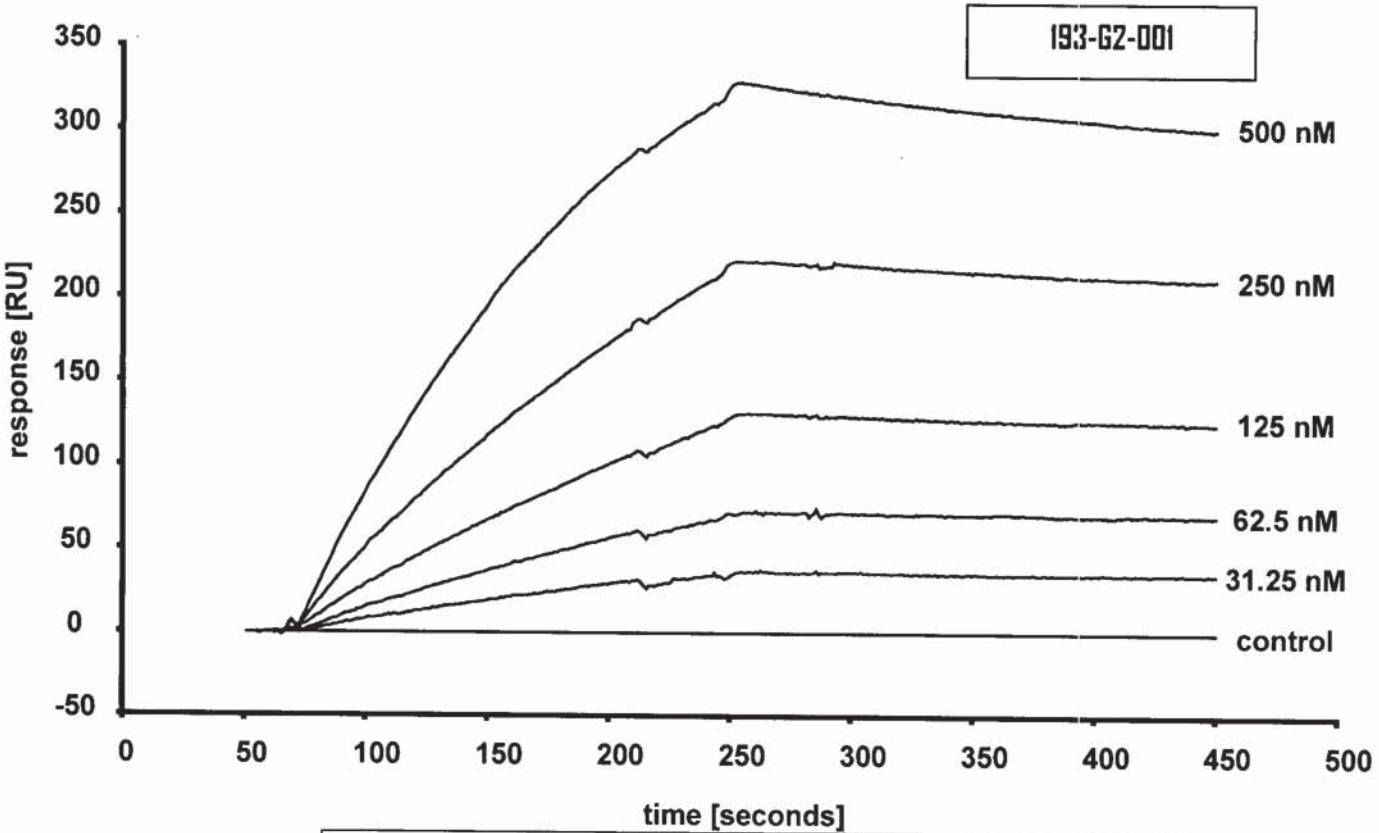

192-A10-008
% of control
80
70
60
50
40
30
20
10
0
0.01
0.1
1
Spiegelmer [nM]

Fig. 16



Spiegelmer	k_a [$M^{-1} x s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
193-G2-001	2.84×10^5	1.42×10^{-4}	0.50

Fig. 17

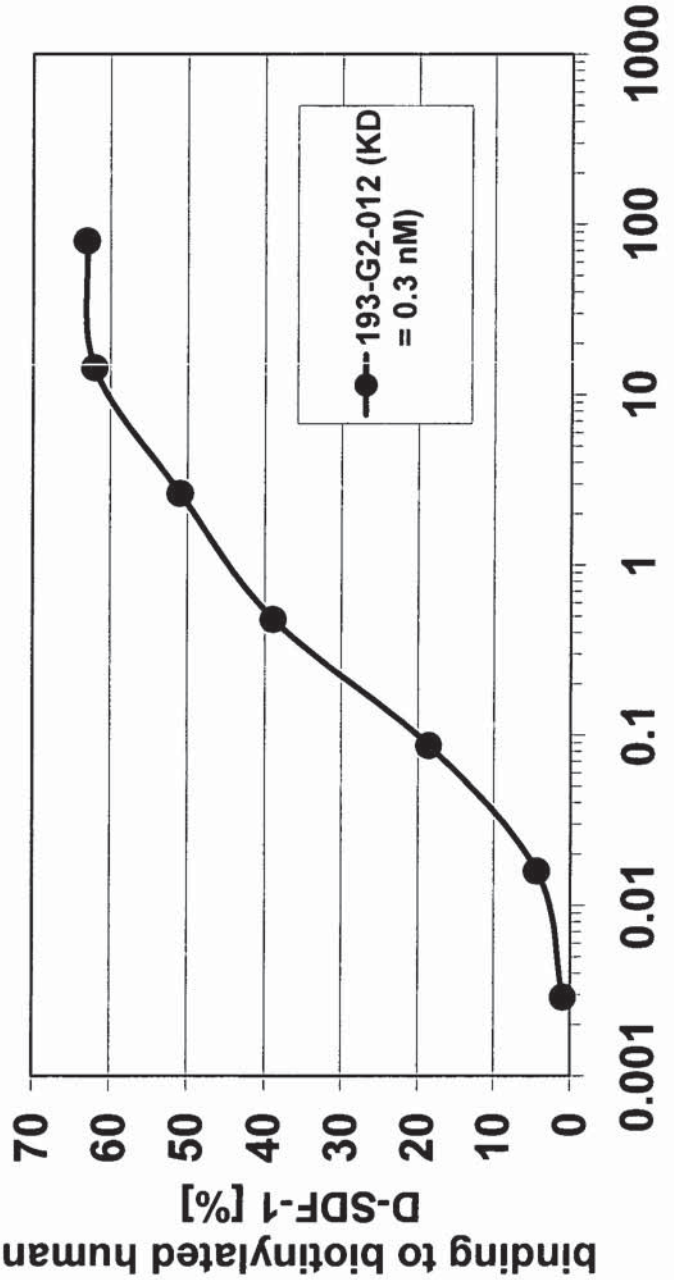

binding to biotinylated human D-SDF-1 [%]
70
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF-1 [nM]
193-G2-012 (KD = 0.3 nM)

Fig. 18

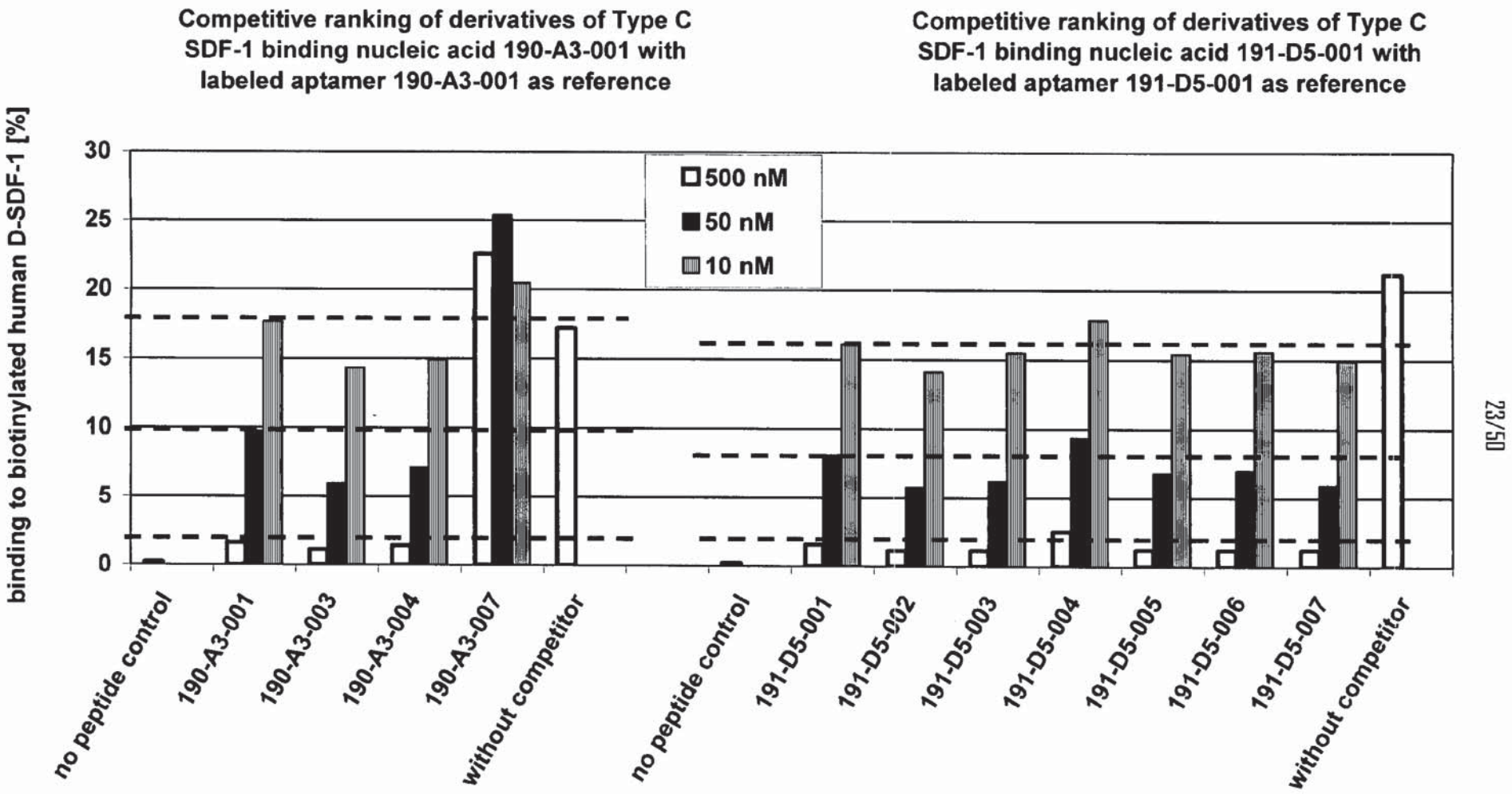

Competitive ranking of derivatives of Type C SDF-1 binding nucleic acid 190-A3-001 with labeled aptamer 190-A3-001 as reference
Competitive ranking of derivatives of Type C SDF-1 binding nucleic acid 191-D5-001 with labeled aptamer 191-D5-001 as reference
binding to biotinylated human D-SDF-1 [%]
30
25
20
15
10
5
0
500 nM
50 nM
10 nM
no peptide control
190-A3-001
190-A3-003
190-A3-004
190-A3-007
without competitor
no peptide control
191-D5-001
191-D5-002
191-D5-003
191-D5-004
191-D5-005
191-D5-006
191-D5-007
without competitor

Fig. 19

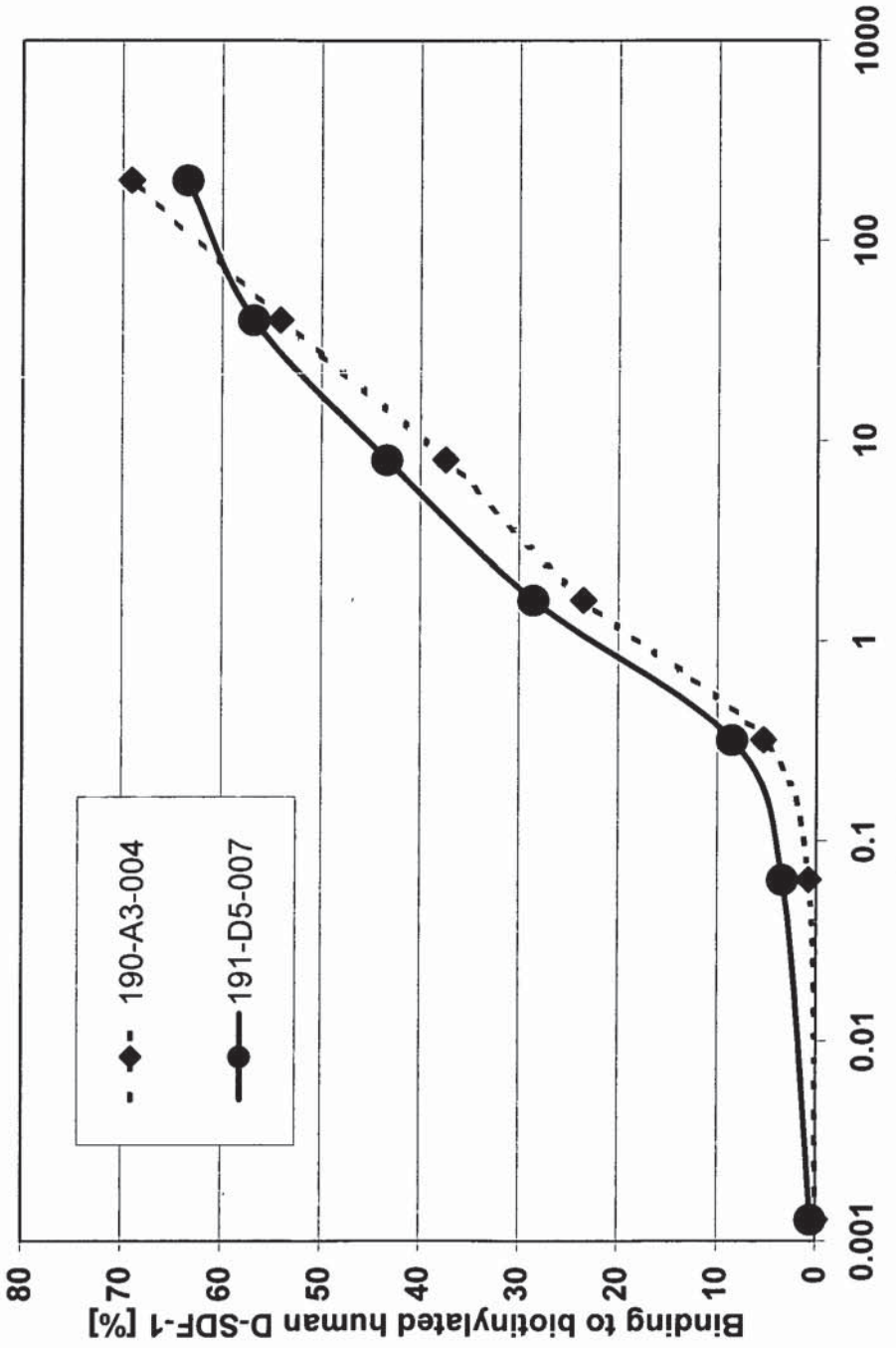
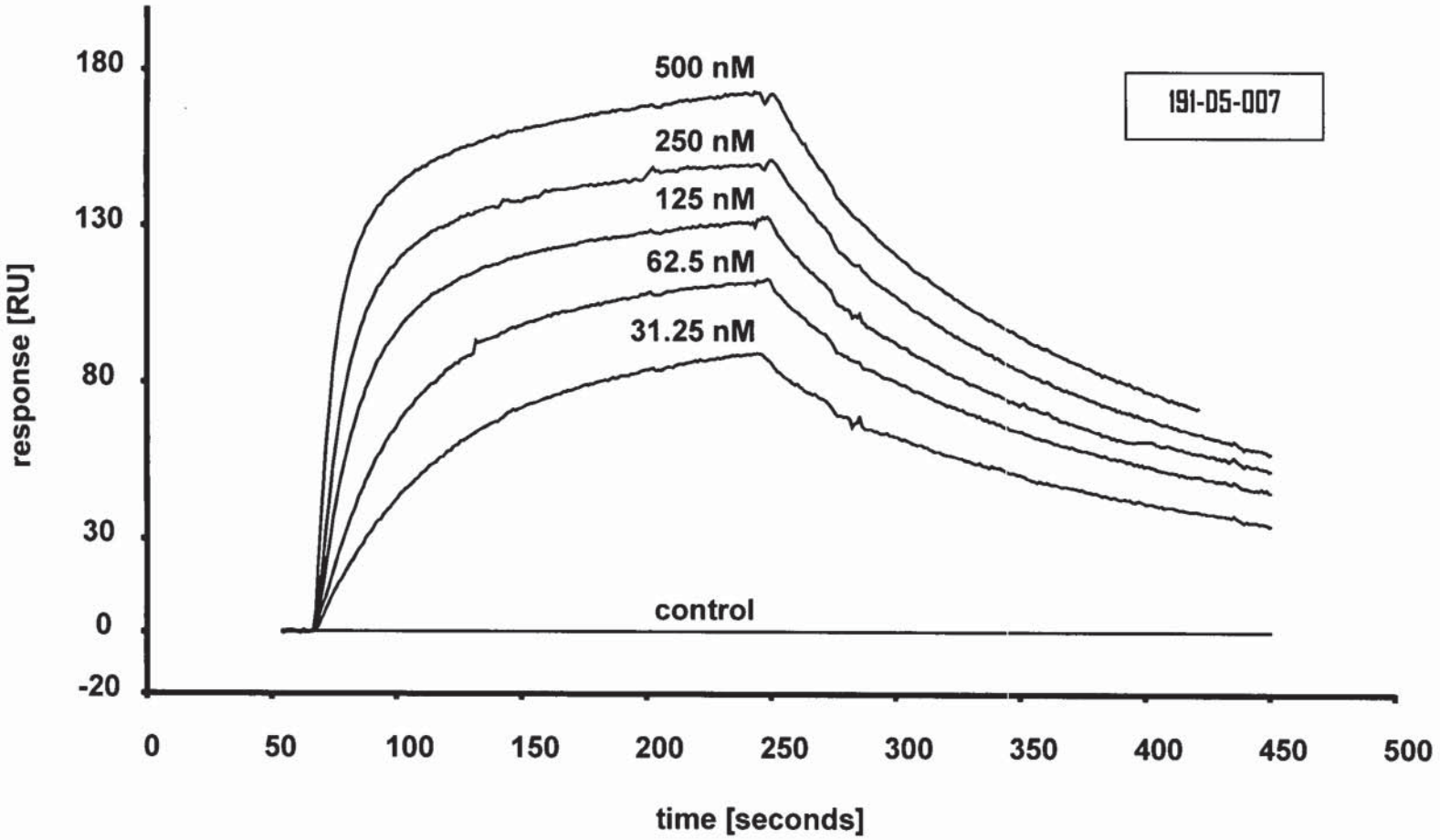

Binding to biotinylated human D-SDF-1 [%]
80
70
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF1 [nM]
190-A3-004
191-D5-007

Fig. 20



Spiegelmer	k_a [$M^{-1} x\ s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
191-05-007	2.68×10^6	2.02×10^{-3}	0.75

Fig. 21

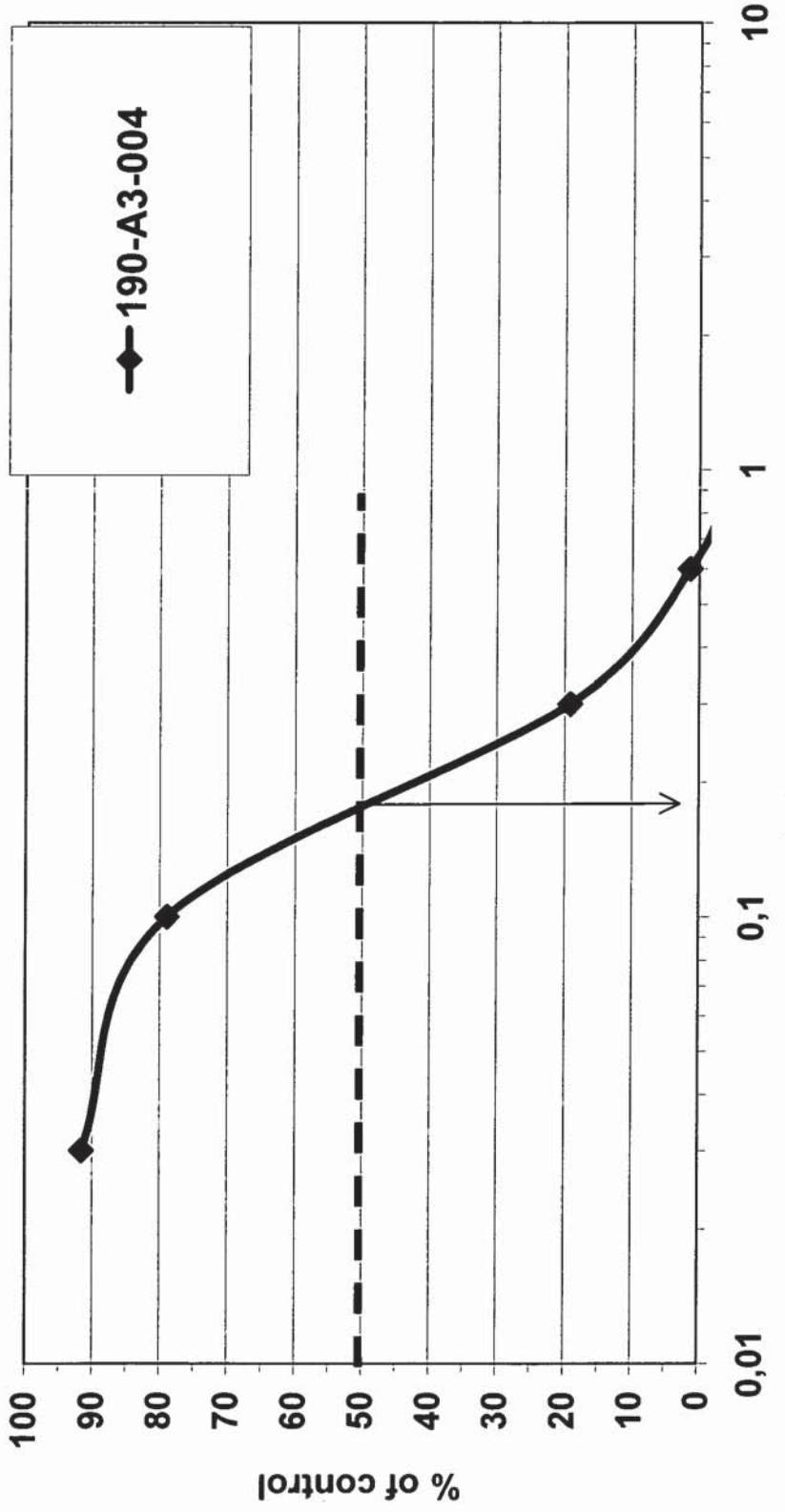

190-A3-004
% of control
100
90
80
70
60
50
40
30
20
10
0
0,01
0,1
1
10
Spiegelmer [nM]

Fig. 22

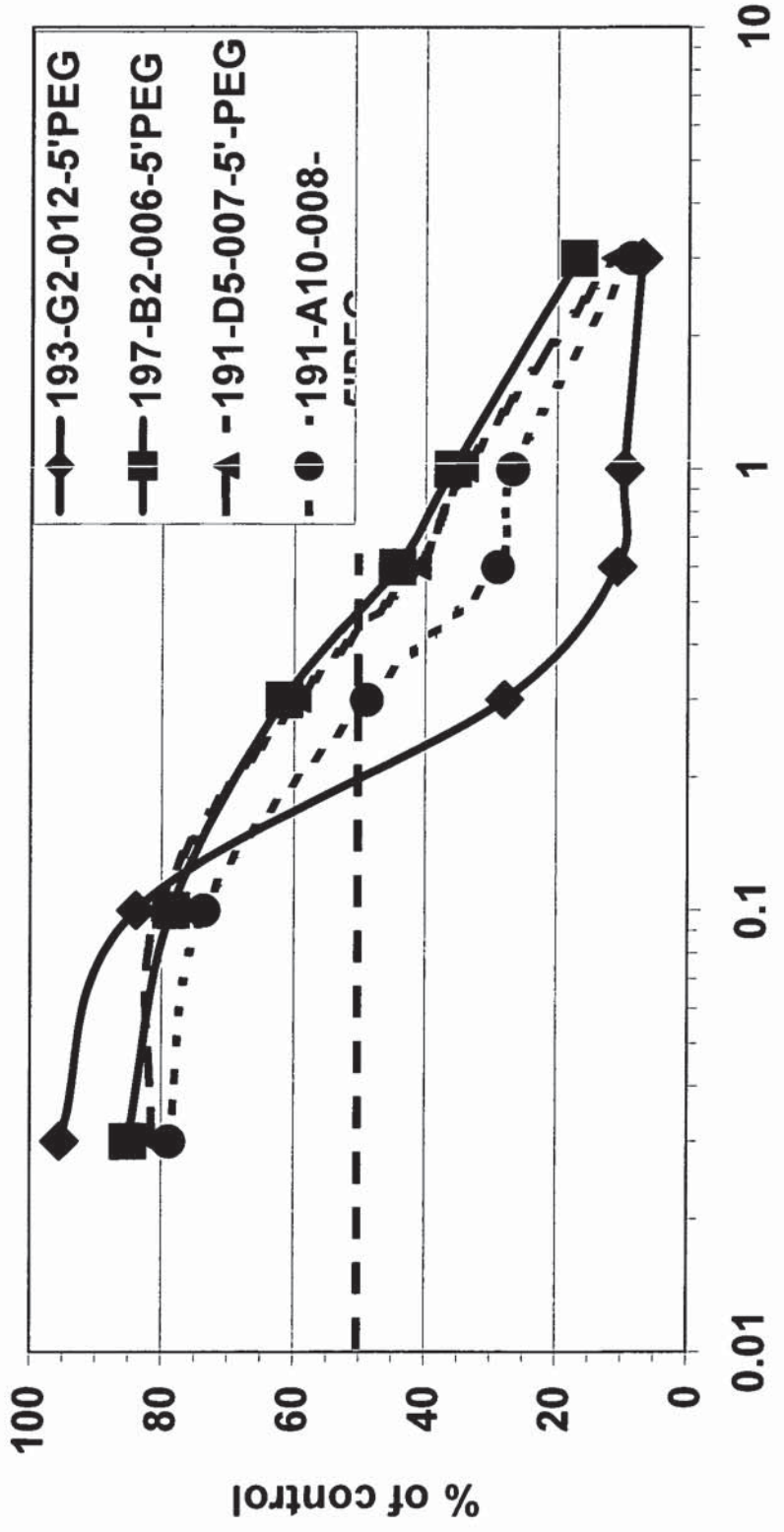

193-G2-012-5'PEG
197-B2-006-5'PEG
191-D5-007-5'-PEG
191-A10-008-
% of control
100
80
60
40
20
0
0.01
0.1
1
10
Spiegelmer [nM]

Fig. 23A

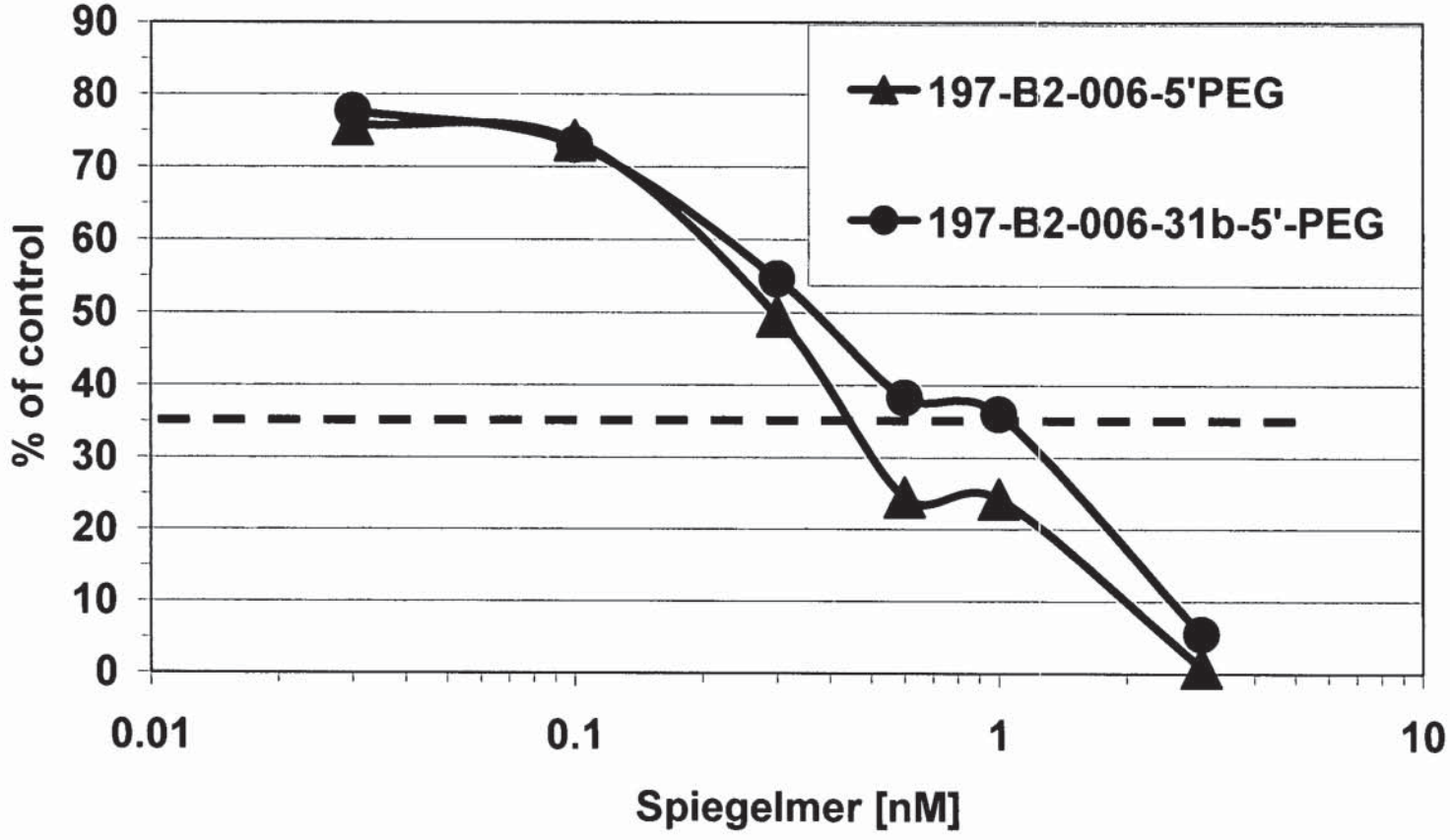
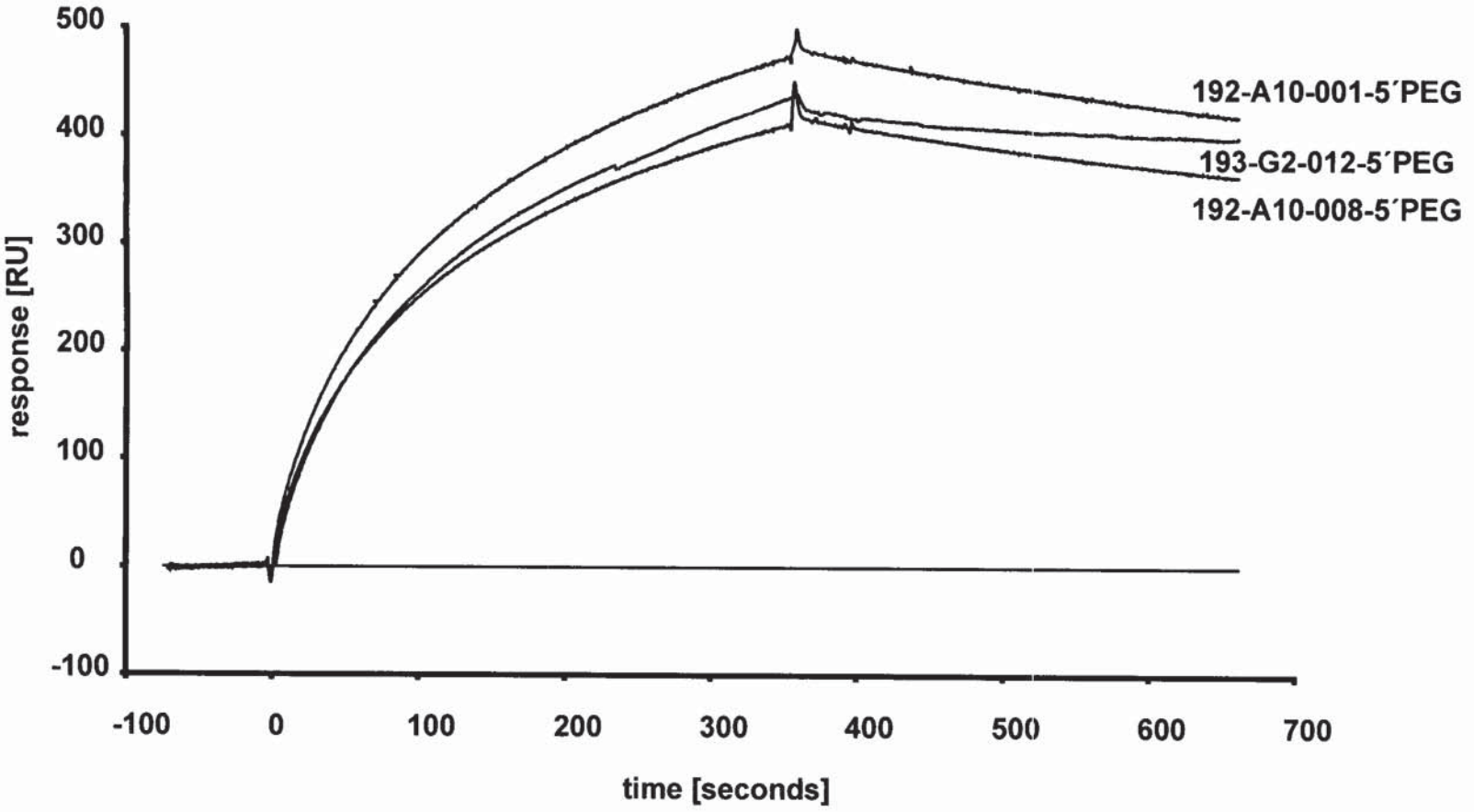
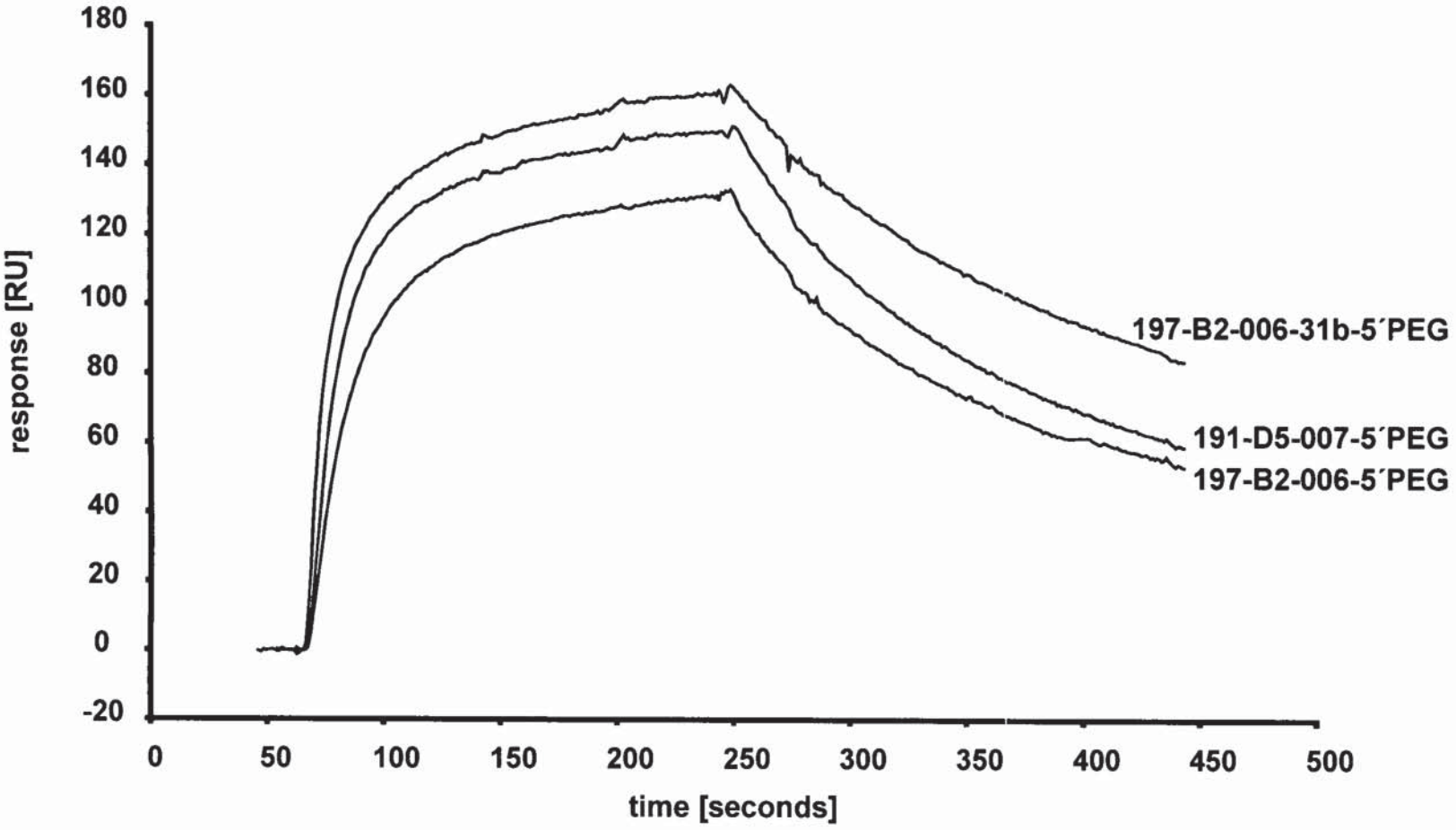

90
80
70
60
50
40
30
20
10
0
% of control
0.01
0.1
1
10
Spiegelmer [nM]
197-B2-006-5'PEG
197-B2-006-31b-5'-PEG

Fig. 23B



Spiegelmer	k_a [$M^{-1} \times s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
192-A10-001-5´PEG	2.08×10^5	5.32×10^{-4}	2.55
192-A10-008-5´PEG	1.7×10^5	6.68×10^{-4}	3.92
193-G2-012-5´PEG	3.42×10^5	2.52×10^{-4}	0.74

Fig. 24 A



Spiegelmer	k_a [$M^{-1} x\ s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
191-D5-007-5´PEG	1.8×10^6 9.05×10^5	4.3×10^{-3} 5.73×10^{-3}	2.4 6.3
197-B2-006-5´PEG	1.47×10^6	4.39×10^{-3}	3.0
197-B2-006-31b-5´PEG	1.96×10^6	3.02×10^{-3}	1.54

Fig. 24B

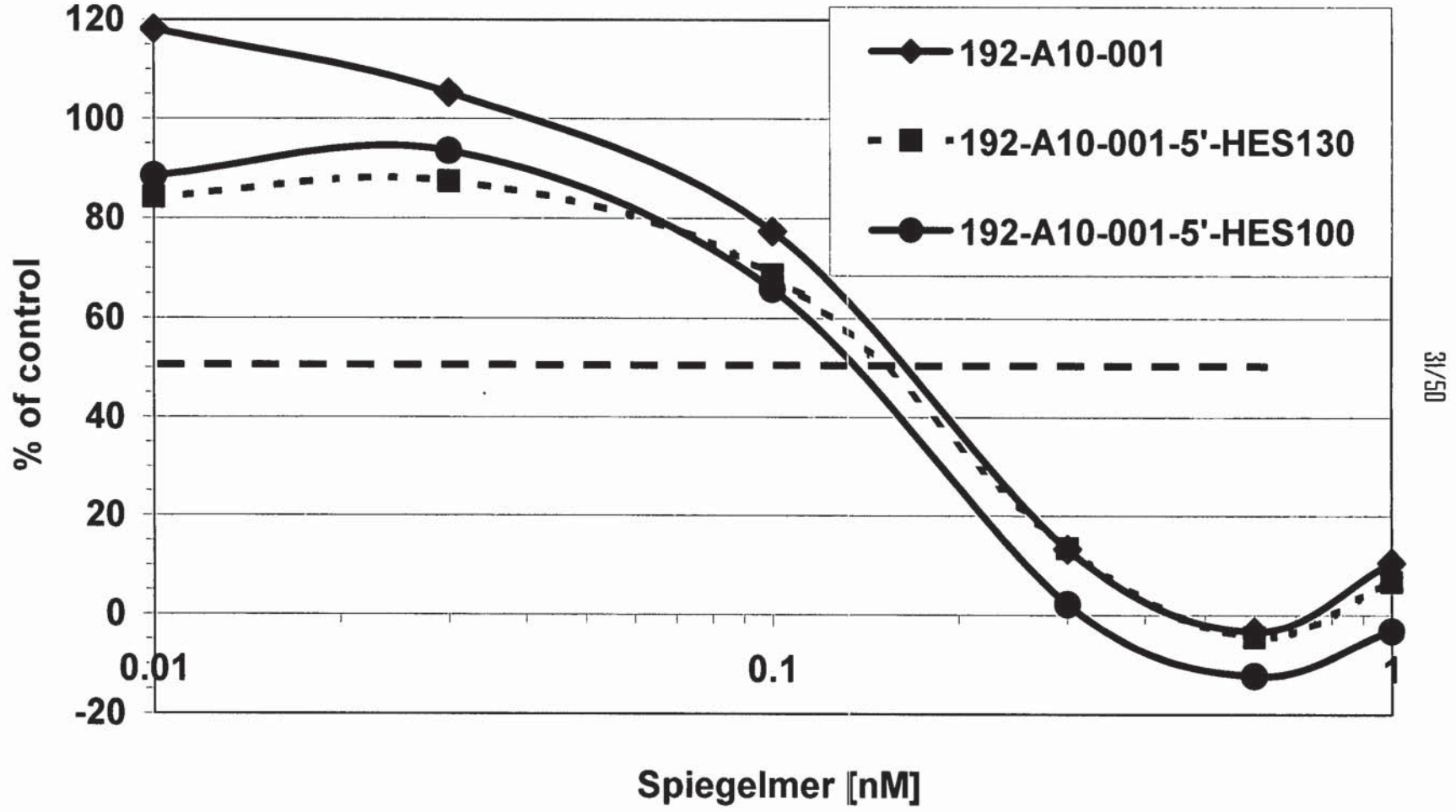

120
100
80
60
40
20
0
-20
% of control
0.01
0.1
1
Spiegelmer [nM]
192-A10-001
192-A10-001-5'-HES130
192-A10-001-5'-HES100

Fig. 25A

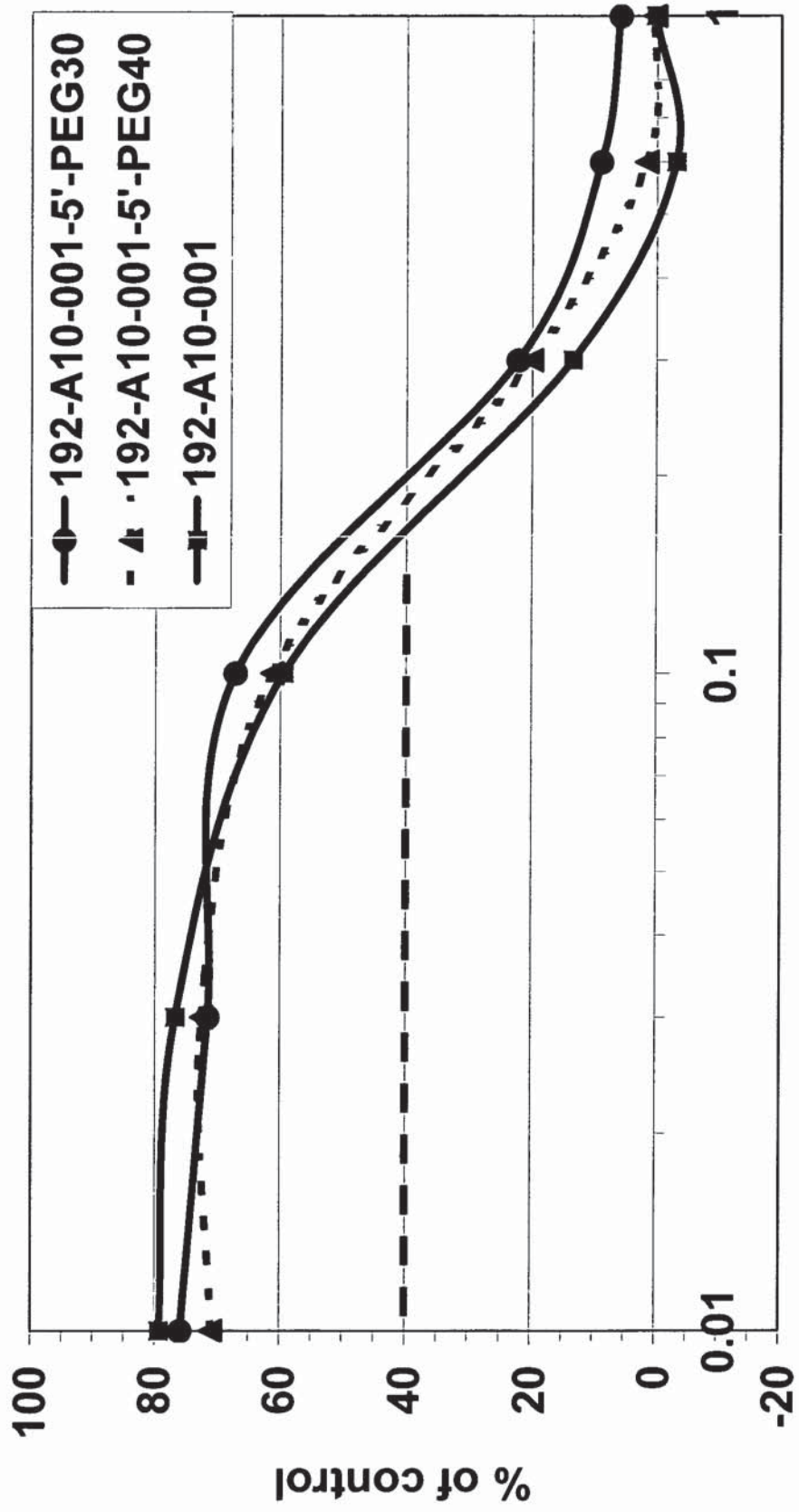

192-A10-001-5'-PEG30
192-A10-001-5'-PEG40
192-A10-001
% of control
100
80
60
40
20
0
-20
0.01
0.1
1
Spiegelmer [nM]

Fig. 25B

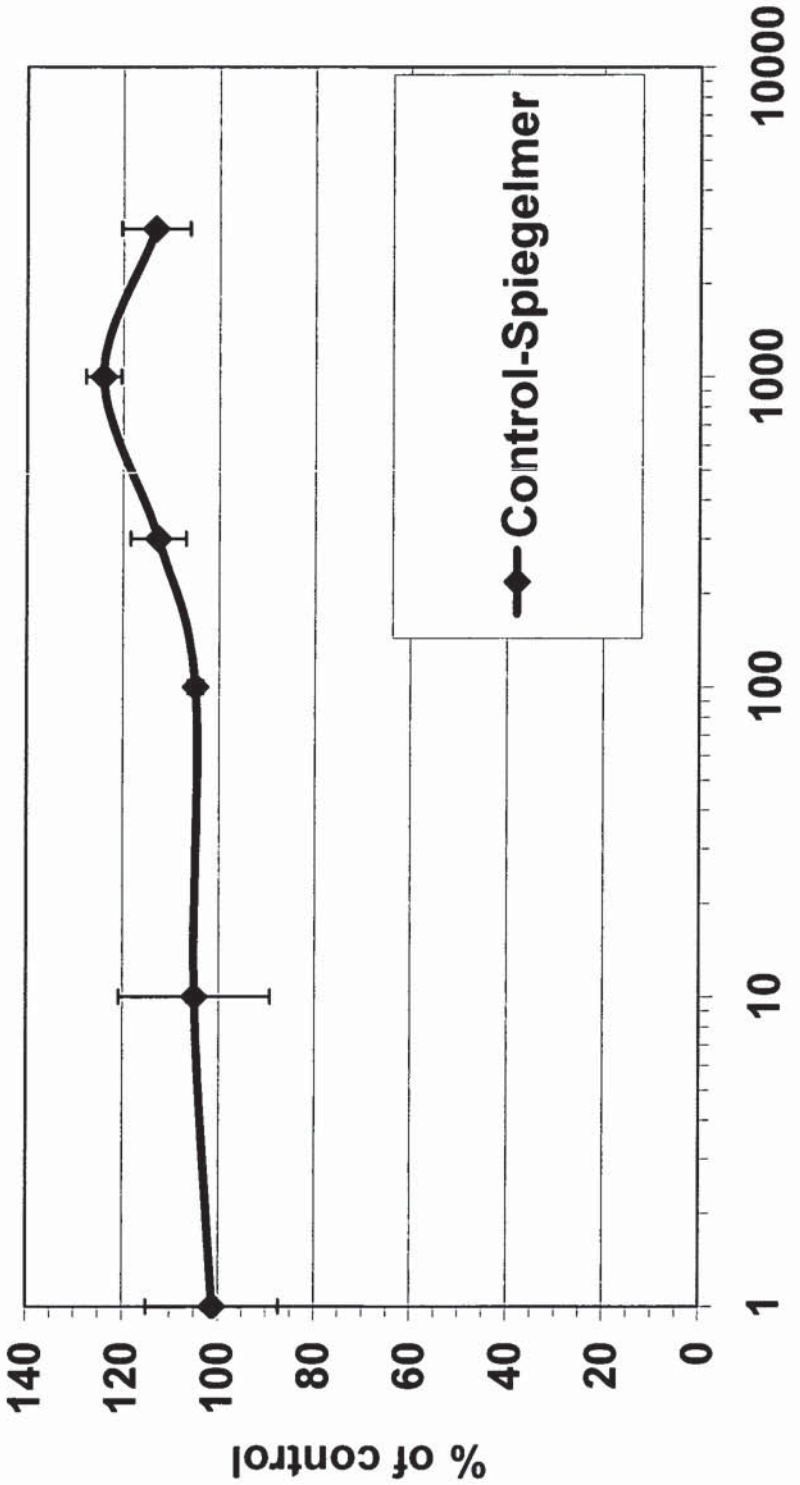

% of control
140
120
100
80
60
40
20
0
1
10
100
1000
10000
Control Spiegelmer [nM]
Control-Spiegelmer

Fig. 26

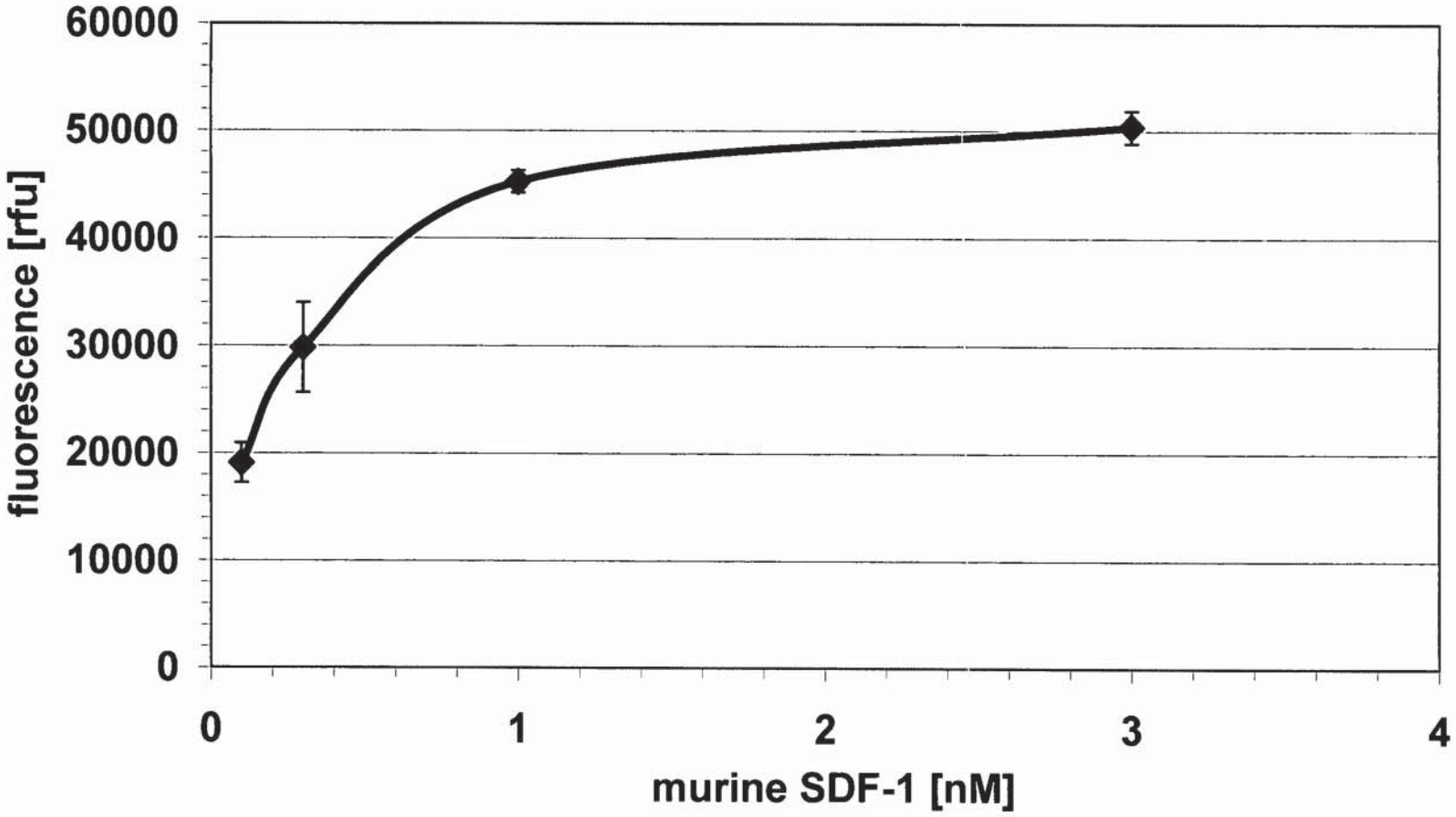

60000
50000
40000
30000
20000
10000
0
fluorescence [rfu]
0
1
2
3
4
murine SDF-1 [nM]

Fig. 27

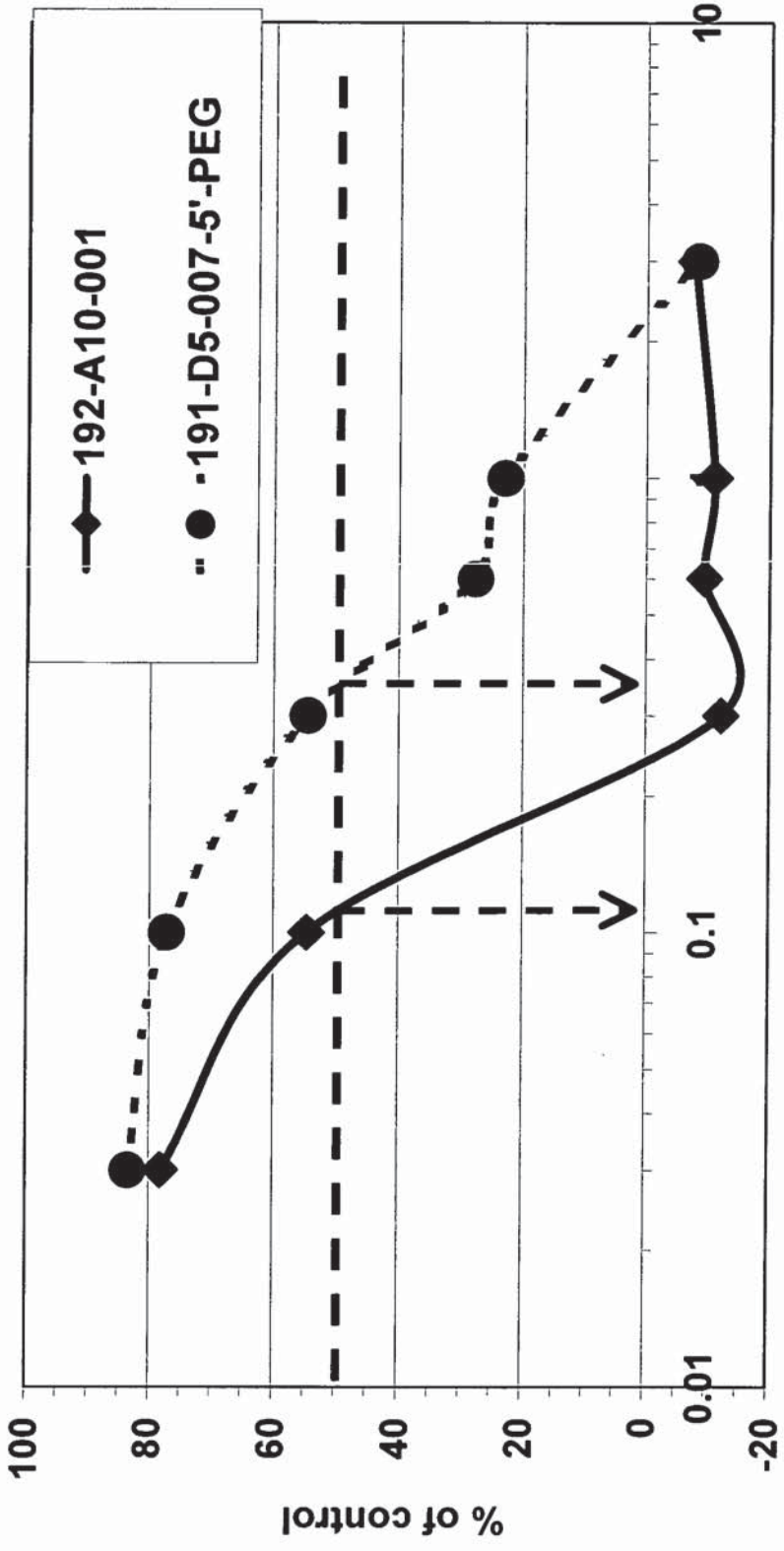

192-A10-001
191-D5-007-5'-PEG
% of control
100
80
60
40
20
0
-20
0.01
0.1
10
Spiegelmer [nM]

Fig. 28

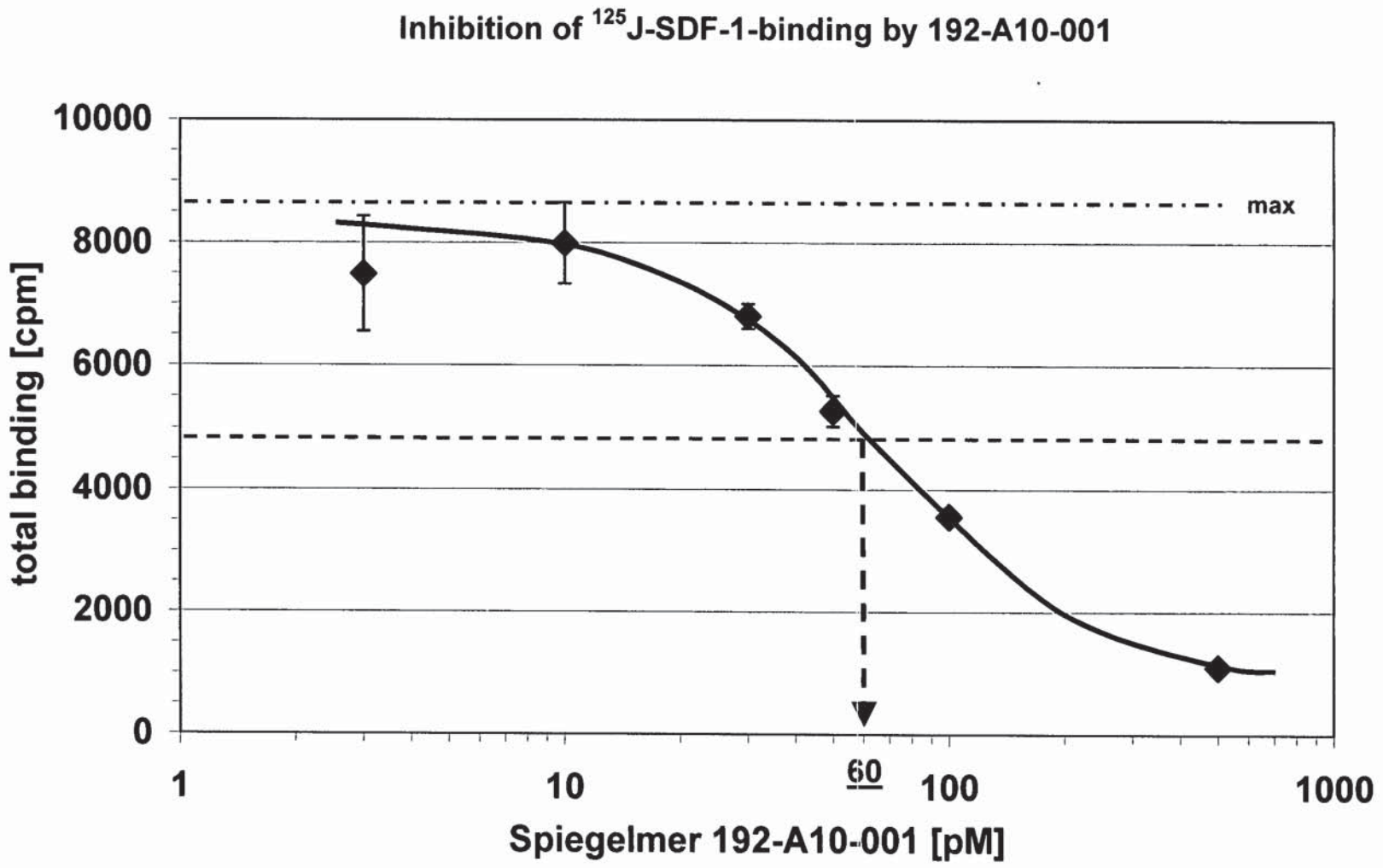
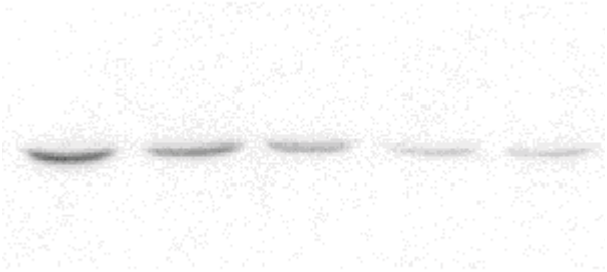

Inhibition of 125J-SDF-1-binding by 192-A10-001
10000
8000
6000
4000
2000
0
total binding [cpm]
max
1
10
60
100
1000
Spiegelmer 192-A10-001 [pM]

Fig. 29



SDF-1 [nM]	1.0	1.0	1.0	1.0	1.0
192-A10-001 [nM]	0	0.1	0.3	1.0	3.0

Fig. 30

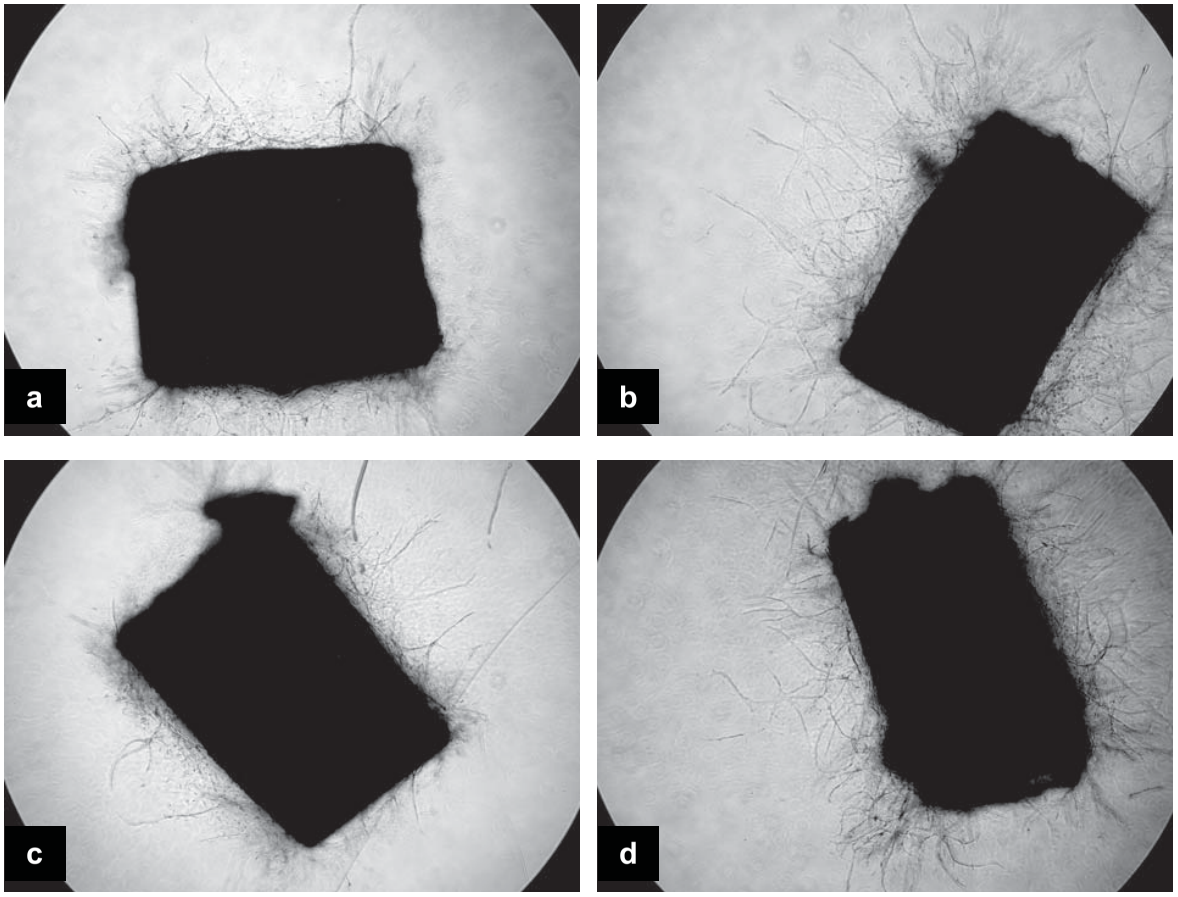


Fig. 31: SDF-1 induced sprouting in an aortic ring sprouting assay. Rings from rat aorta were embedded in collagen matrix and incubated for 6 days with SDF-1 with or without Spiegelmers. **a**: control; **b**: 10 nM SDF-1; **c**: 10 nM SDF-1 + 1 µM 193-G2-012-5'-PEG; **d**: 10 nM SDF-1 + 1 µM PEGylated Control Spiegelmer

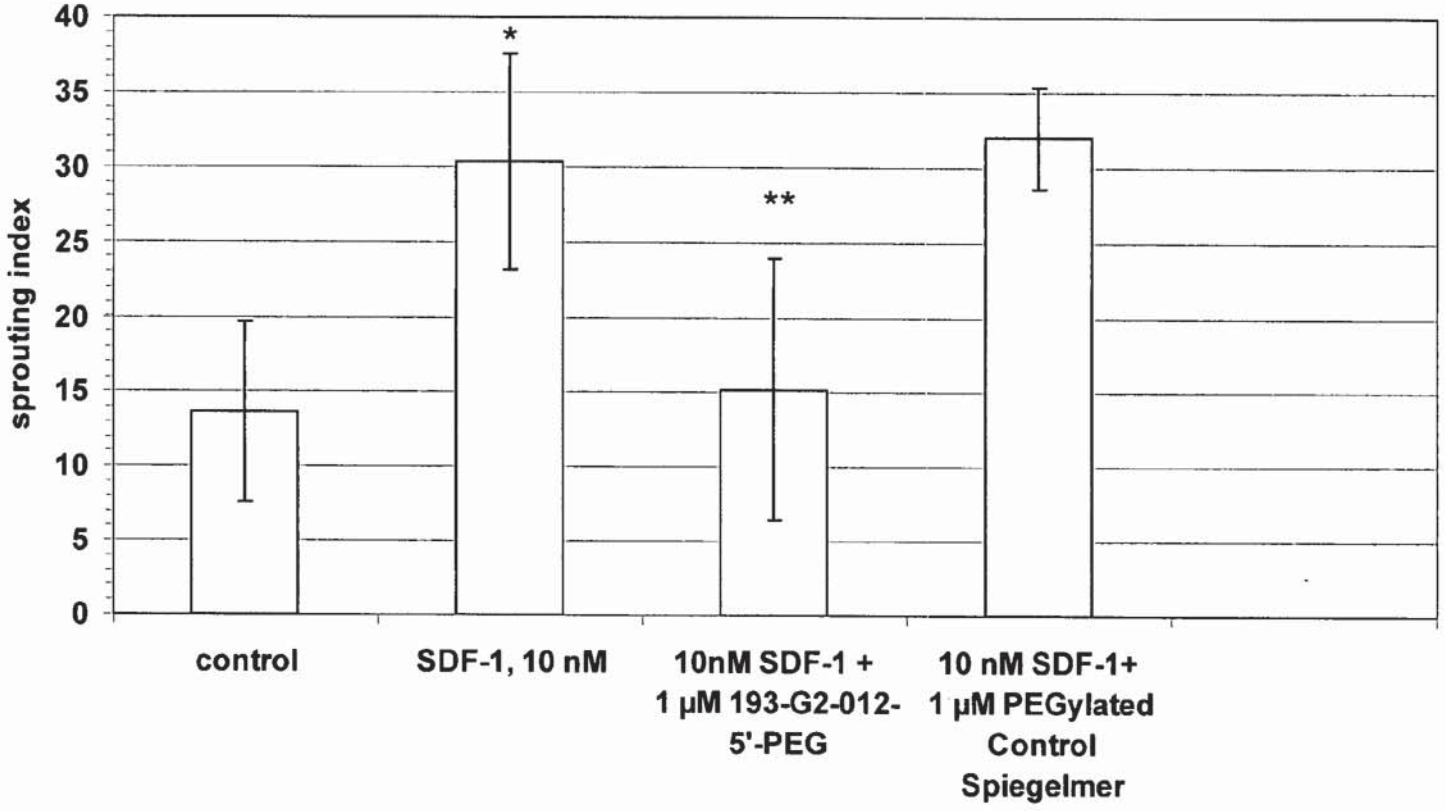


Fig. 32: SDF-1 induced sprouting and the blockage thereof by Spiegelmers in an aortic ring sprouting assay. Rings from rat aorta were embedded in collagen matrix and incubated for 6 days with SDF-1 with or without Spiegelmers. Sprouting indices are shown as mean +/- SD for 5 rings per condition. *: the value for SDF-1 is significantly different from control (Mann-Whitney-test; p= 0.009); **: the value for SDF-1 + 193-G2-012-5'-PEG is significantly different from that for SDF-1 (Mann-Whitney-test; p= 0.028).

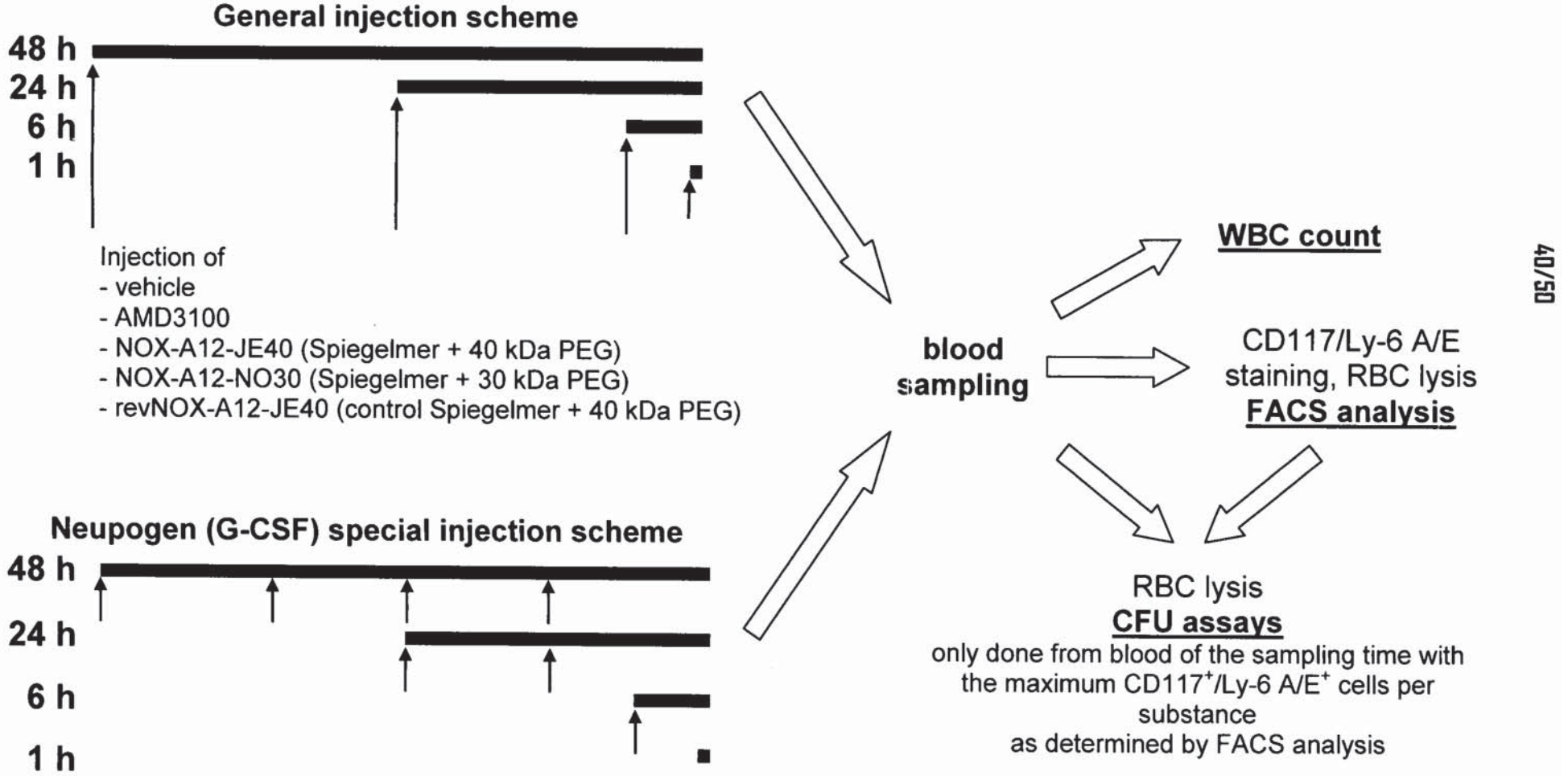

General injection scheme
48 h
24 h
6 h
1 h
Injection of
- vehicle
- AMD3100
- NOX-A12-JE40 (Spiegelmer + 40 kDa PEG)
- NOX-A12-NO30 (Spiegelmer + 30 kDa PEG)
- revNOX-A12-JE40 (control Spiegelmer + 40 kDa PEG)
Neupogen (G-CSF) special injection scheme
48 h
24 h
6 h
1 h
blood sampling
WBC count
CD117/Ly-6 A/E staining, RBC lysis
FACS analysis
RBC lysis
CFU assays
only done from blood of the sampling time with the maximum CD117+/Ly-6 A/E+ cells per substance
as determined by FACS analysis

Fig. 33

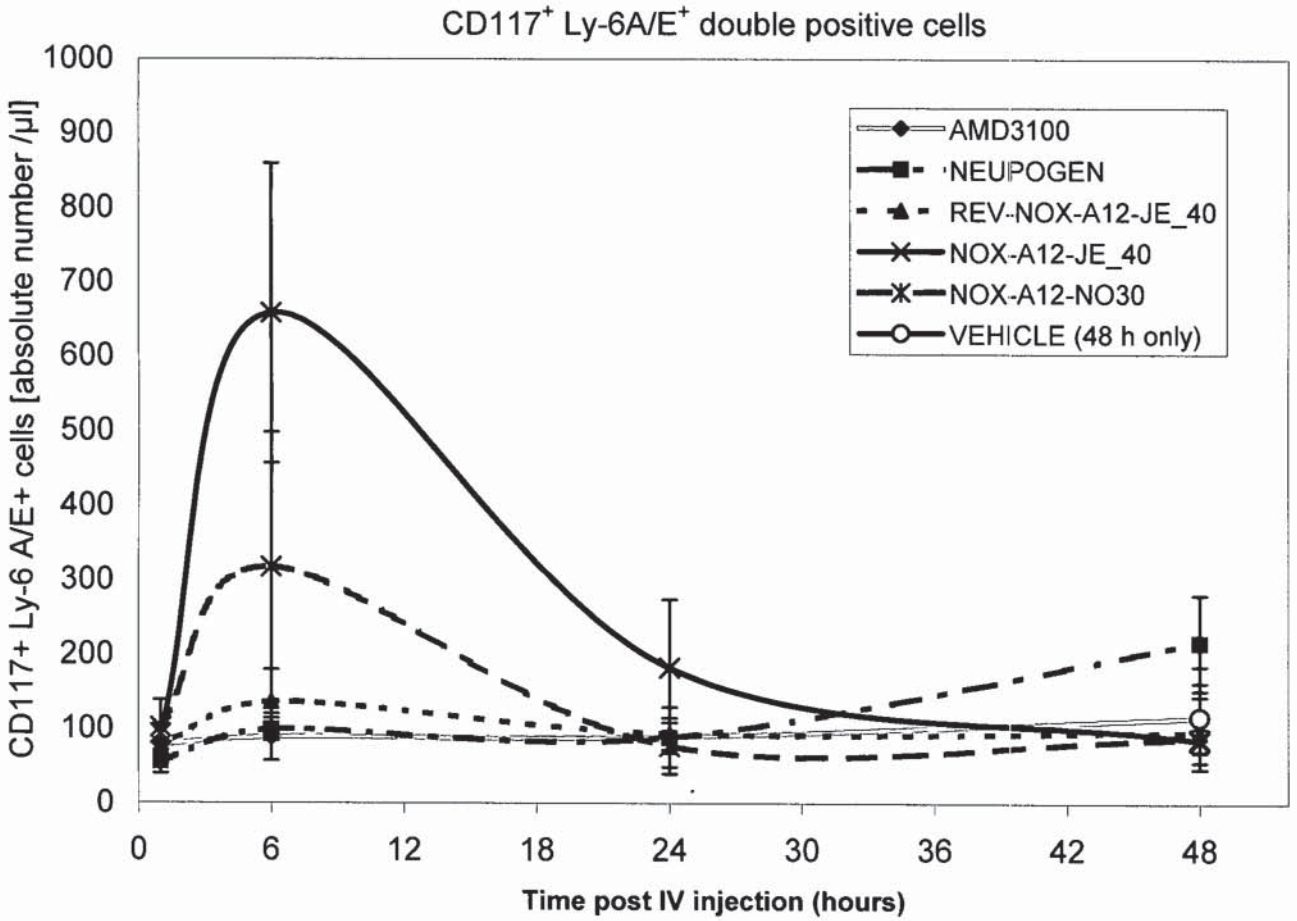

CD117+ Ly-6A/E+ double positive cells
CD117+ Ly-6 A/E+ cells [absolute number /µl]
1000
900
800
700
600
500
400
300
200
100
0
0
6
12
18
24
30
36
42
48
Time post IV injection (hours)
AMD3100
NEUPOGEN
REV-NOX-A12-JE_40
NOX-A12-JE_40
NOX-A12-NO30
VEHICLE (48 h only)

Fig. 34

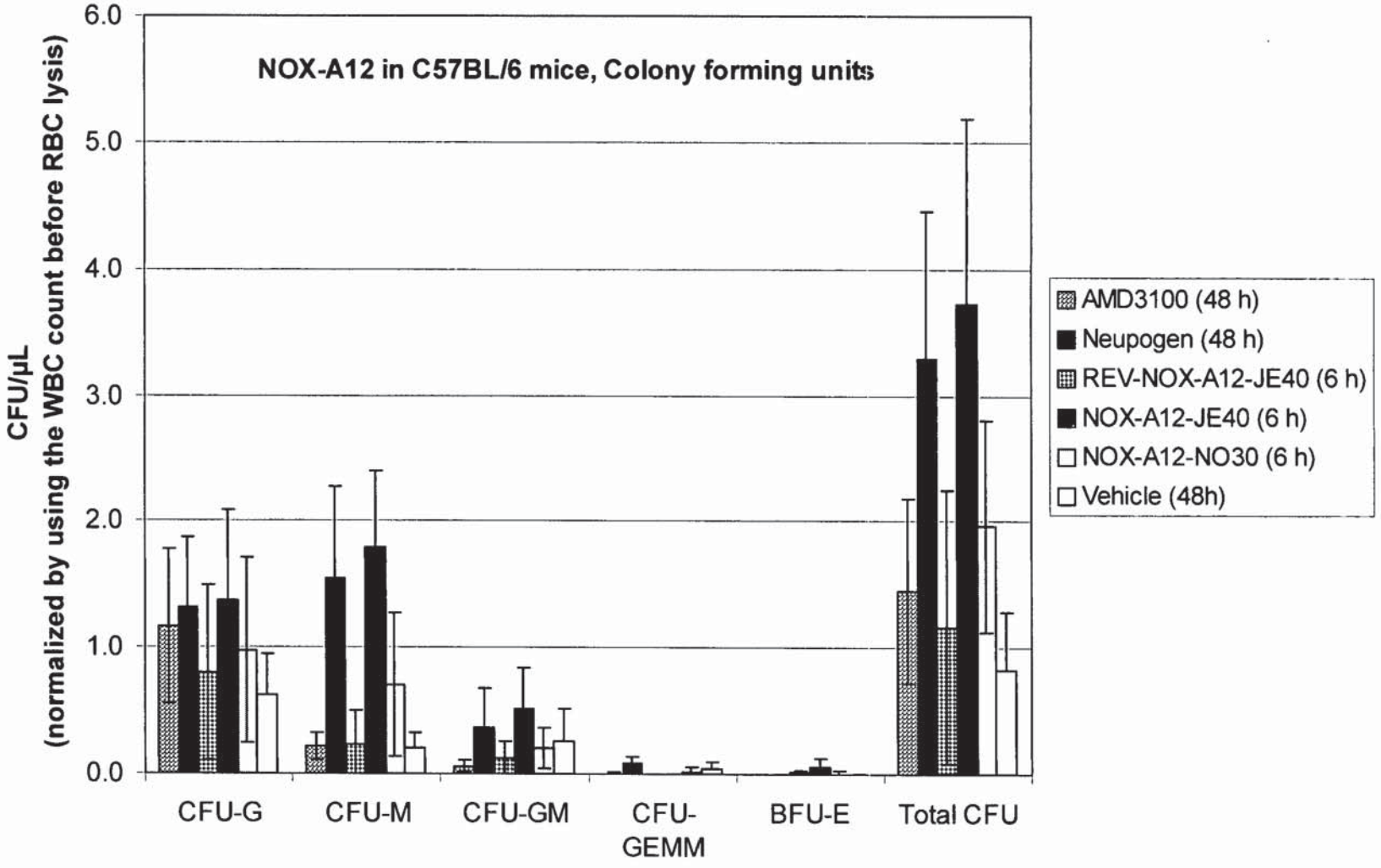
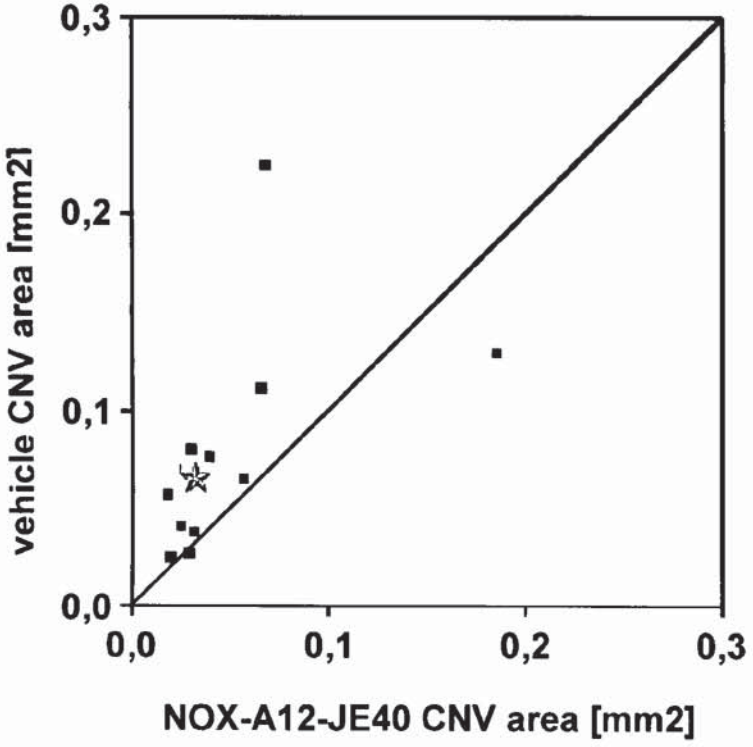
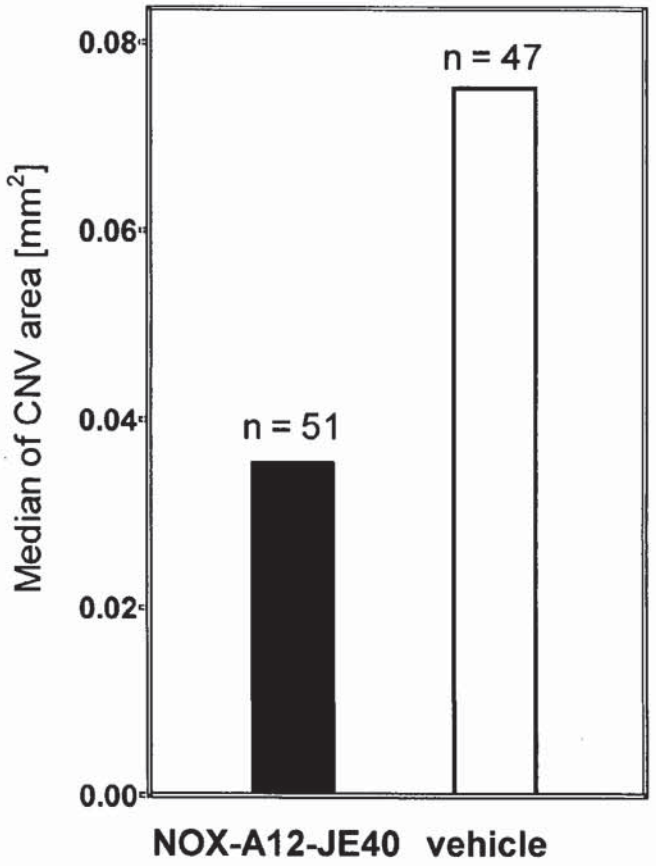

NOX-A12 in C57BL/6 mice, Colony forming units
CFU/µL
(normalized by using the WBC count before RBC lysis)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
CFU-G
CFU-M
CFU-GM
CFU-GEMM
BFU-E
Total CFU
AMD3100 (48 h)
Neupogen (48 h)
REV-NOX-A12-JE40 (6 h)
NOX-A12-JE40 (6 h)
NOX-A12-NO30 (6 h)
Vehicle (48h)

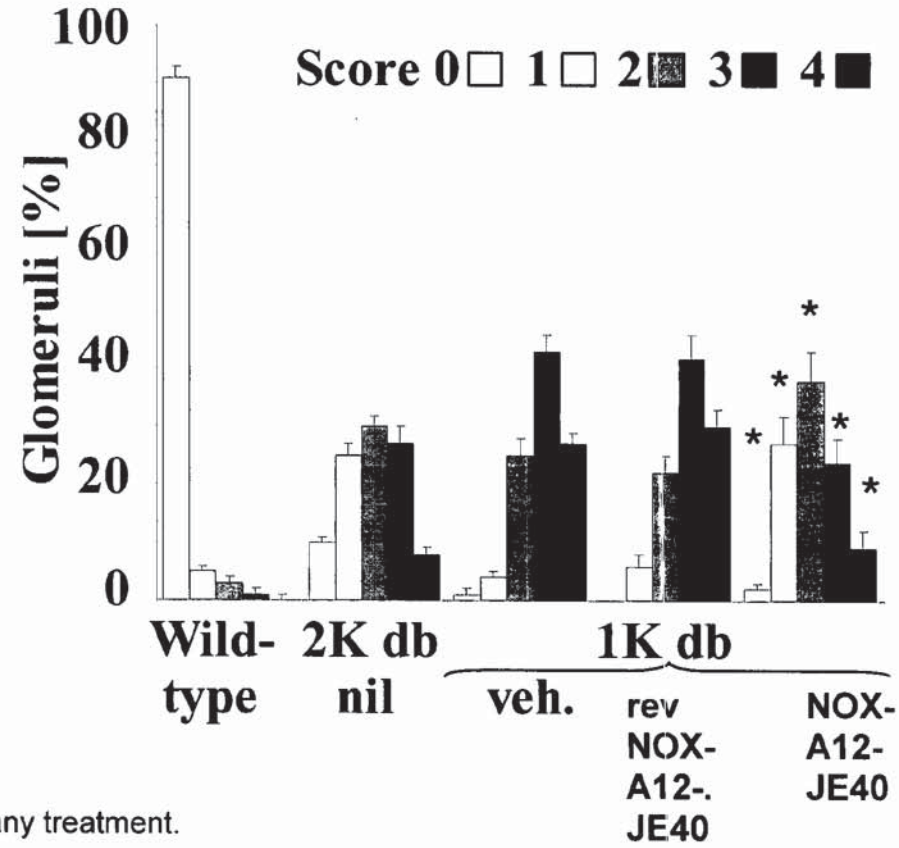
Fig. 35





n = number of evaluated laser burns per group

Fig. 36



Wild type = wild type mice without any treatment.

2K db nil = diabetic mice with two kidneys without any treatment.

1K db = diabetic mice after uninephrectomy (1 kidney left)

veh. = vehicle treated (5 % glucose for injection)

Score 0-4 = Glomerulosclerosis score from 0 = healthy to 4 = highly fibrotic.

Fig. 37

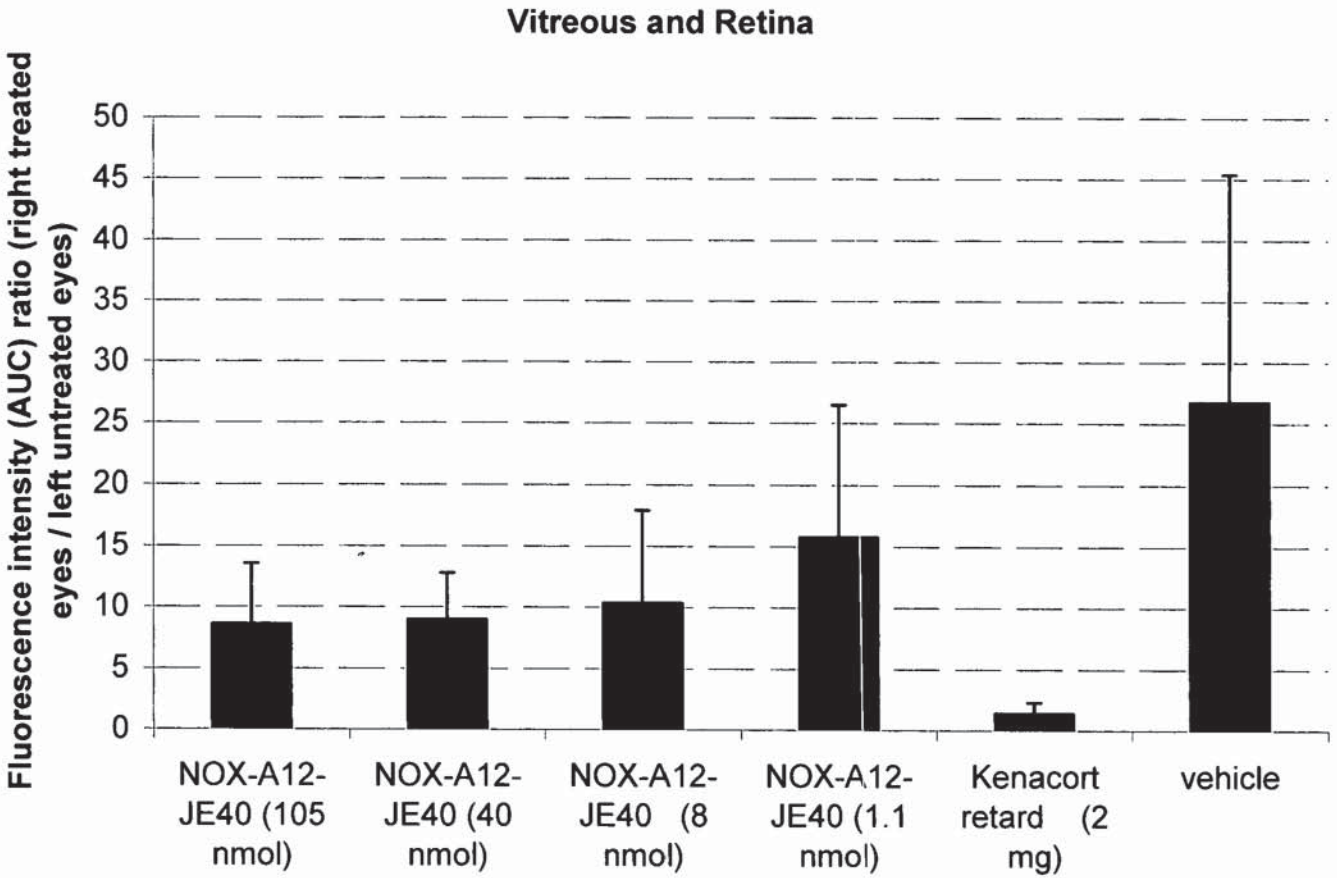
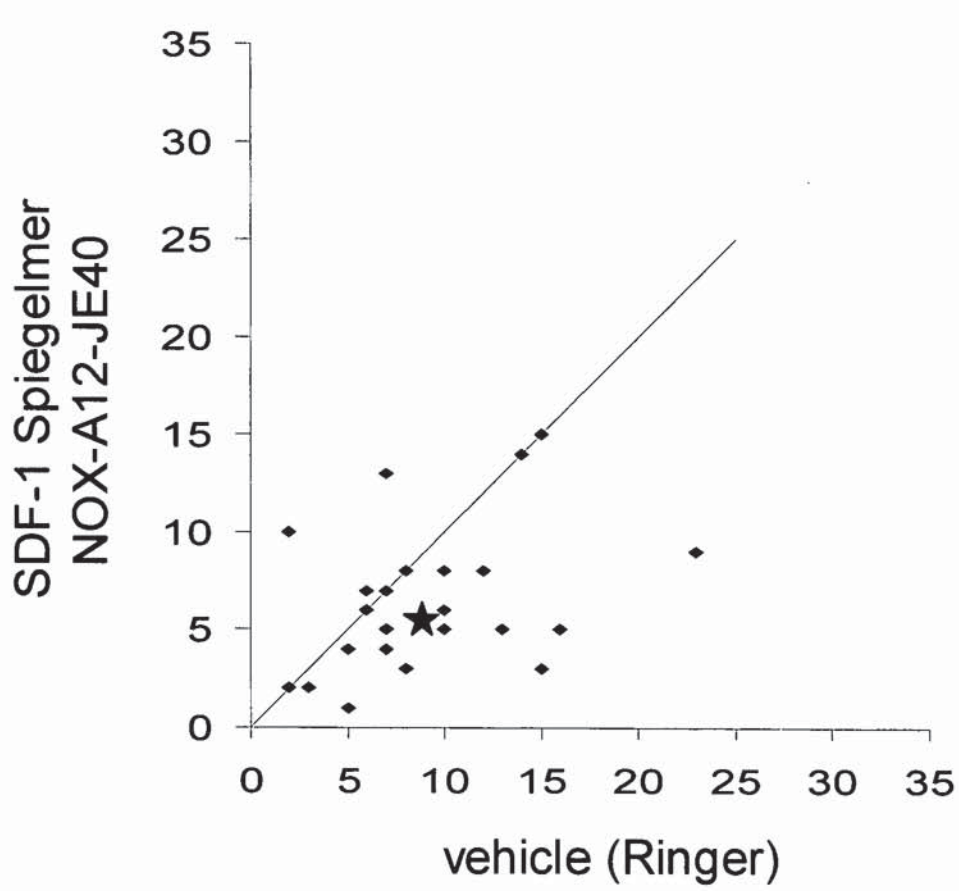

Vitreous and Retina
Fluorescence intensity (AUC) ratio (right treated eyes / left untreated eyes)
50
45
40
35
30
25
20
15
10
5
0
NOX-A12-JE40 (105 nmol)
NOX-A12-JE40 (40 nmol)
NOX-A12-JE40 (8 nmol)
NOX-A12-JE40 (1.1 nmol)
Kenacort retard (2 mg)
vehicle

Fig. 38



The mean retinopathy scores is depicted as a star.

Fig. 39

Statistics: Wilcoxon-Signed-Rank Test / p-values

	Fluorescein (n=24)	Isolectin (n=15)
Clusters (n)	**0.210**	**0.057**
Cluster-area absolute	**0.210**	**0.501**
Cluster-area relative	**0.501**	**0.365**
Tufts (n)	**0.008**	**0.0215**
Avascular zone absolute	**0.3531**	**0.2524**
Avascular zone relative	**0.398**	**0.359**
Retinopathy Score	**0.009**	

Fig. 40

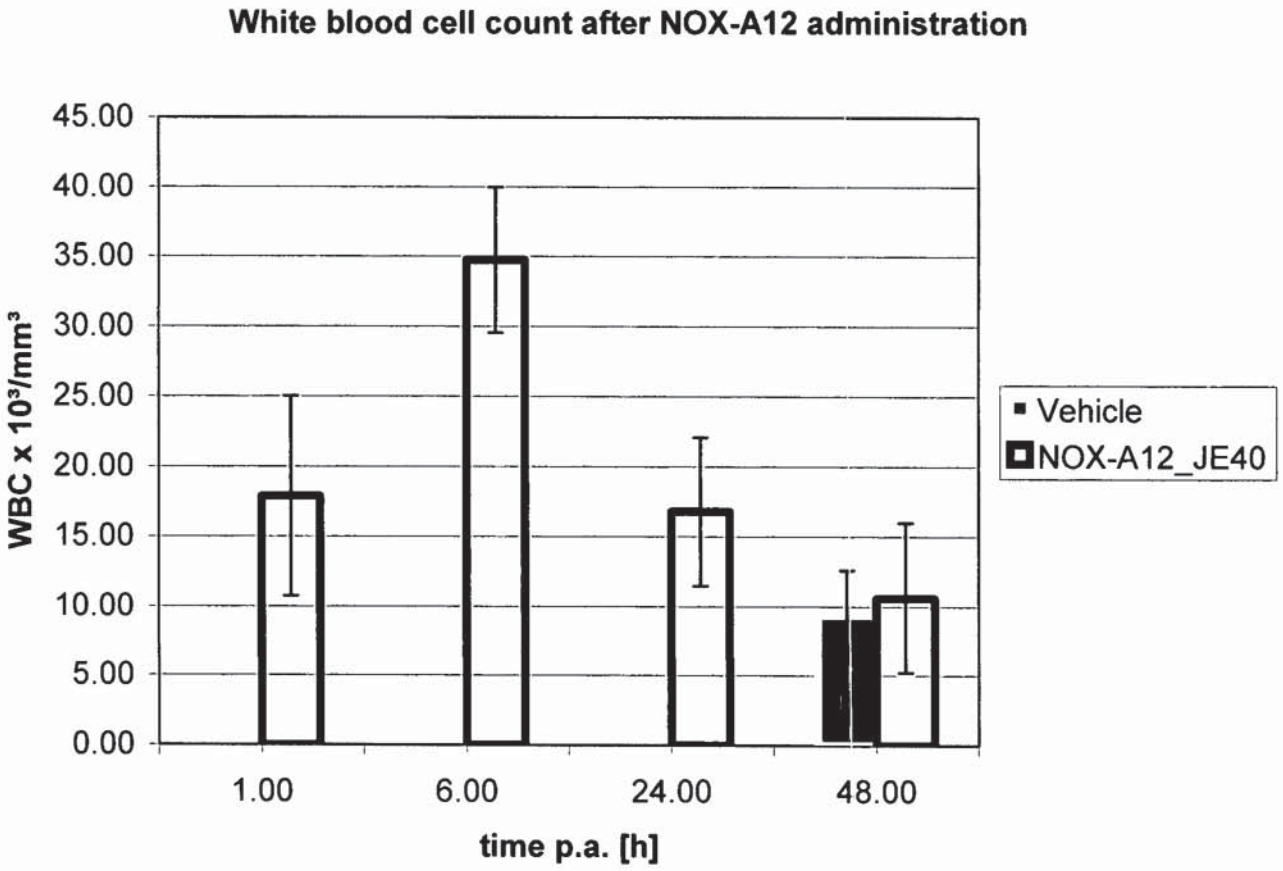

White blood cell count after NOX-A12 administration
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
WBC x 10³/mm³
1.00
6.00
24.00
48.00
time p.a. [h]
Vehicle
NOX-A12_JE40

Fig. 41

Indications for allogeneic HSCT in Europe 1990-2000

	No. of patients			
	Total 1990-2000	%	Total 2000	%
Leukemias	33 509	75.9	4653	72.7
Acute myeloid leukemia	10 990	24.9	1627	25.4
Acute lymphocytic leukemia	8 871	20.1	1135	17.7
Chronic myeloid leukemia	10 559	23.9	1315	20.5
Myelodysplastic syndromes	2 680	6.1	454	7.1
Chronic lymphocytic leukemia	409	0.9	122	1.9
Lymphoproliferative disorders	3 930	8.9	820	12.8
Multiple myeloma	1 470	3.3	295	4.6
Hodgkin disease	320	0.7	68	1.1
Non-Hodgkin lymphoma	2 140	4.8	457	7.1
Solid tumors	272	0.6	104	1.6
Neuroblastoma	30	0.1	1	0.0
Glioma	2	0.0	1	0.0
Soft tissue sarcoma	13	0.0	5	0.1
Germinal tumors	10	0.0	3	0.0
Breast cancer	57	0.1	16	0.2
Ewing sarcoma	28	0.1	4	0.1
Lung cancer	1	0.0	0	0.0
Ovarian cancer	11	0.0	7	0.1
Other solid tumors	120	0.3	67	1.0
Nonmalignant disorders	5 695	12.9	700	10.9
Aplastic anemia + Fanconi	2 483	5.6	287	4.5
Thalassemia	1 349	3.1	147	2.3
Combined immune deficiencies	724	1.6	103	1.6
Inborn errors	1 112	2.5	153	2.4
Autoimmune diseases	27	0.1	10	0.2
Others	759	1.7	127	2.0
Total	44 165		6404	

Fig. 42

. Indications for autologous HSCT in Europe 1990-2000

	No. of patients			
	Total 1990-2000	%	Total 2000	%
Leukemias	15 052	17.0	1 764	13.9
Acute myeloid leukemia	8 129	9.2	1 047	8.2
Acute lymphocytic leukemia	3 765	4.2	302	2.4
Chronic myeloid leukemia	1 967	2.2	148	1.2
Myelodysplastic syndromes	297	0.3	50	0.4
Chronic lymphocytic leukemia	894	1.0	217	1.7
Lymphoproliferative disorders	48 917	55.1	8 498	66.7
Multiple myeloma	16 206	18.3	3 388	26.6
Hodgkin disease	9 078	10.2	1 226	9.6
Non-Hodgkin lymphoma	23 633	26.6	3 884	30.5
Solid tumors	24 016	27.0	2 286	18.0
Neuroblastoma	1 912	2.2	262	2.1
Glioma	544	0.6	73	0.6
Soft tissue sarcoma	1 013	1.1	144	1.1
Germinal tumors	2 658	3.0	304	2.4
Breast cancer	12 598	14.2	781	6.1
Ewing sarcoma	1 401	1.6	244	1.9
Lung cancer	318	0.4	62	0.5
Ovarian cancer	628	0.7	100	0.8
Other solid tumors	2 944	3.3	316	2.5
Nonmalignant disorders	321	0.4	100	0.8
Aplastic anemia + Fanconi	7	0.0	1	0.0
Thalassemia	0	0.0	0	0.0
Combined immune deficiencies	10	0.0	2	0.0
Inborn errors	4	0.0	0	0.0
Autoimmune diseases	300	0.3	97	0.8
Others	492	0.6	84	0.7
Total	88 798		12 732	

Fig. 43