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**CA**CAGC	<
192-F10	38	**GCUGUG**AAAGUAACACGUCAA-UGAAAGGUAAC**CGCAGC**	<
192-B11	38	**GCUGUG**AAAGUAACACGUCAA-UGAAAGGUAAC**CA**CAGC	=
192-C9	38	**GCUGUA**AAAGUAACAUGUCAA-UGAAAGGUAAC**UA**CAGC	<
192-E10	38	**GCUGUA**AAAGUAACAAGUCAA-UGAAAGGUAAC**UA**CAGC	<
192-C10	38	**GCUGUG**AAAGUAACAAGUCAA-UGAAAGGUAAC**CA**CAGC	=
192-D11	38	**GCAGUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CA**CAGC	<
192-G11	38	**GC**U**GUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CA**C**U**GC	<
192-H11	38	**GCUAUG**AAAGUAACAUGUCAA-UGAAAGGUAAC**CAUAGC**	<
192-D10	38	**GCUGCG**AAAGCGACAUGUCAA-UGAAAGGUAGC**CGCAGC**	<<
192-E9	38	**GCUGUG**AAAGCAACAUGUCAA-UGAAAGGUAGC**CA**CAGC	<<
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

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**		<	

10/50

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

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

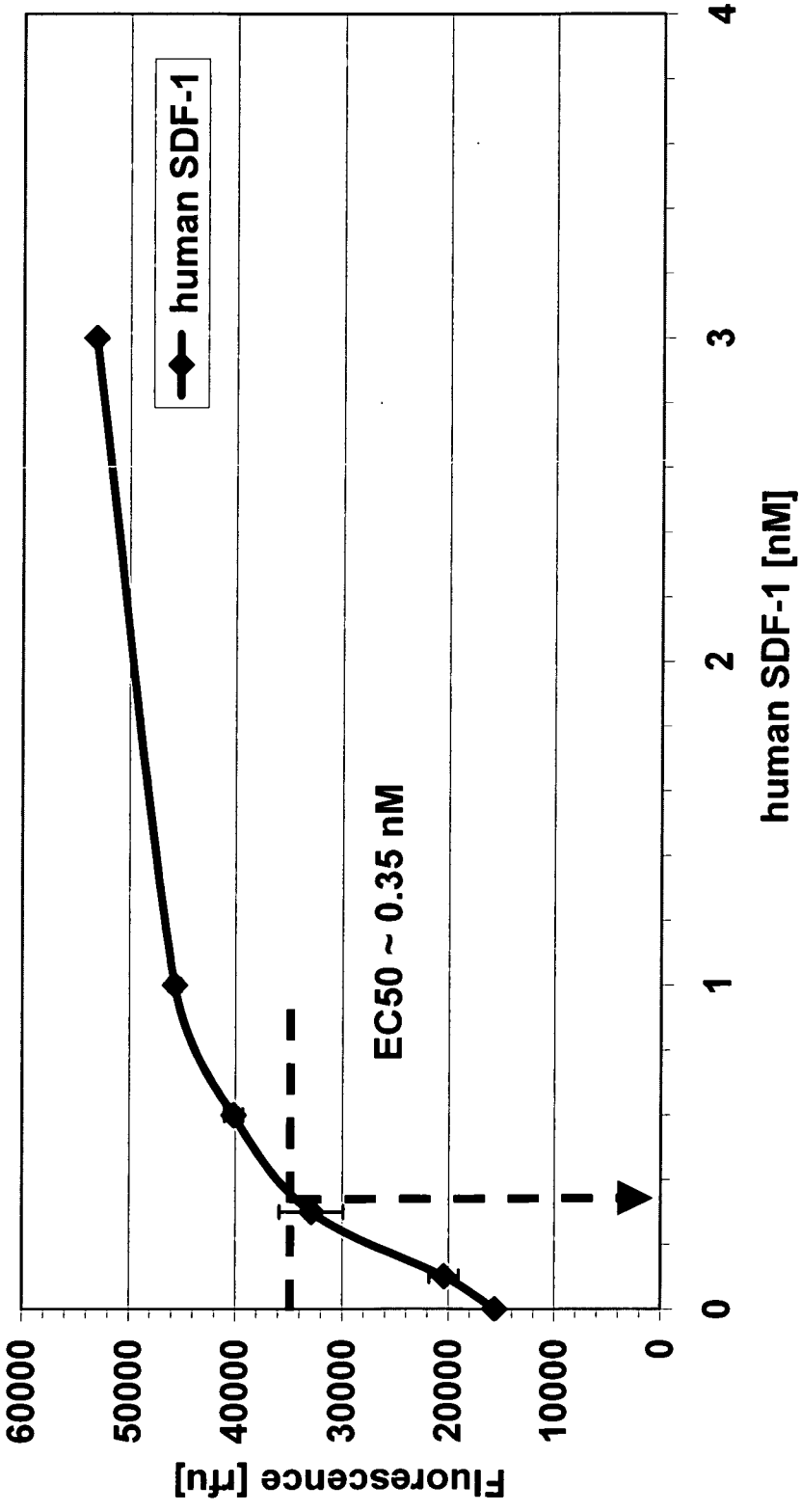

human SDF-1
EC50 ~ 0.35 nM
Fluorescence [rfu]
human SDF-1 [nM]
0
10000
20000
30000
40000
50000
60000
0
1
2
3
4

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

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

Fig. 12

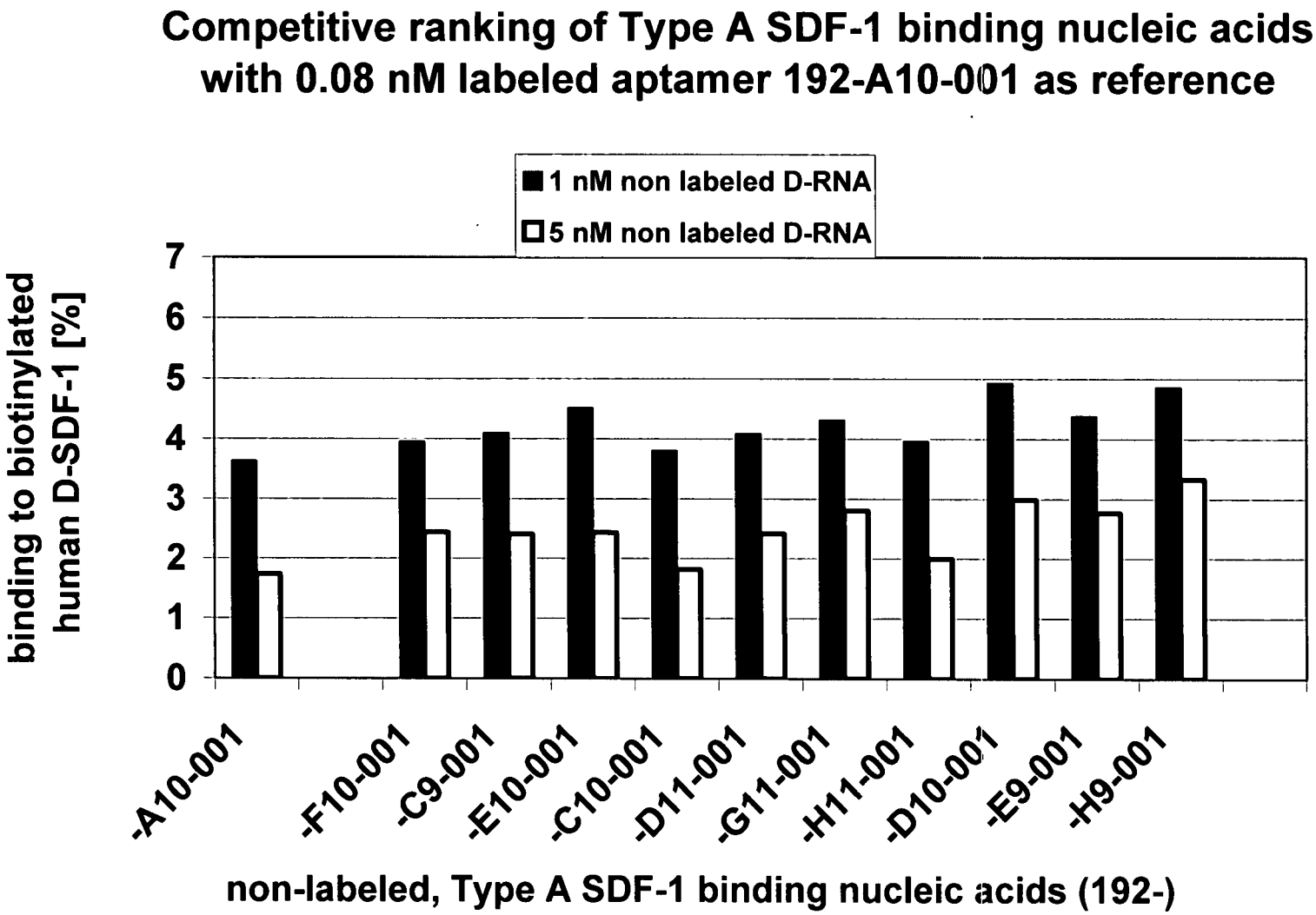
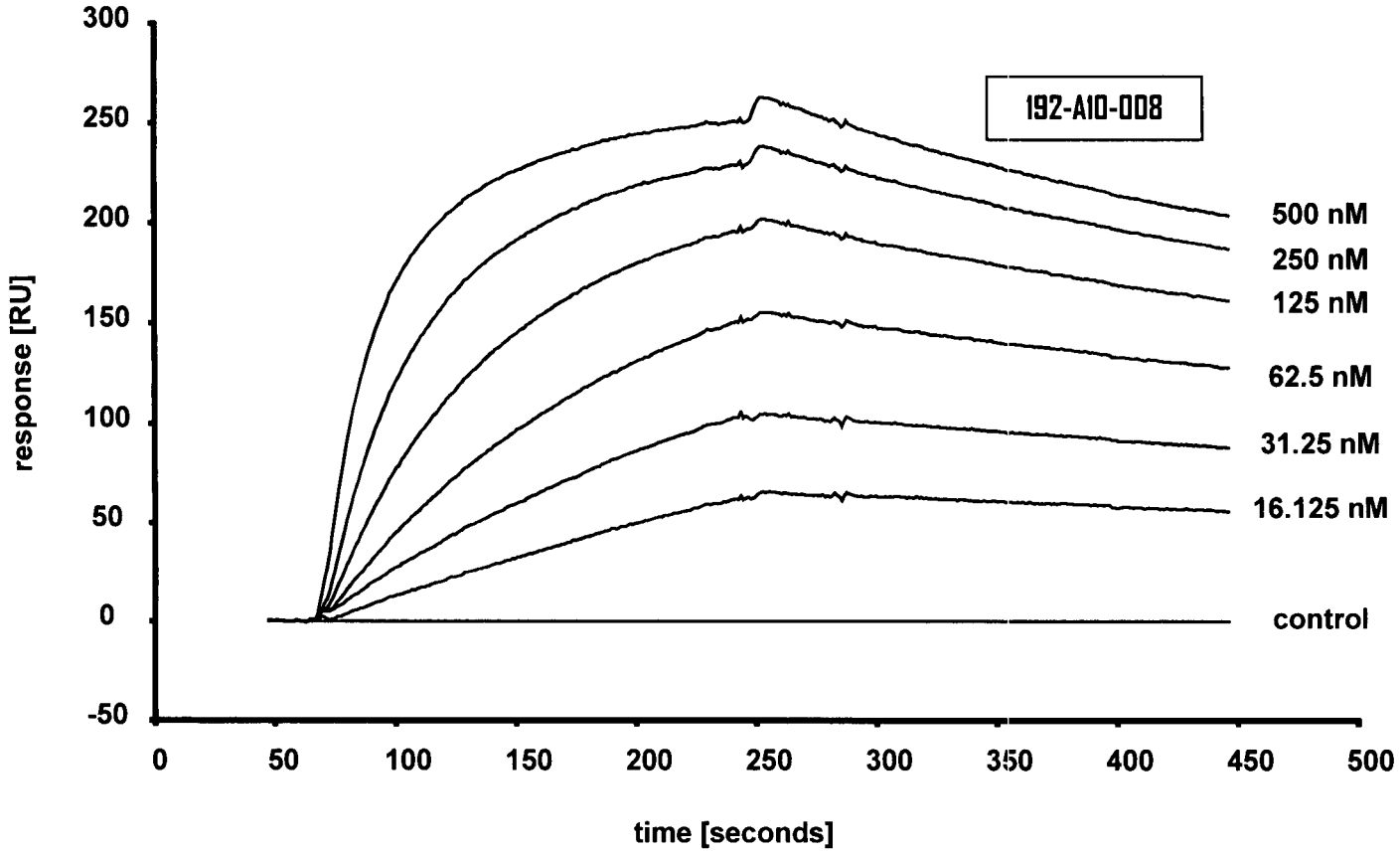

Competitive ranking of Type A SDF-1 binding nucleic acids
with 0.08 nM labeled aptamer 192-A10-001 as reference
1 nM non labeled D-RNA
5 nM non labeled D-RNA
binding to biotinylated
human D-SDF-1 [%]
0
1
2
3
4
5
6
7
-A10-001
-F10-001
-C9-001
-E10-001
-C10-001
-D11-001
-G11-001
-H11-001
-D10-001
-E9-001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

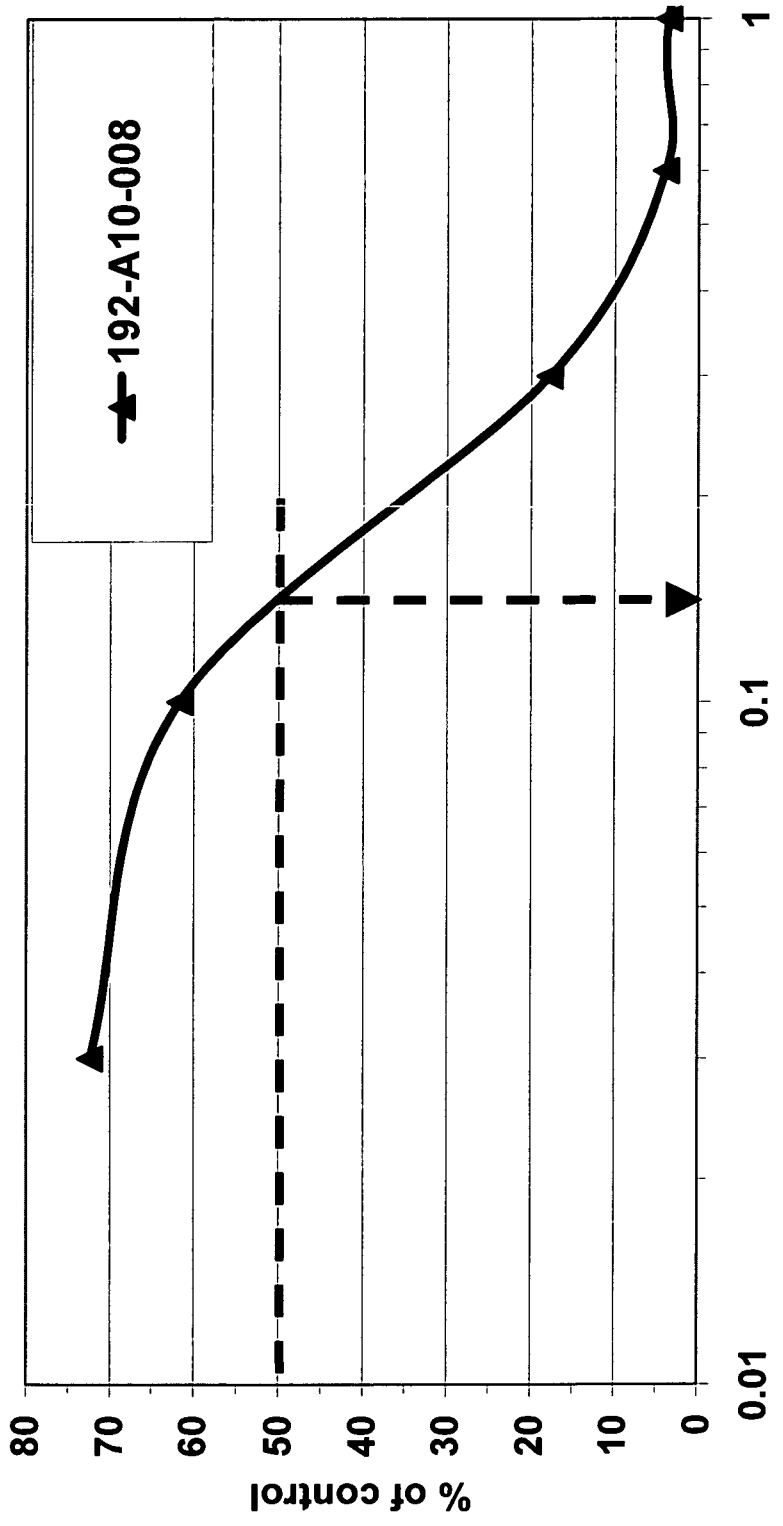
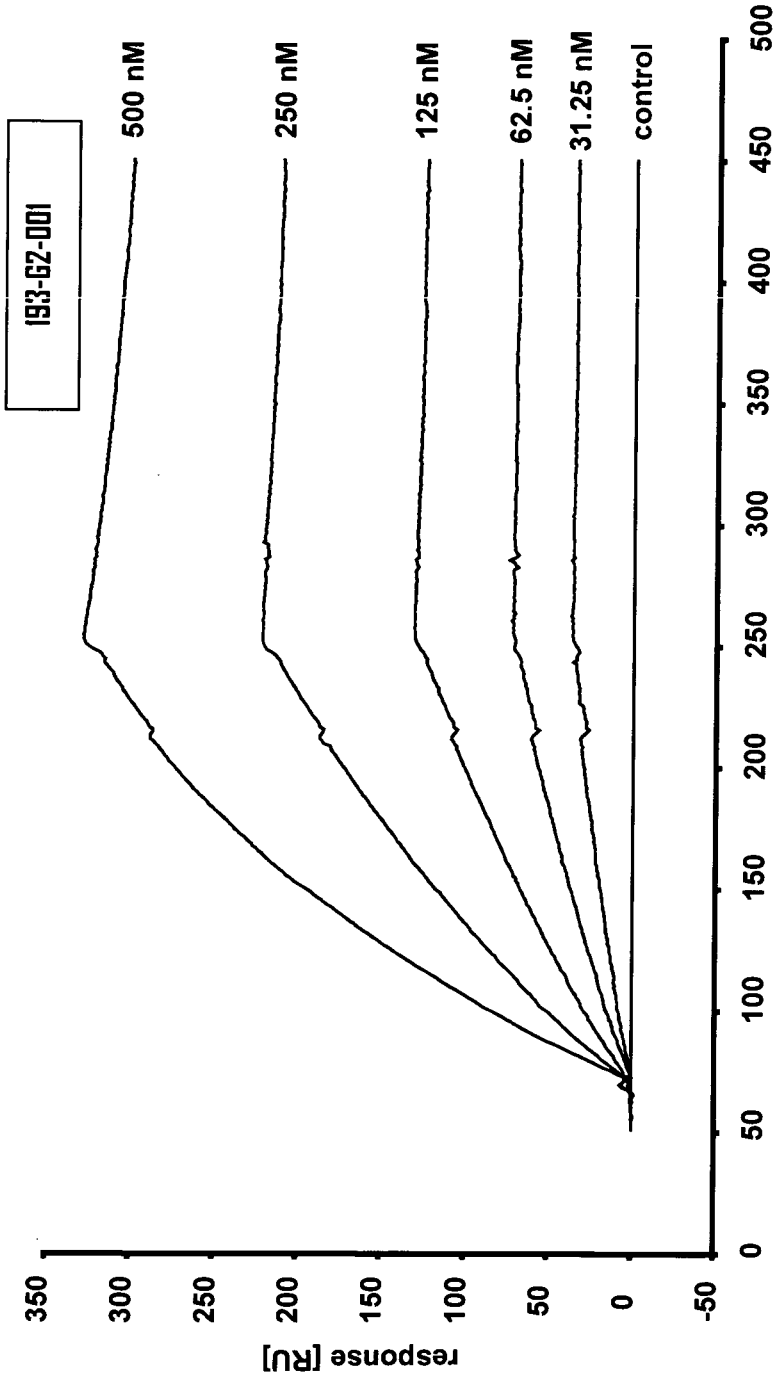

192-A10-008
% of control
0
10
20
30
40
50
60
70
80
0.01
0.1
1
Spiegelmer [nM]

Fig. 16



Spiegelmer	k_a [$M^{-1} \times s^{-1}$]	k_{off} [s^{-1}]	K_D [nM]
193-62-001	2.84×10^5	1.42×10^{-4}	0.50

Fig. 17

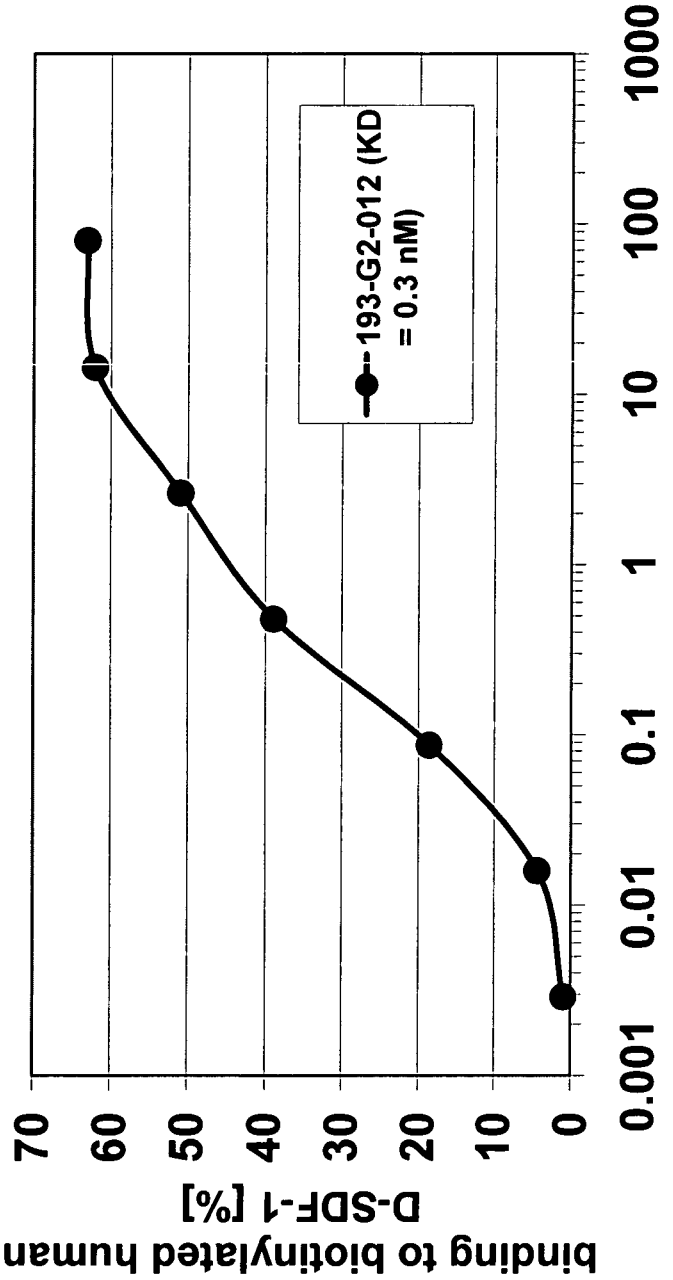

binding to biotinylated human D-SDF-1 [%]
0
10
20
30
40
50
60
70
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF-1 [nM]
193-G2-012 (KD = 0.3 nM)

Fig. 18

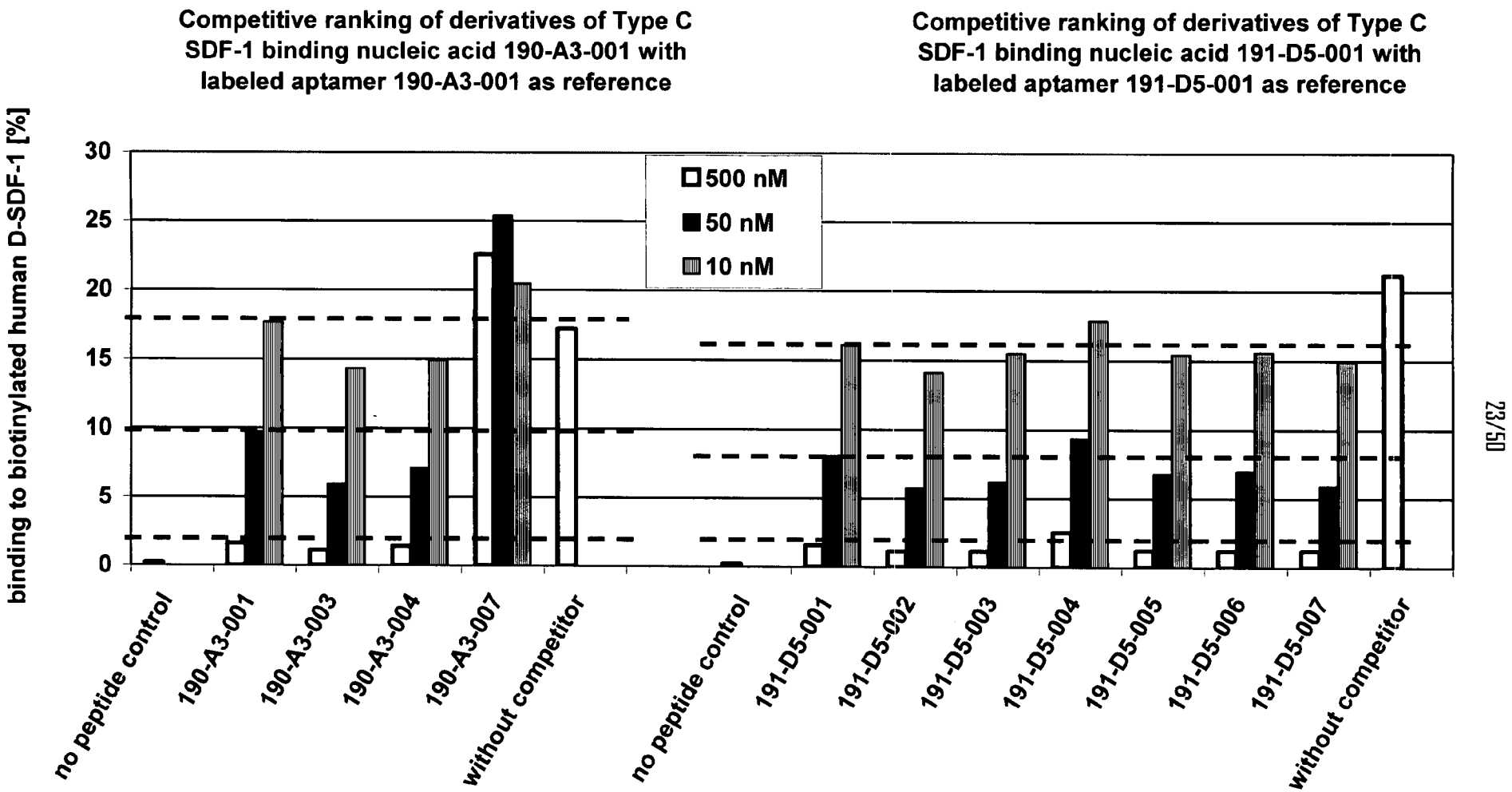

Competitive ranking of derivatives of Type C SDF-1 binding nucleic acid 190-A3-001 with labeled aptamer 190-A3-001 as reference
Competitive ranking of derivatives of Type C SDF-1 binding nucleic acid 191-D5-001 with labeled aptamer 191-D5-001 as reference
binding to biotinylated human D-SDF-1 [%]
30
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

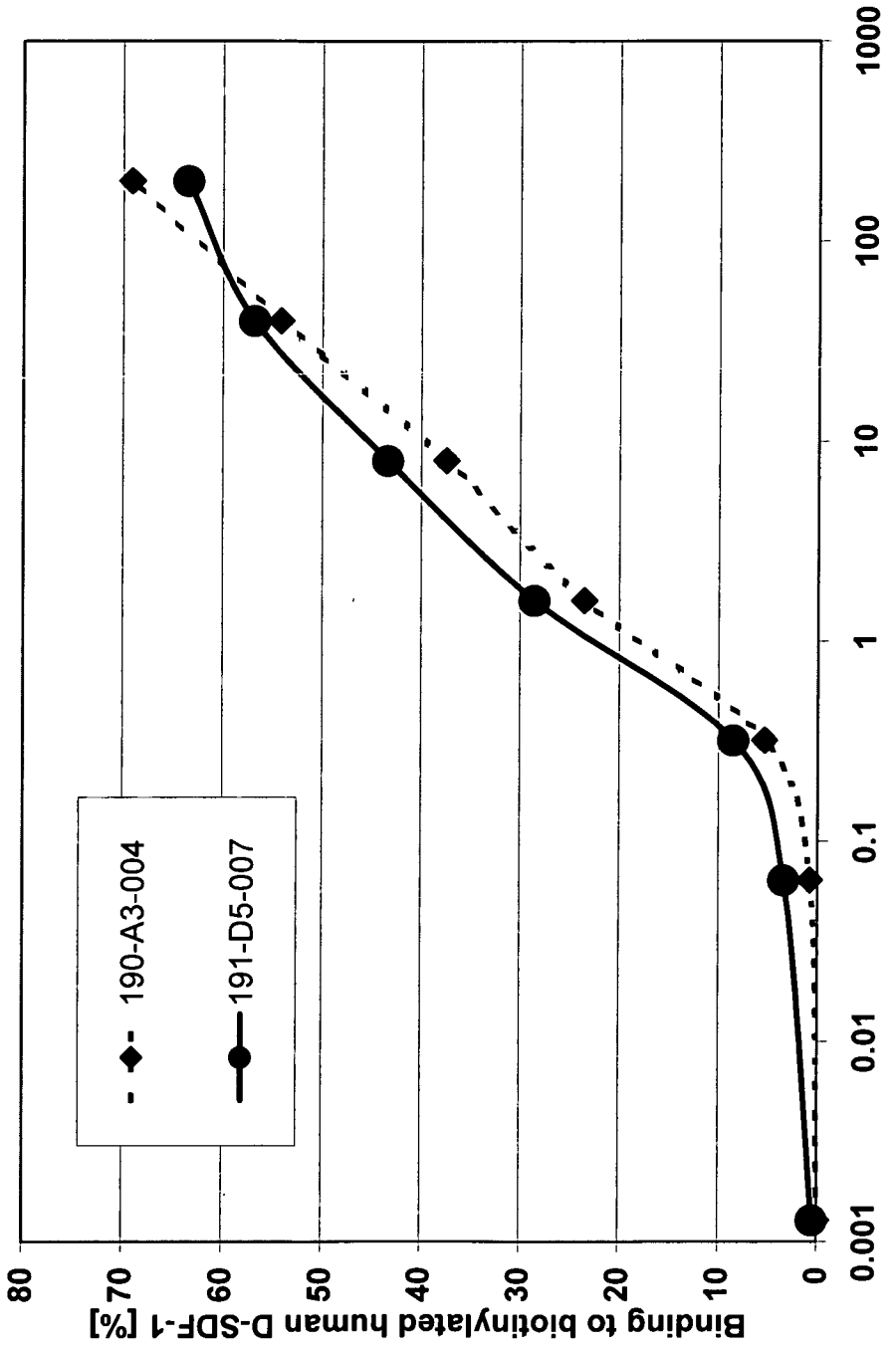
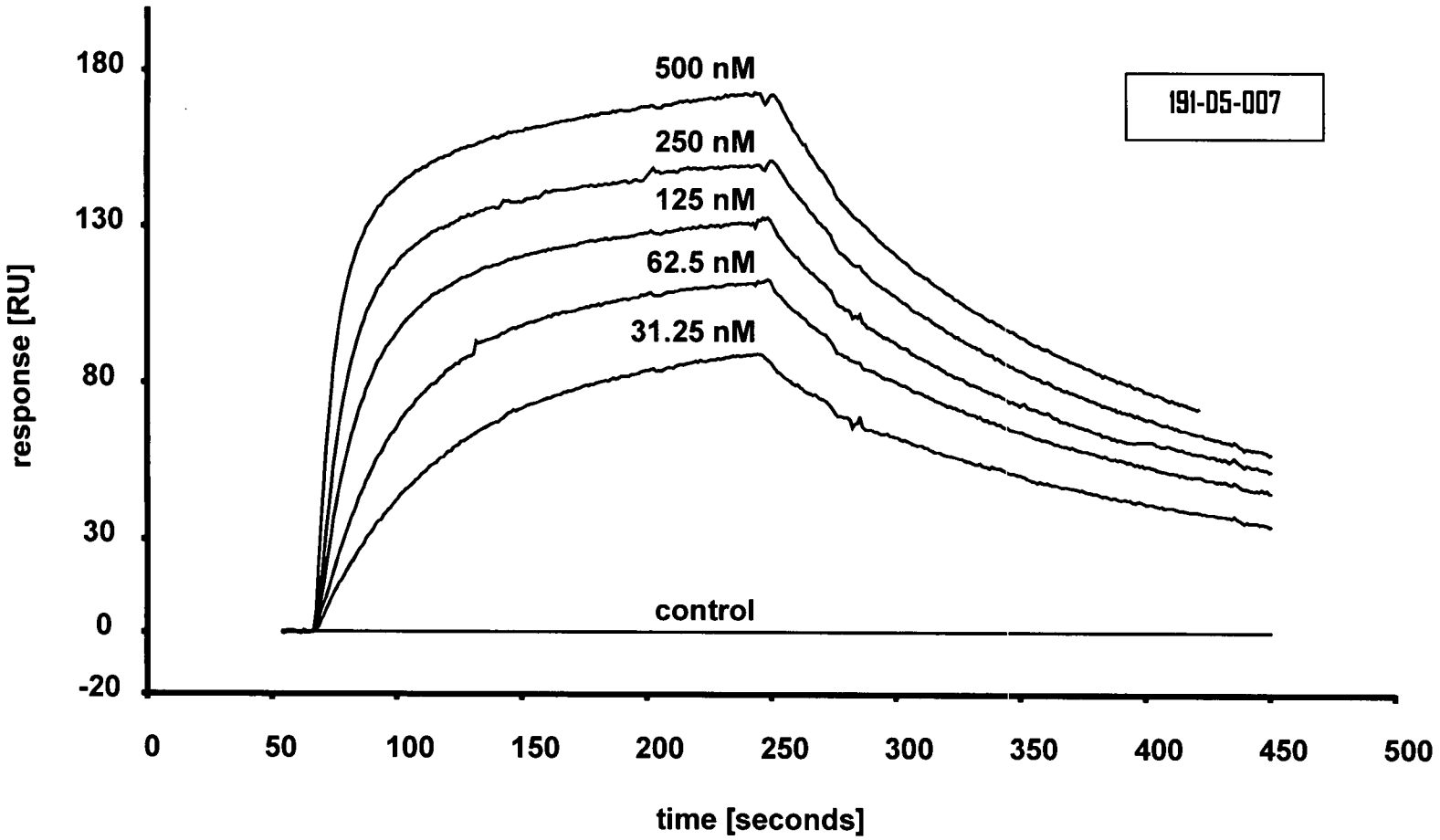

Binding to biotinylated human D-SDF-1 [%]
0
10
20
30
40
50
60
70
80
0.001
0.01
0.1
1
10
100
1000
biotinylated human D-SDF1 [nM]
190-A3-004
191-D5-007

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

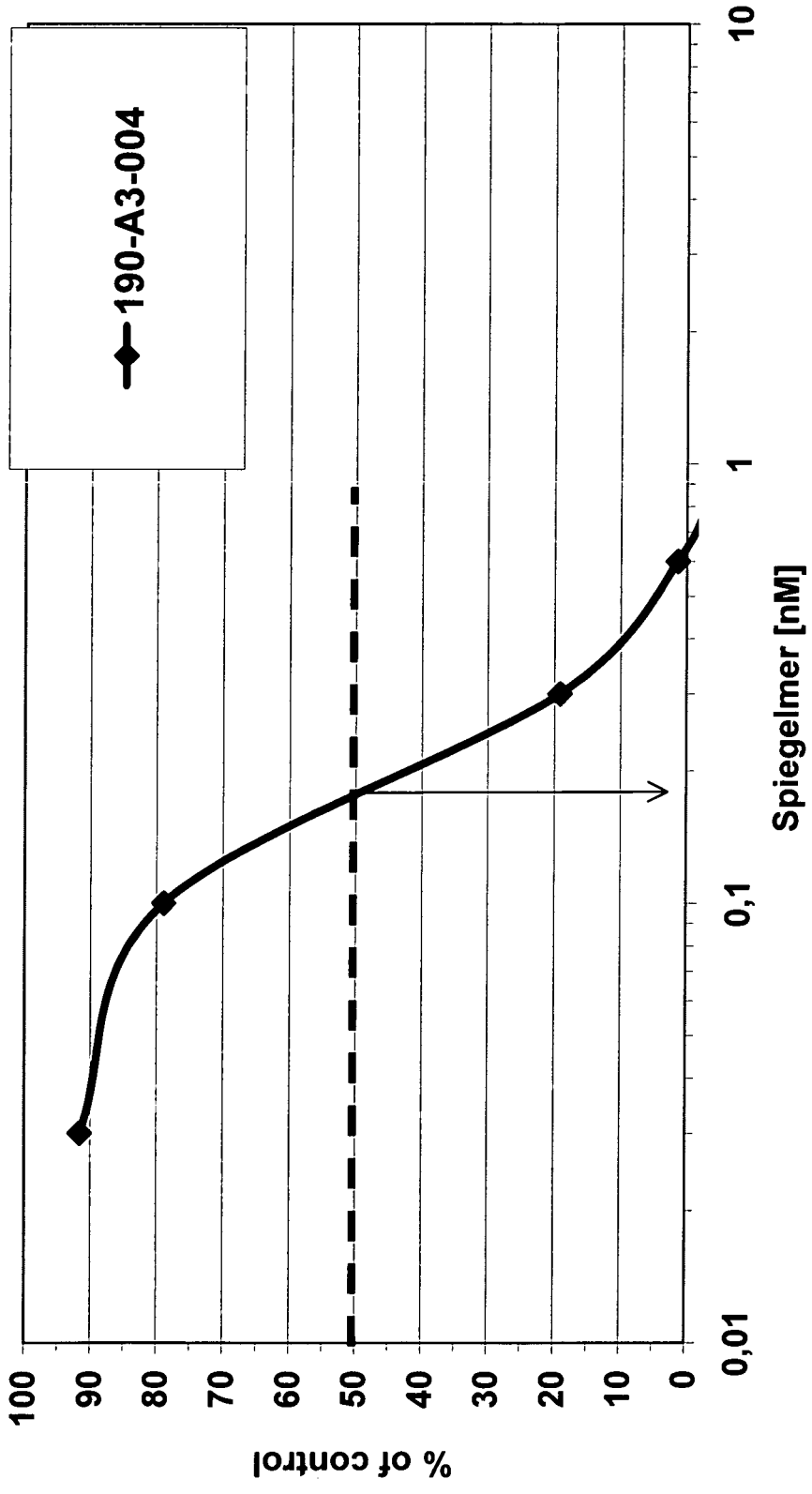

190-A3-004
% of control
100
90
80
70
60
50
40
30
20
10
0
0,01
0,1
1
10
Spiegelmer [nM]

Fig. 22

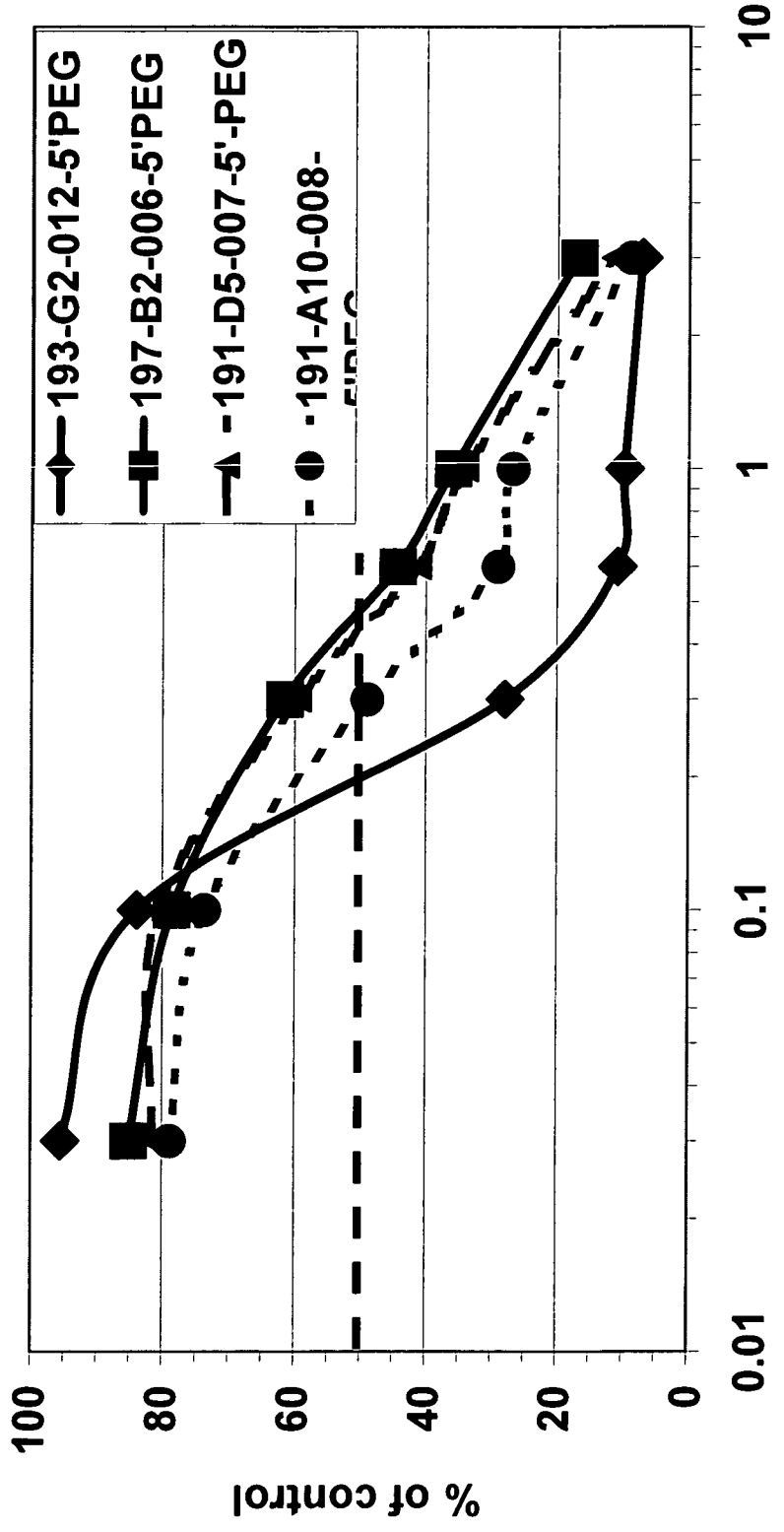

193-G2-012-5'PEG
197-B2-006-5'PEG
191-D5-007-5'-PEG
191-A10-008-
% of control
100
80
60
40
20
0
0.01
0.1
1
10
Spiegelmer [nM]

Fig. 23A

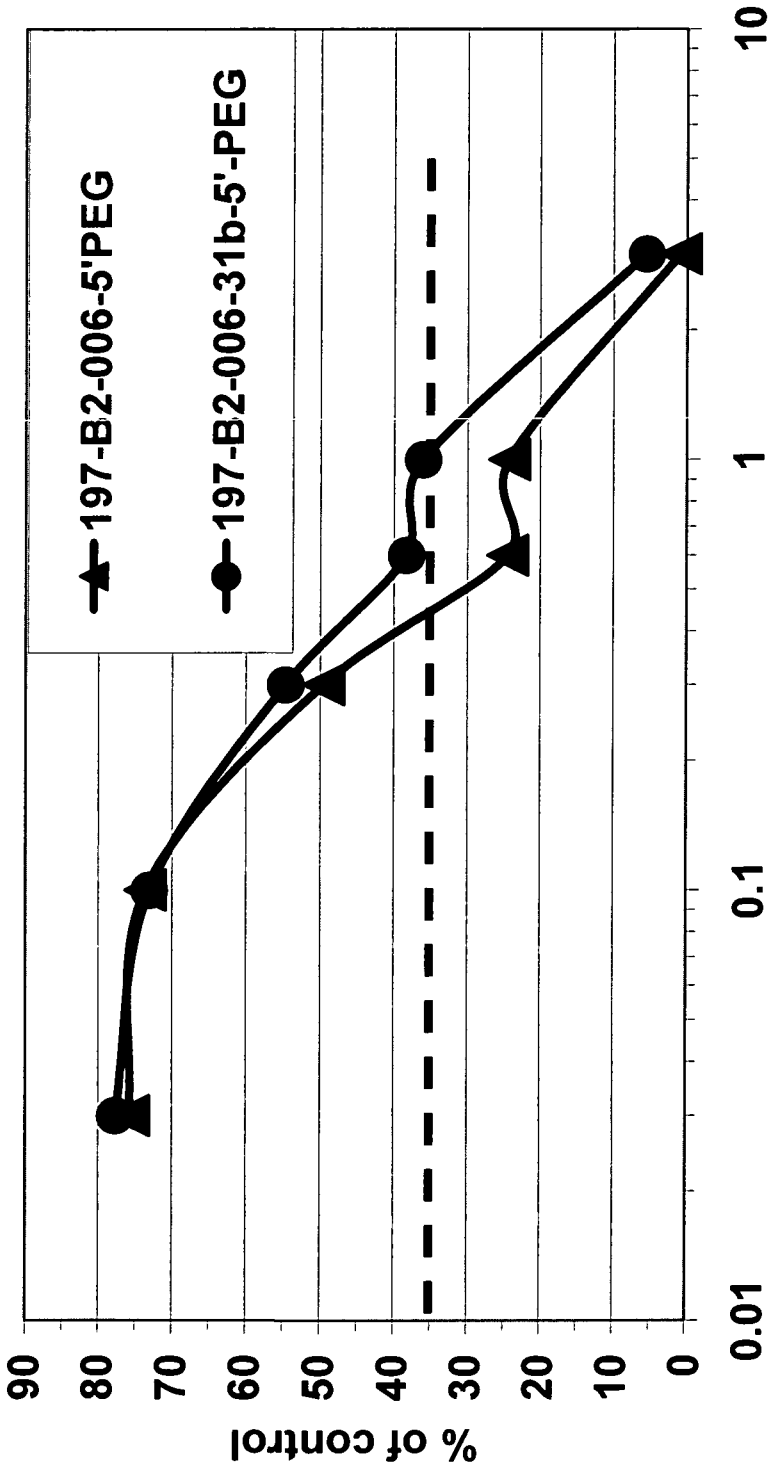
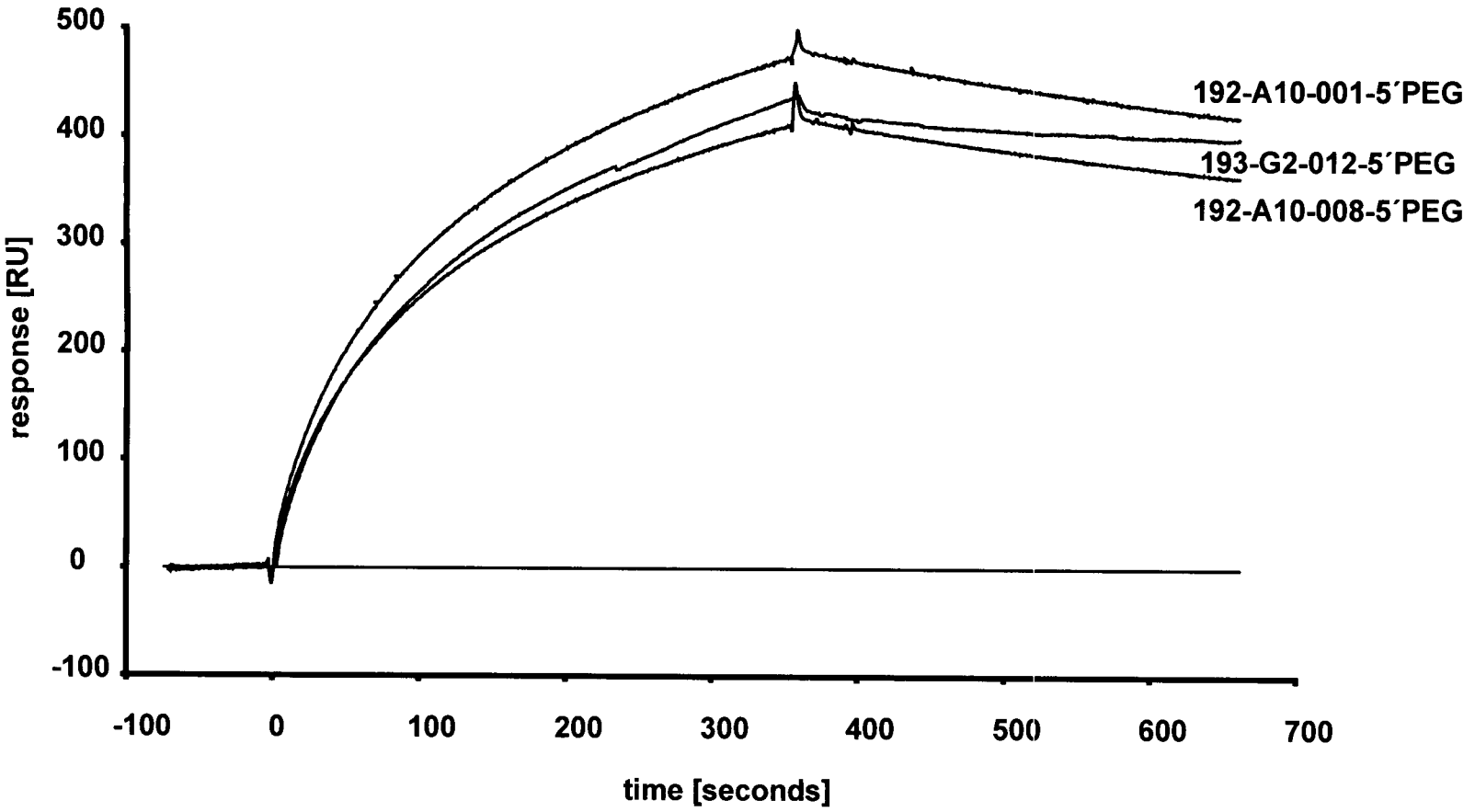
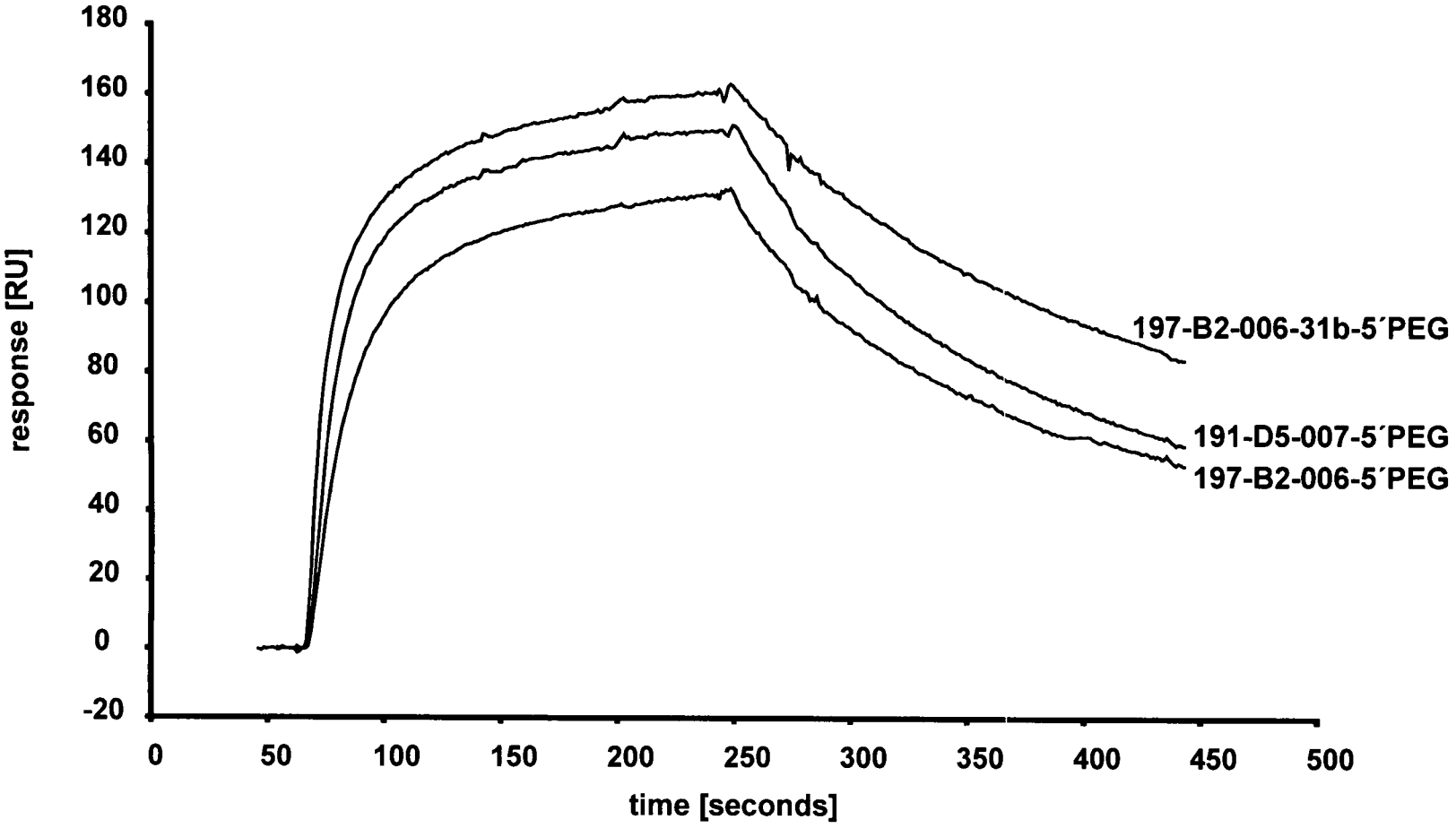

197-B2-006-5'PEG
197-B2-006-31b-5'-PEG
% of control
0
10
20
30
40
50
60
70
80
90
0.01
0.1
1
10
Spiegelmer [nM]

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	$1.8 x10^6$ $9.05 x10^5$	$4.3 x 10^{-3}$ $5.73 x 10^{-3}$	2.4 6.3
197-B2-006-5´PEG	$1.47 x10^6$	$4.39 x 10^{-3}$	3.0
197-B2-006-31b-5´PEG	$1.96 x10^6$	$3,02 x 10^{-3}$	1.54

Fig. 24B

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

Fig. 25A

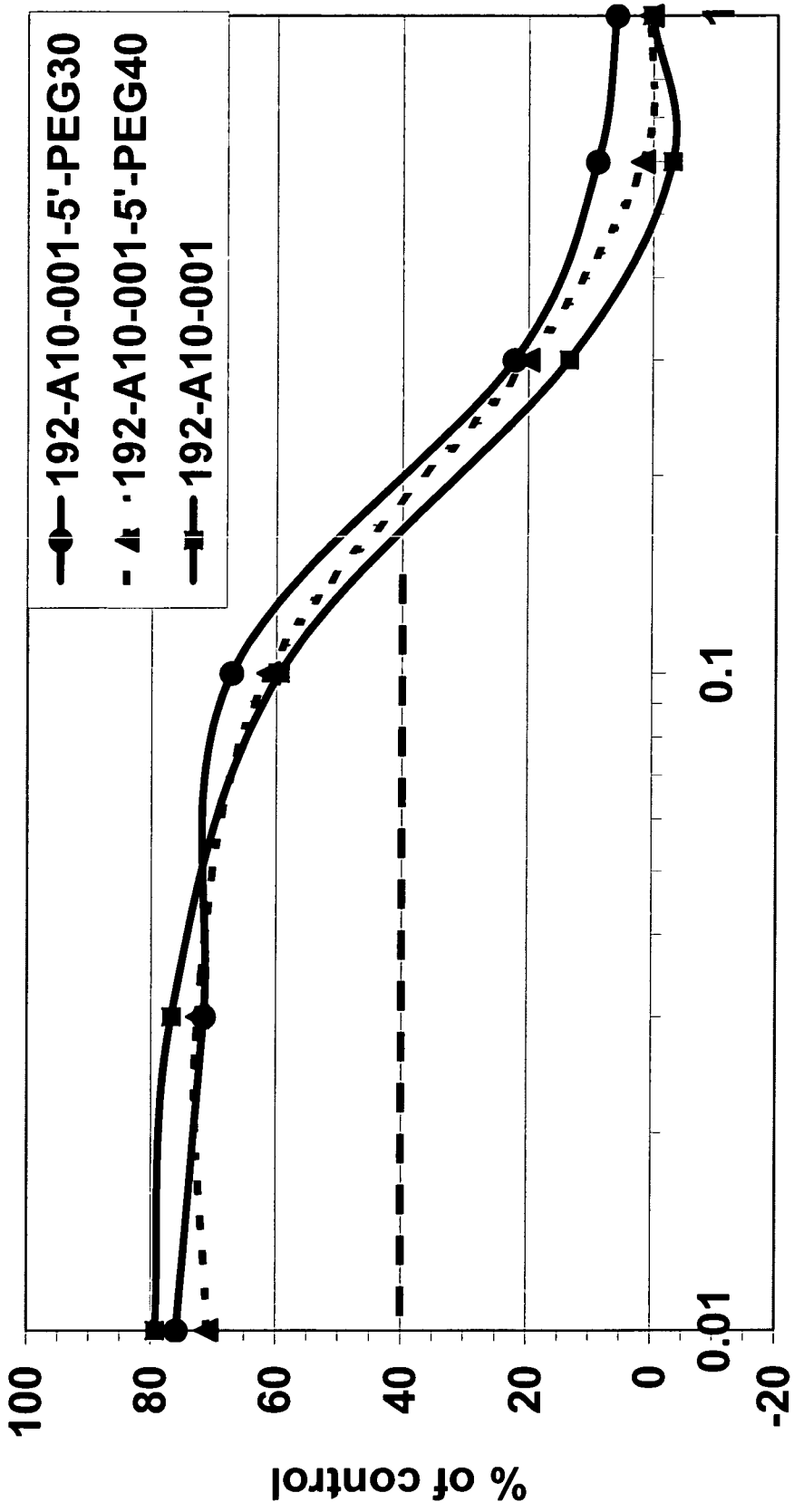

192-A10-001-5'-PEG30
192-A10-001-5'-PEG40
192-A10-001
% of control
100
80
60
40
20
0
-20
0.01
0.1
1
Spiegelmer [nM]

Fig. 25B

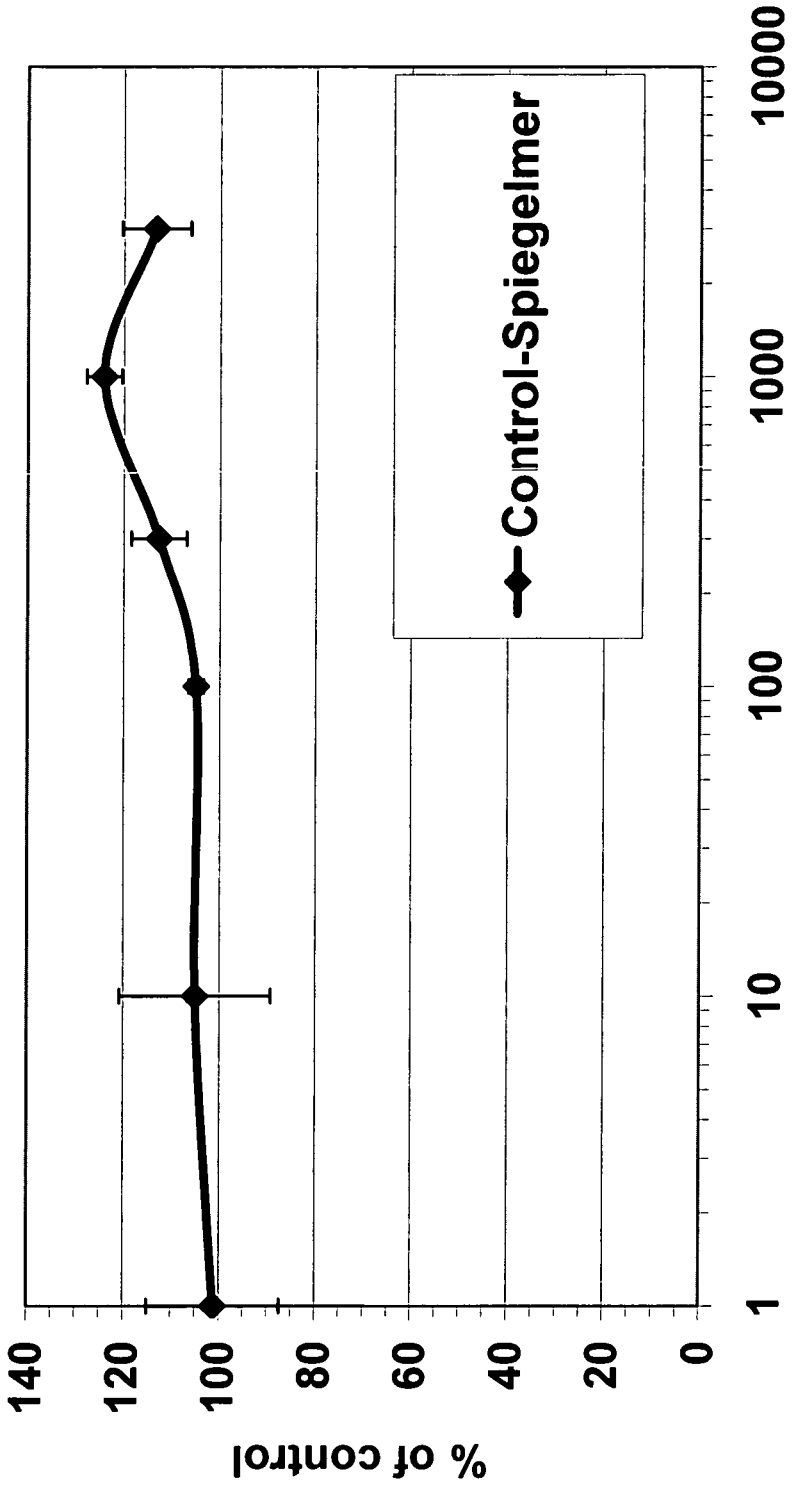

% of control
140
120
100
80
60
40
20
0
1
10
100
1000
10000
Control Spiegelmer [nM]
Control-Spiegelmer

Fig. 26

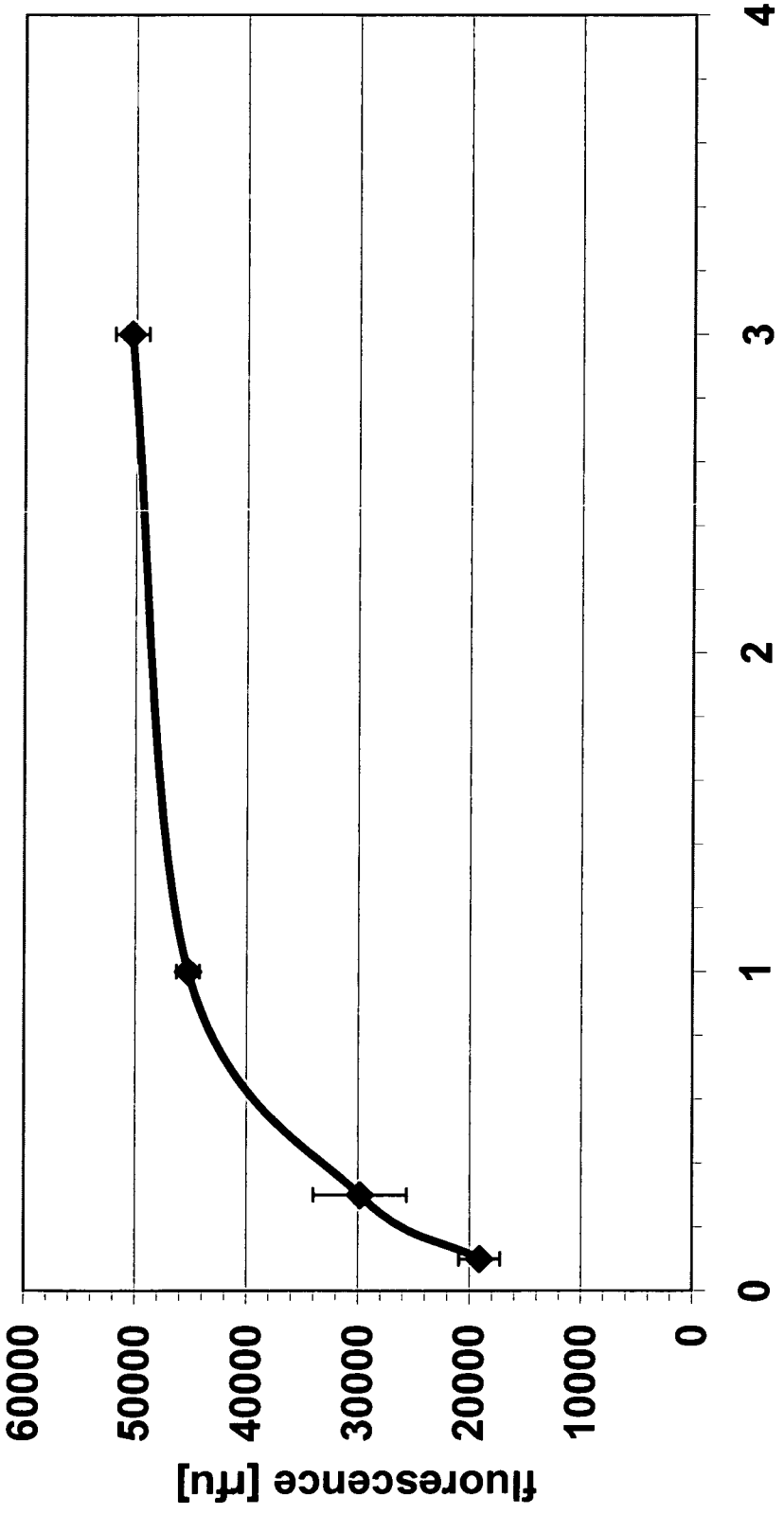

fluorescence [rfu]
60000
50000
40000
30000
20000
10000
0
0
1
2
3
4
murine SDF-1 [nM]

Fig. 27

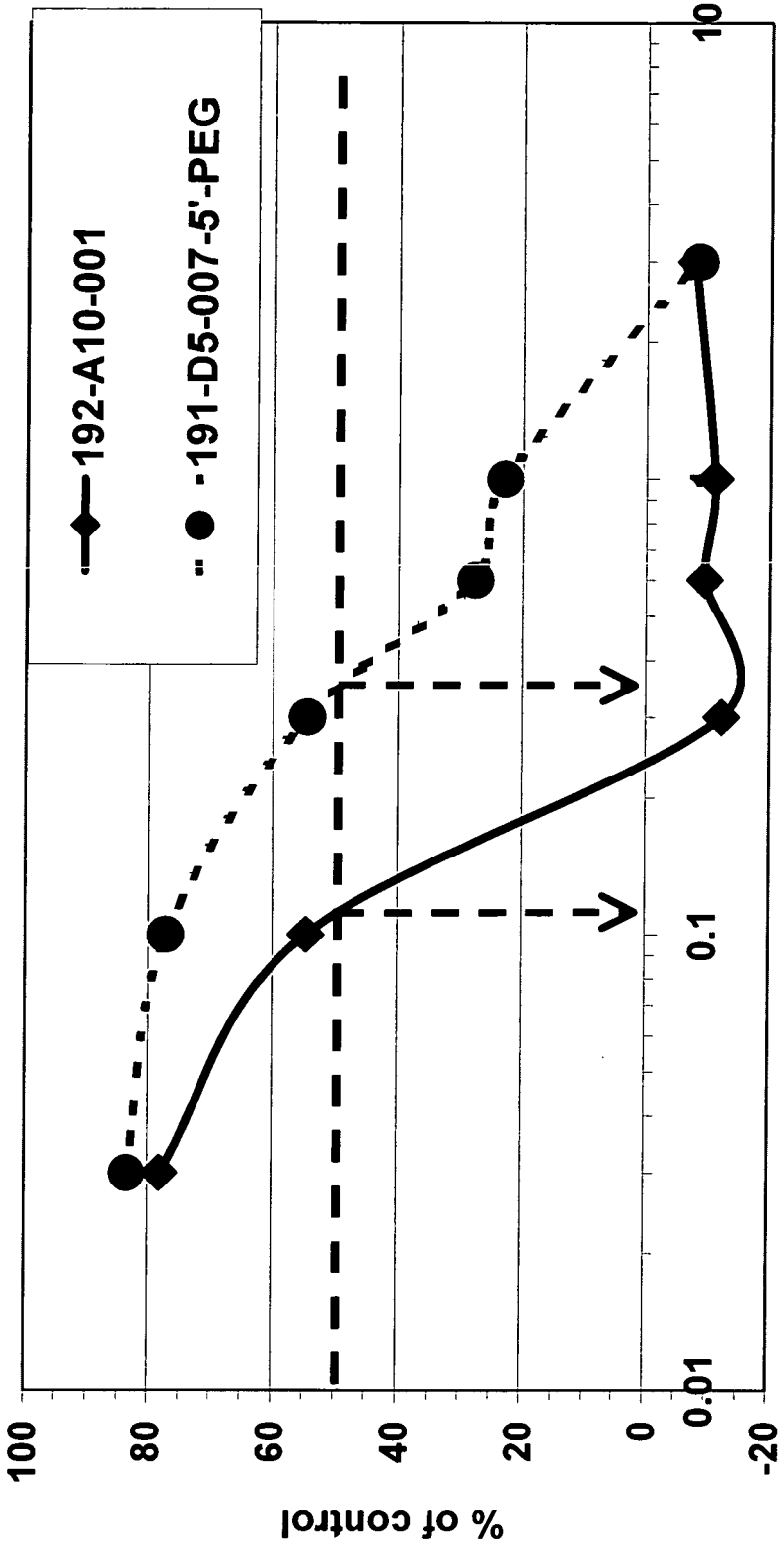

192-A10-001
191-D5-007-5'-PEG
% of control
100
80
60
40
20
0
-20
0.01
0.1
10
Spiegelmer [nM]

Fig. 28

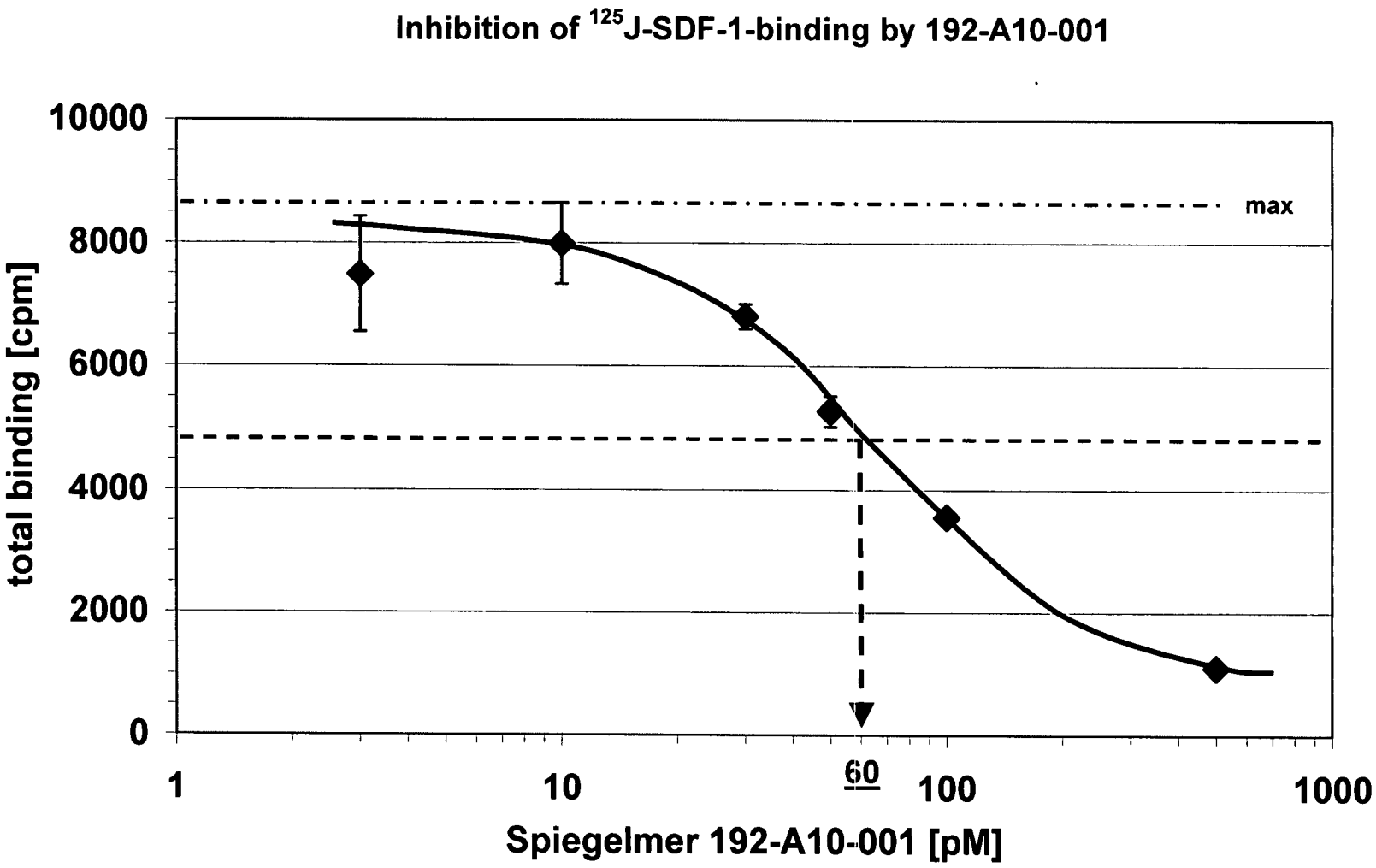
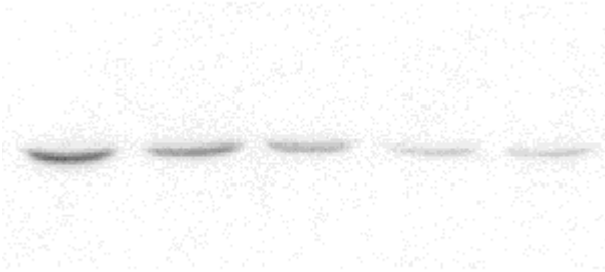

Inhibition of 125J-SDF-1-binding by 192-A10-001
10000
8000
6000
4000
2000
0
total binding [cpm]
max
1
10
60
100
1000
Spiegelmer 192-A10-001 [pM]

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

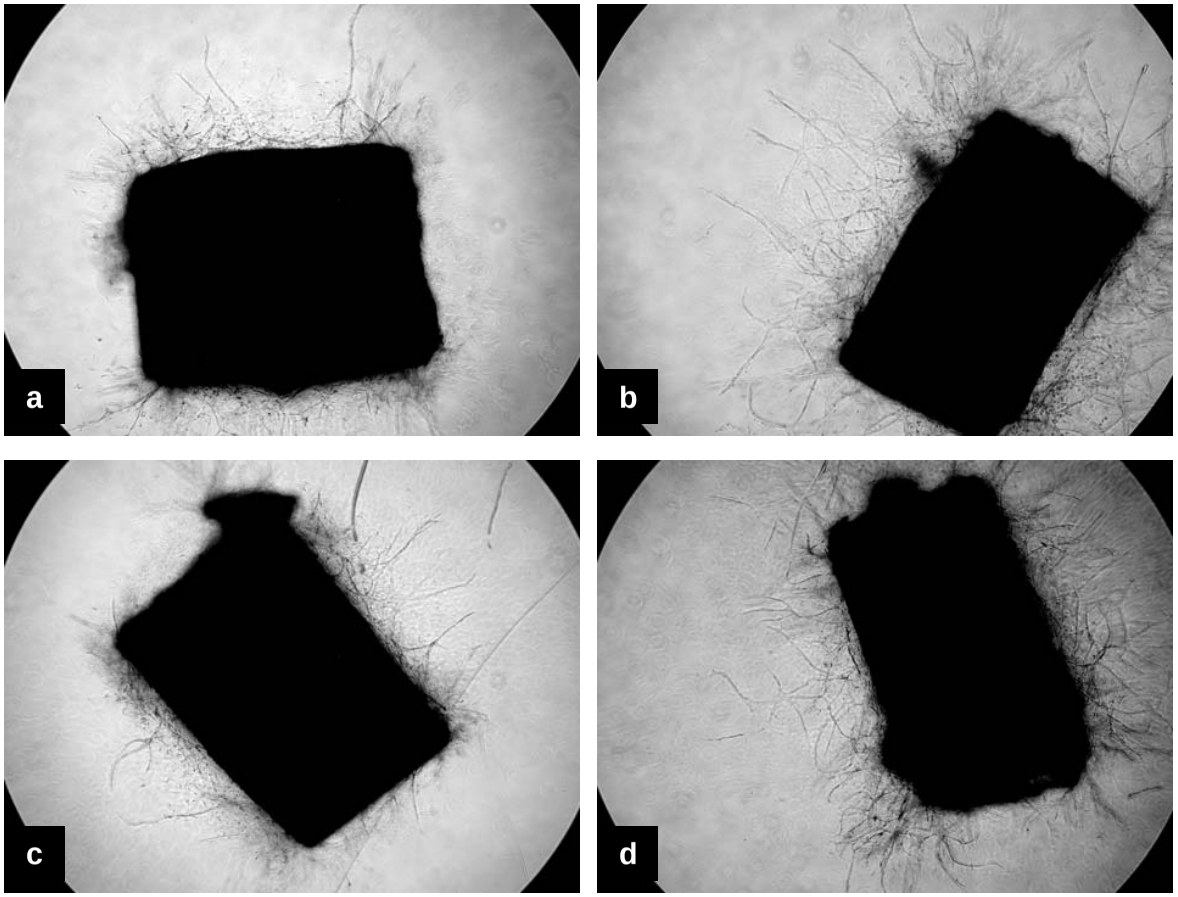


Fig. 31: SDF-1 induced sprouting in an aortic ring sprouting assay. Rings from rat aorta were embedded in collagen matrix and incubated for 6 days with SDF-1 with or without Spiegelmers. **a**: control; **b**: 10 nM SDF-1; **c**: 10 nM SDF-1 + 1 µM 193-G2-012-5'-PEG; **d**: 10 nM SDF-1 + 1 µM PEGylated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

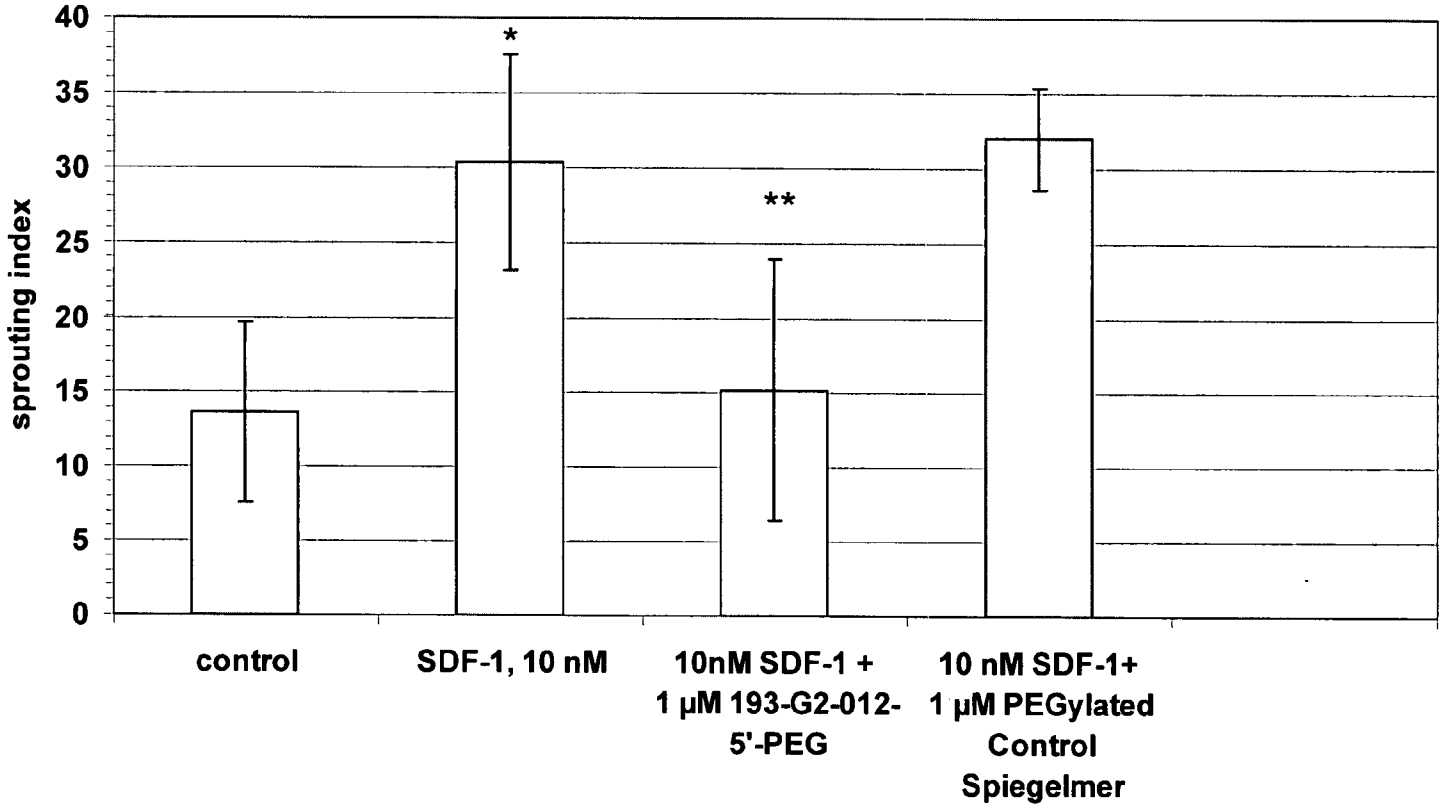


Fig. 32: SDF-1 induced sprouting and the blockage thereof by Spiegelmers in an aortic ring sprouting assay. Rings from rat aorta were embedded in collagen matrix and incubated for 6 days with SDF-1 with or without Spiegelmers. Sprouting indices are shown as mean +/- SD for 5 rings per condition. *: the 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).

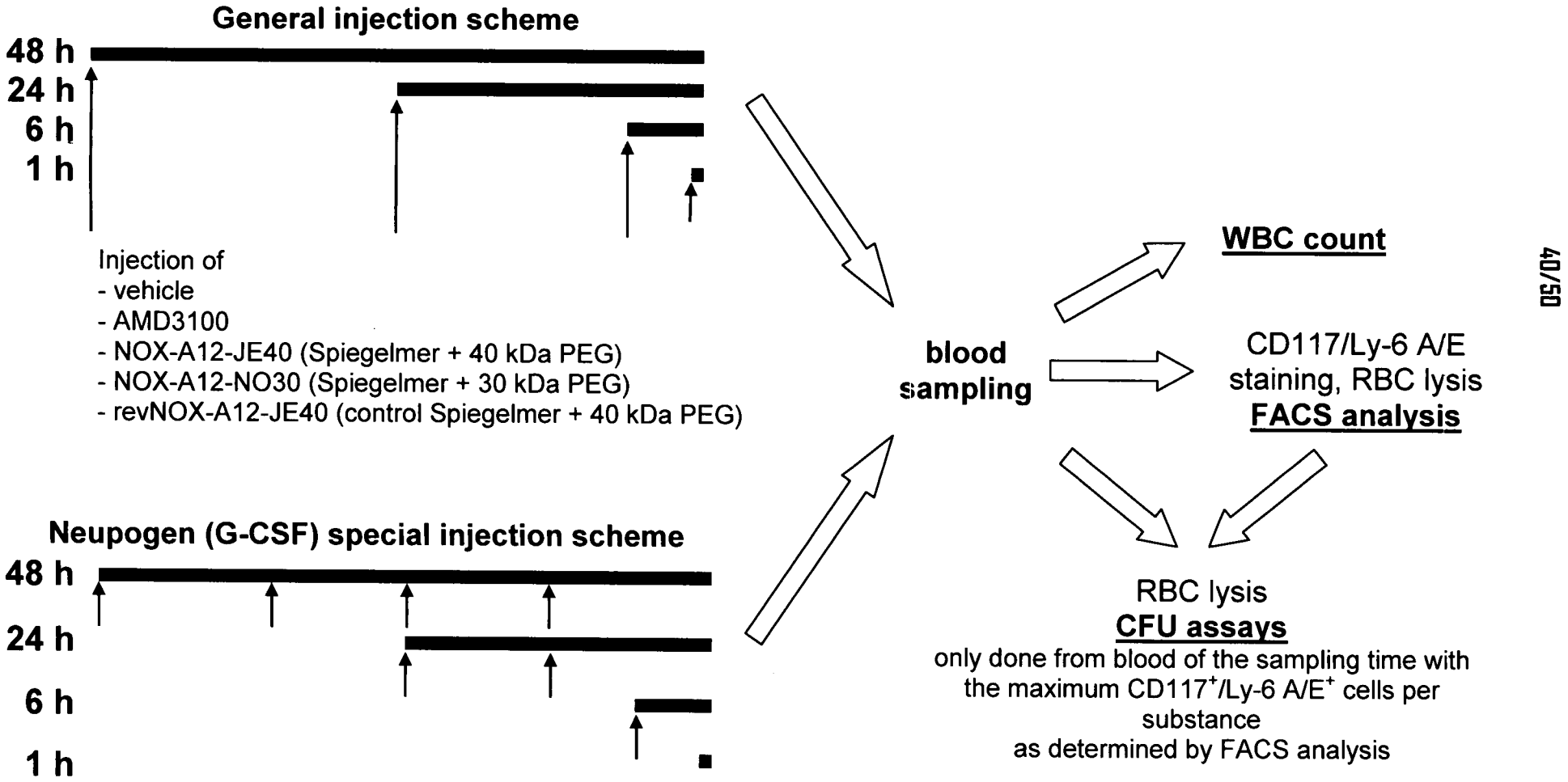

General injection scheme
48 h
24 h
6 h
1 h
Injection of
- vehicle
- AMD3100
- NOX-A12-JE40 (Spiegelmer + 40 kDa PEG)
- NOX-A12-NO30 (Spiegelmer + 30 kDa PEG)
- revNOX-A12-JE40 (control Spiegelmer + 40 kDa PEG)
Neupogen (G-CSF) special injection scheme
48 h
24 h
6 h
1 h
blood sampling
WBC count
CD117/Ly-6 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

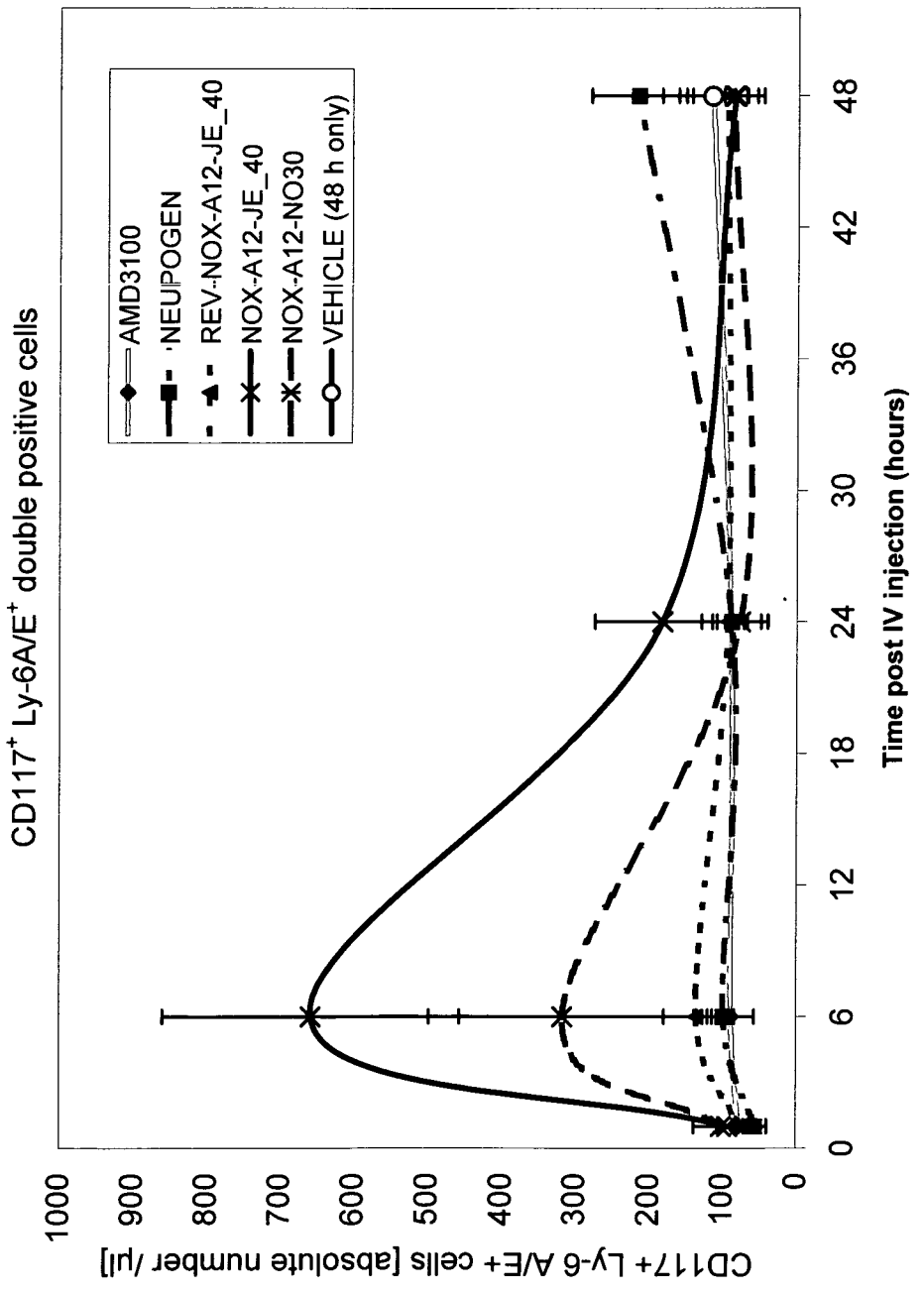

CD117+ Ly-6A/E+ double positive cells
CD117+ Ly-6 A/E+ cells [absolute number /µl]
1000
900
800
700
600
500
400
300
200
100
0
0
6
12
18
24
30
36
42
48
Time post IV injection (hours)
AMD3100
NEUPOGEN
REV-NOX-A12-JE_40
NOX-A12-JE_40
NOX-A12-NO30
VEHICLE (48 h only)

Fig. 34

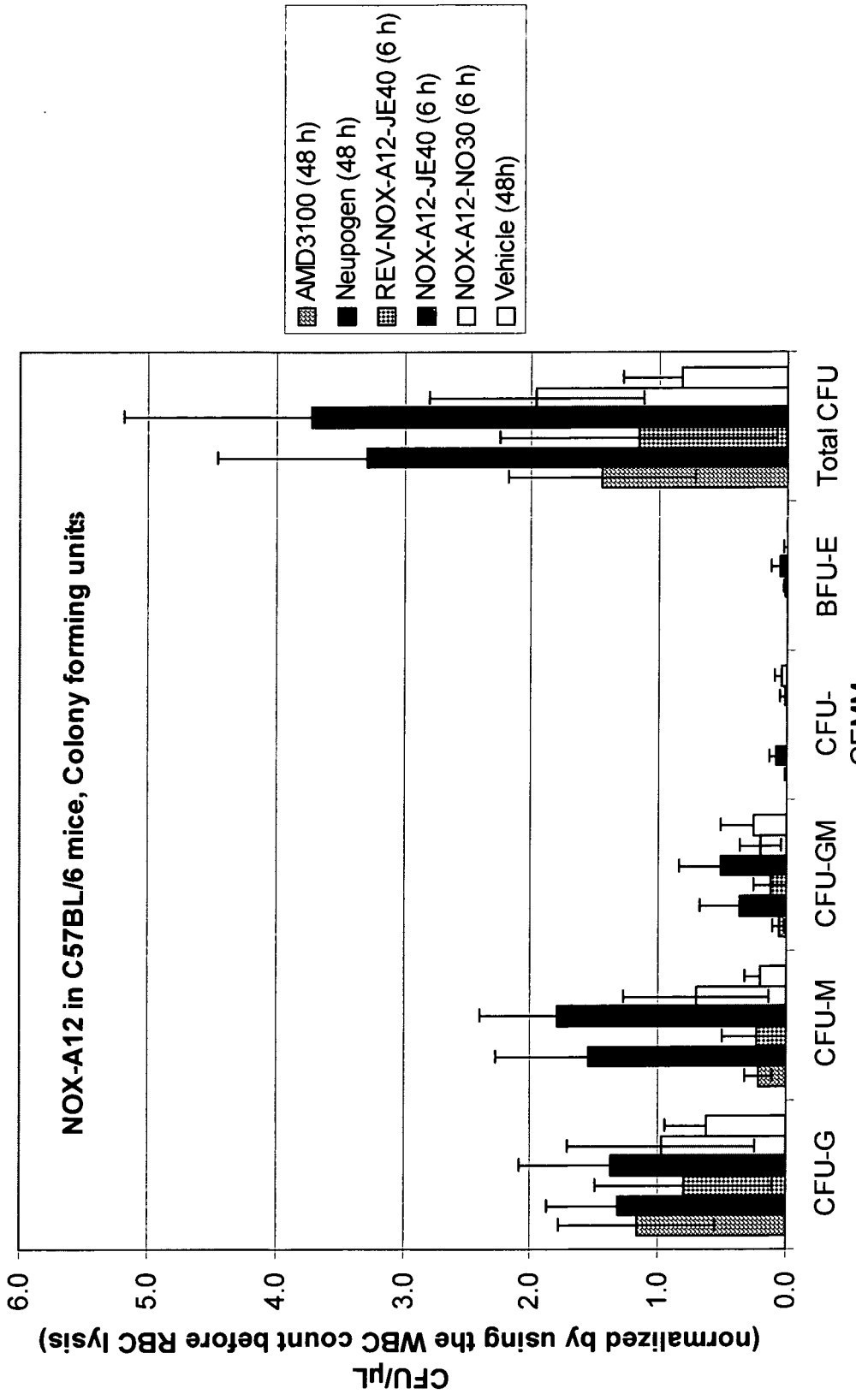
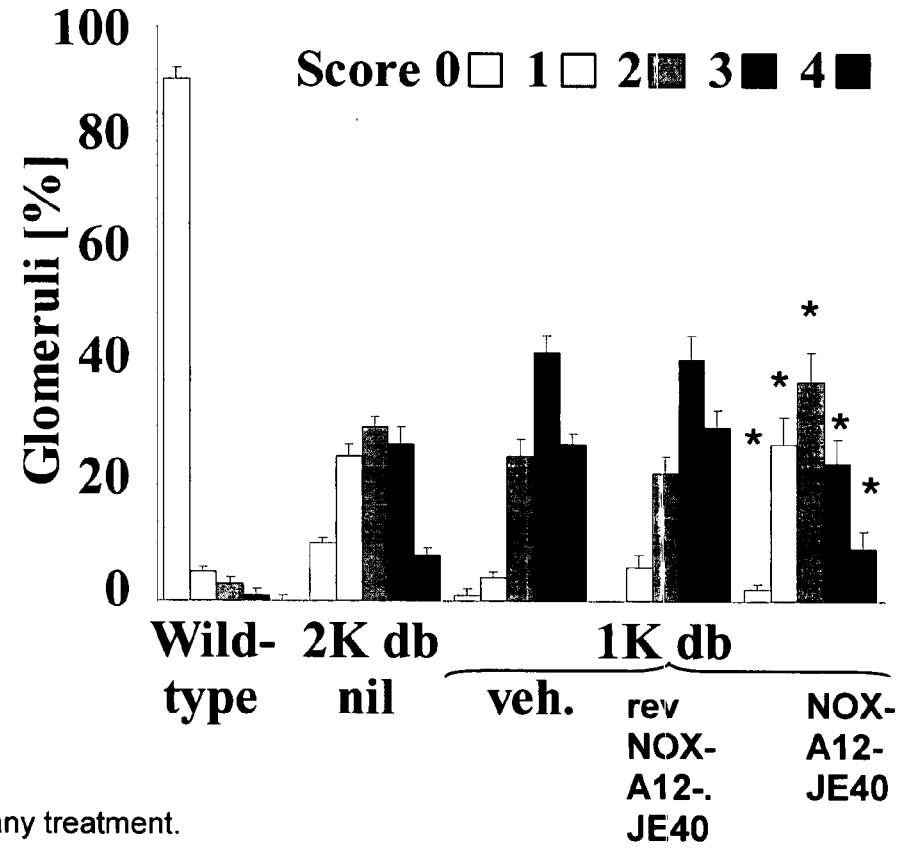

NOX-A12 in C57BL/6 mice, Colony forming units
CFU/µL
(normalized by using the WBC count before RBC lysis)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
AMD3100 (48 h)
Neupogen (48 h)
REV-NOX-A12-JE40 (6 h)
NOX-A12-JE40 (6 h)
NOX-A12-NO30 (6 h)
Vehicle (48h)
CFU-G
CFU-M
CFU-GM
CFU-GEMM
BFU-E
Total CFU

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

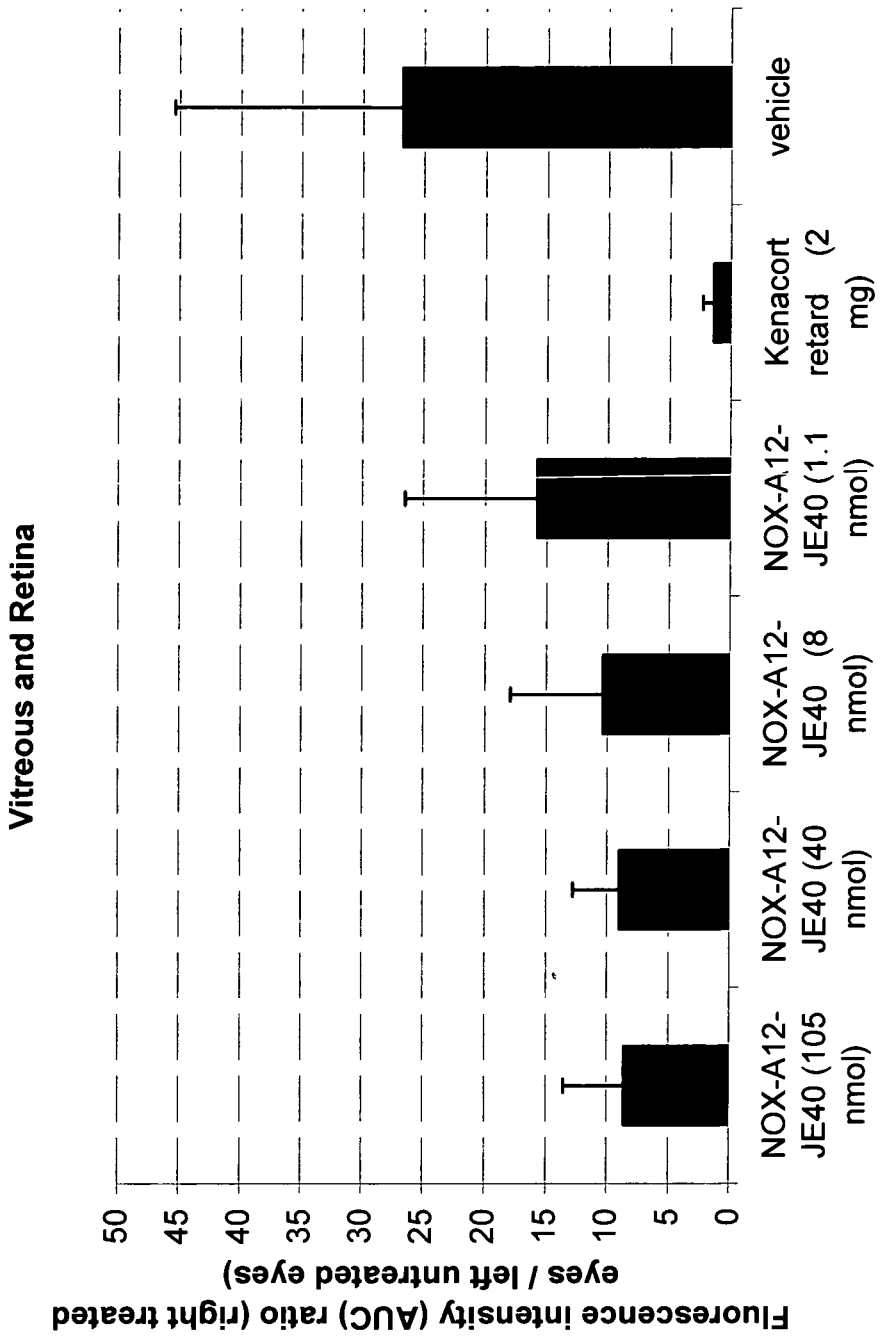
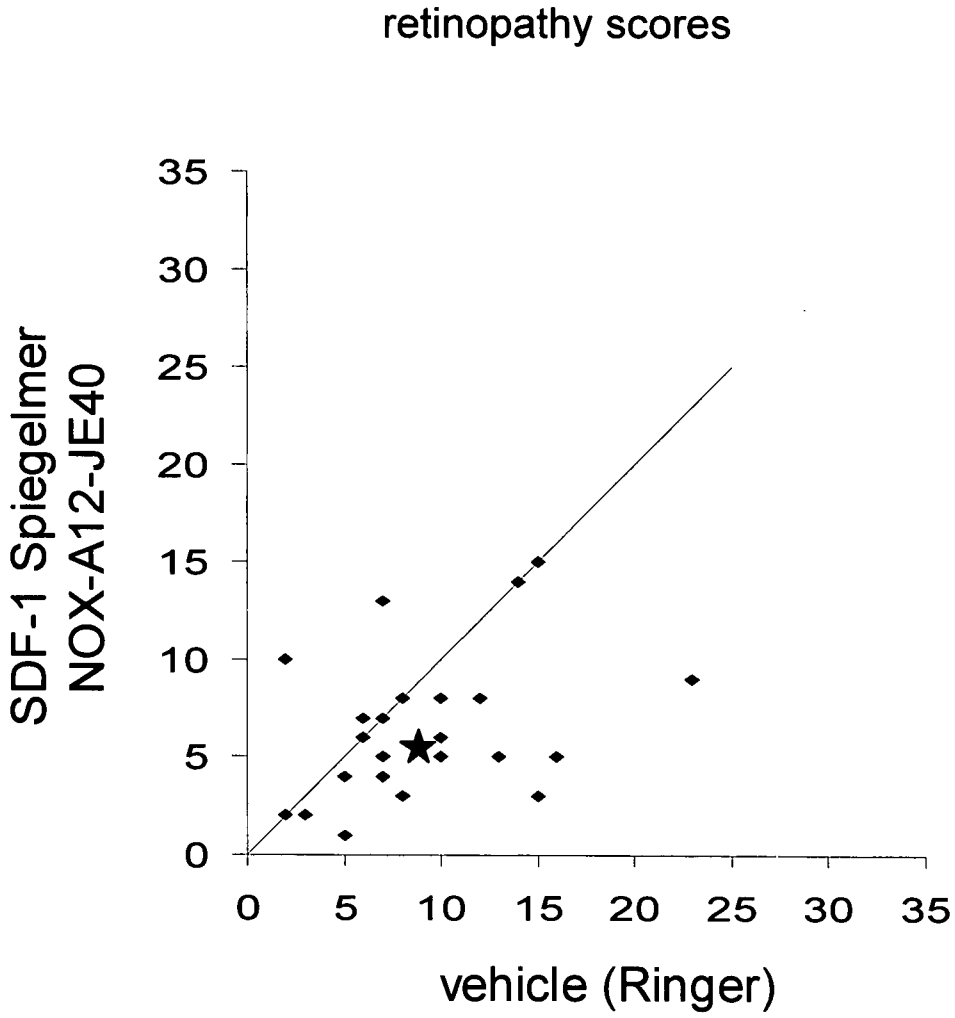

Vitreous and Retina
Fluorescence intensity (AUC) ratio (right treated eyes / left untreated eyes)
0
5
10
15
20
25
30
35
40
45
50
NOX-A12-JE40 (105 nmol)
NOX-A12-JE40 (40 nmol)
NOX-A12-JE40 (8 nmol)
NOX-A12-JE40 (1.1 nmol)
Kenacort retard (2 mg)
vehicle

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

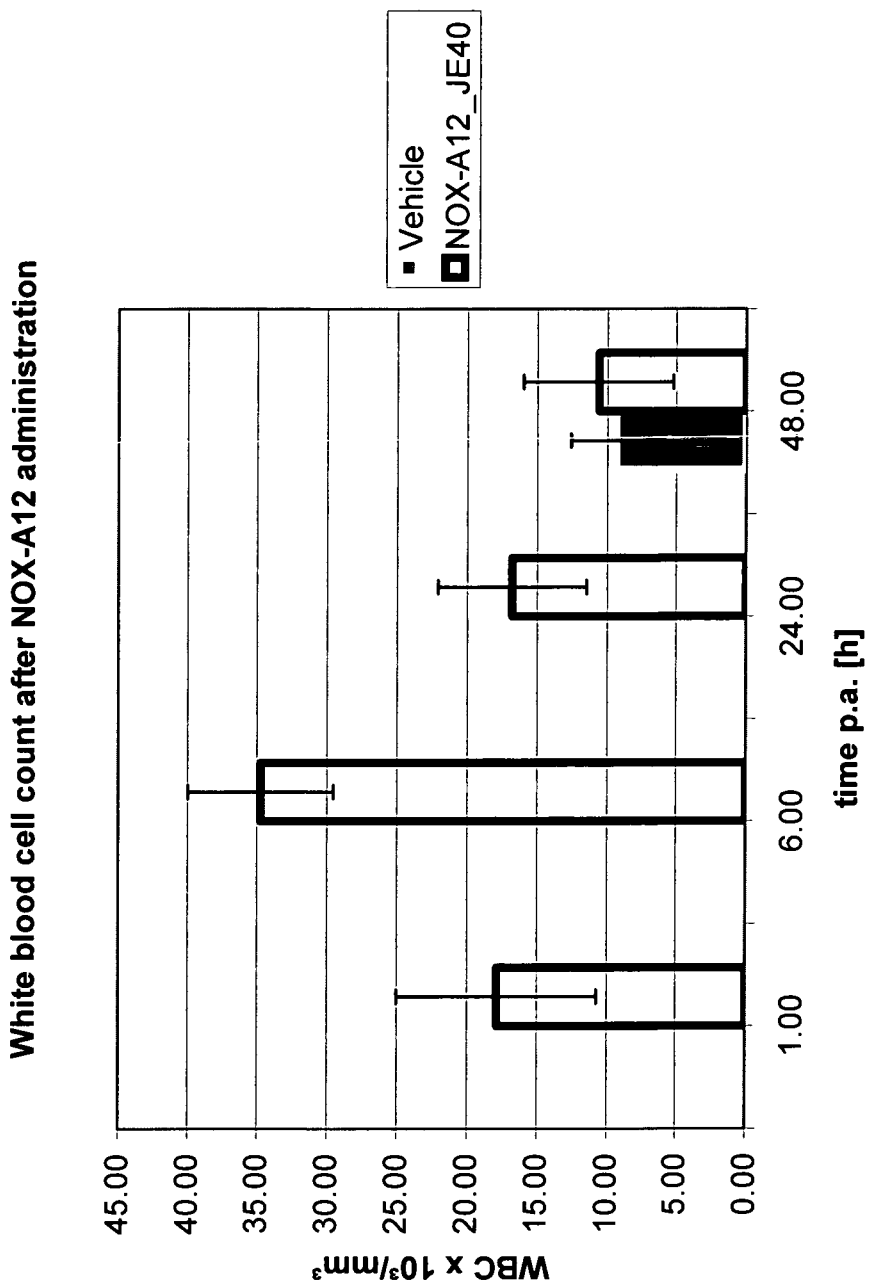

White blood cell count after NOX-A12 administration
Vehicle
NOX-A12_JE40
WBC x 10³/mm³
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
1.00
6.00
24.00
48.00
time p.a. [h]

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

SEQUENCE LISTING

<110> NOXXON Pharma AG

<120> SDF-1 binding nucleic acids and the use thereof

<130> SG1559A

<160> 241

<170> PatentIn version 3.1

<210> 1

<211> 68

<212> PRT

<213> Homo sapiens

<400> 1

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser
1 5 10 15

His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr Pro
20 25 30

Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg Gln
35 40 45

Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys
50 55 60

Ala Leu Asn Lys
65

<210> 2

<211> 72

<212> PRT

<213> Homo sapiens

<400> 2

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser
1 5 10 15

His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr Pro
20 25 30

Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg Gln
35 40 45

Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys
50 55 60

Ala Leu Asn Lys Arg Phe Lys Met
65 70

<210> 3

<211> 68

<212> PRT

<213> Mus musculus

<400> 3

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser
1 5 10 15

His Ile Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr Pro
20 25 30

Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg Gln
35 40 45

Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys
50 55 60

Ala Leu Asn Lys
65

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Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser
1 5 10 15

His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr Pro
20 25 30

Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg Gln
35 40 45

Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys
50 55 60

Ala Leu Asn Lys Arg Phe Lys
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<211> 38

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<210> 6

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<211> 39

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<222> (1)..(26)

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<211> 6

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<400> 24
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<211> 36

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<222> (1)..(36)

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<210> 26

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<210> 27

<211> 32

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<222> (1)..(32)

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<400> 27
gugaaagcaa caugucaaug aaagguagcc gc 32

<210> 28

<211> 30

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<222> (1)..(30)

<223> L-RNA

<400> 28
ugaaagcaac augucaauga aagguagccg 30

<210> 29

<211> 28

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<222> (1)..(28)

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gaaagcaaca ugucaaugaa agguagcc 28

<210> 30

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<222> (1)..(26)

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<400> 30
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<210> 31

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gcgugaaagc aacaugucaa ugaaagguag ccgcgc 36

<210> 32

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<210> 33

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<210> 34

<211> 34

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<210> 35

<211> 34

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<210> 36

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<210> 37

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<210> 38

<211> 34

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<210> 40

<211> 34

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<210> 41

<211> 34

<212> RNA

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<210> 42

<211> 5

<212> RNA

<213> Artificial sequence

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<222> (1)..(1)

<223> s or absent

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sbbbs 5

<210> 43

<211> 5

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<222> (1)..(5)

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<222> (5)..(5)

<223> s or absent

<400> 43
sbbvs 5

<210> 44

<211> 6

<212> RNA

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<222> (3)..(3)

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<222> (4)..(4)

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<222> (1)..(6)

<223> L-RNA

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<222> (1)..(1)

<223> R or absent

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<222> (2)..(2)

<223> s or absent

<400> 44
rsnnbv 6

<210> 45

<211> 6

<212> RNA

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<222> (5)..(5)

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<222> (6)..(6)

<223> y or absent

<400> 45
bnbnry 6

<210> 46

<211> 47

<212> RNA

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<222> (1)..(47)

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agcguggugu gaucuagaug uaguggcuga uccuagucag guacgcu 47

<210> 47

<211> 47

<212> RNA

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<223> L-RNA

<400> 47
agcguggugu gaucuagaug uauuggcuga uccuagucag guacgcu 47

<210> 48

<211> 47

<212> RNA

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<220>

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<222> (1)..(47)

<223> L-RNA

<400> 48
agcguggugu gaucuagaug uaauggcuga uccuagucag gugcgcu 47

<210> 49

<211> 45

<212> RNA

<213> Artificial sequence

<220>

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<220>

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<222> (1)..(45)

<223> L-RNA

<400> 49
gcgaggugug aucuagaugu aguggcugau ccuagucagg ugcgc 45

<210> 50

<211> 45

<212> RNA

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<223> synthetic

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<222> (1)..(45)

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gcguggugug aucuagaugu aguggcugau ccuagucagg ugcgc 45

<210> 51

<211> 45

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<210> 52

<211> 45

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<223> L-RNA

<400> 52
gcguggugug aucuagaugu aauggcugau ccuagucagg gacgc 45

<210> 53

<211> 45

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gcguggugug aucuagaugu agaggcugau ccuagucagg uacgc 45

<210> 54

<211> 45

<212> RNA

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gcguggugug aucuagaugu aaaggcugau ccuagucagg uacgc 45

<210> 55

<211> 45

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<210> 56

<211> 45

<212> RNA

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<210> 57

<211> 35

<212> RNA

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<222> (1)..(35)

<223> L-RNA

<400> 57
gugugaucua gauguadwgg cugwuccuag uyagg 35

<210> 58

<211> 35

<212> RNA

<213> Artificial sequence

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<222> (1)..(35)

<223> L-RNA

<400> 58
gugugaucua gauguadugg cugauccuag ucagg 35

<210> 59

<211> 6

<212> RNA

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<223> L-RNA

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<222> (1)..(1)

<223> A or absent

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agcrwg 6

<210> 60

<211> 6

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<222> (6)..(6)

<223> U or absent

<400> 60
kryscu 6

<210> 61

<211> 45

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<222> (1)..(45)

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<210> 62

<211> 43

<212> RNA

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<222> (1)..(43)

<223> L-RNA

<400> 62
cgugguguga ucuagaugua guggcugauc cuagucaggu acg 43

<210> 63

<211> 41

<212> RNA

<213> Artificial Sequence

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<222> (1)..(41)

<223> L-RNA

<400> 63

guggugugau cuagauguag uggcugaucc uagucaggua c 41

<210> 64

<211> 39

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<222> (1)..(39)

<223>

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<222> (1)..(39)

<223> L-RNA

<400> 64
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<210> 65

<211> 37

<212> RNA

<213> Artificial sequence

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<222> (1)..(37)

<223> L-RNA

<400> 65
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<210> 66

<211> 35

<212> RNA

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<222> (1)..(35)

<223> L-RNA

<400> 66
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<210> 67

<211> 45

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<223> L-RNA

<400> 67
gcguggugug aucuagaugu auuggcugau ccuagucagg uacgc 45

<210> 68

<211> 45

<212> RNA

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<222> (1)..(45)

<223> L-RNA

<400> 68
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<210> 69

<211> 43

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<222> (1)..(43)

<223> L-RNA

<400> 69
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<210> 70

<211> 43

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<223> L-RNA

<400> 70
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<210> 71

<211> 43

<212> RNA

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<400> 71
ggccguguga ucuagaugua uuggcugauc cuagucaggg gcc 43

<210> 72

<211> 43

<212> RNA

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<220>

<223> synthetic

<220>

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<222> (1)..(43)

<223> L-RNA

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gcccguguga ucuagaugua uuggcugauc cuagucaggg ggc 43

<210> 73

<211> 5

<212> RNA

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<222> (1)..(1)

<223> G or absent

<400> 73
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<210> 74

<211> 5

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<222> (1)..(5)

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<222> (5)..(5)

<223> C or absent

<400> 74
bvssc 5

<210> 75

<211> 6

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<222> (1)..(6)

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<222> (1)..(1)

<223> A or absent

<400> 75
agcgug 6

<210> 76

<211> 6

<212> RNA

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<222> (1)..(6)

<223> L-RNA

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<222> (6)..(6)

<223> U or absent

<400> 76
uacgcu 6

<210> 77

<211> 6

<212> RNA

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<222> (1)..(6)

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<223> A or absent

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<222> (2)..(2)

<223> G or absent

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<210> 78

<211> 6

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<222> (1)..(6)

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<222> (5)..(5)

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<210> 83

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<210> 89

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<210> 90

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<211> 36

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<210> 96

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<210> 97

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<211> 32

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<210> 101

<211> 31

<212> RNA

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<222> (1)..(31)

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<400> 101
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<210> 102

<211> 29

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<400> 102
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<210> 103

<211> 27

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<400> 103
gggagguuag ggcuagaagu cgguccc 27

<210> 104

<211> 27

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<223> L-RNA

<400> 104
ccgcgguuag ggcuagaagu cgggcgg 27

<210> 105

<211> 27

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<220>

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<223> L-RNA

<400> 105
cccggguuag ggcuagaagu cggcggg 27

<210> 106

<211> 27

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<223> L-RNA

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<210> 107

<211> 29

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<210> 108

<211> 29

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<210> 109

<211> 29

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<211> 29

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<210> 114

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<210> 115

<211> 31

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<211> 29

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<222> (1)..(29)

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<400> 117
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<210> 118

<211> 31

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<222> (1)..(31)

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<210> 119

<211> 31

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<400> 119
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<211> 10

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<400> 120
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<210> 121

<211> 10

<212> RNA

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<222> (3)..(3)

<223> n is any nucleotide

<220>

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<222> (3)..(3)

<223> nucleotide = a, g, c or u

<400> 121
yynrcassmy 10

<210> 122

<211> 10

<212> RNA

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<222> (1)..(10)

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<400> 122
rksbugsvgr 10

<210> 123

<211> 10

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<222> (3)..(3)

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<222> (3)..(3)

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<210> 124

<211> 5

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<210> 125

<211> 5

<212> RNA

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<222> (5)..(5)

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<400> 125
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<210> 126

<211> 5

<212> RNA

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<210> 127

<211> 5

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<210> 128

<211> 5

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<210> 129

<211> 5

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<222> (1)..(5)

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<210> 130

<211> 5

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<400> 130
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<210> 131

<211> 5

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<210> 132

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<222> (1)..(1)

<223> 40 kDa-PEG

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<211> 36

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<223> L-RNA

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<222> (1)..(1)

<223> 40 kDa-PEG

<400> 133
gcgugaaagc aacaugucaa ugaaagguag ccgcgc 36

<210> 134

<211> 29

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<222> (1)..(29)

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<222> (1)..(1)

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<400> 134
cgggagguua gggcuagaag ucggucccg 29

<210> 135

<211> 29

<212> RNA

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<222> (1)..(1)

<223> 40 kDa-PEG

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<210> 136

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<212> RNA

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<210> 137

<211> 38

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<400> 137
gcugugaaag caacauguca augaaaggua gccgcagc 38

<210> 138

<211> 40

<212> RNA

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<222> (1)..(40)

<223> L-RNA

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<210> 139

<211> 38

<212> RNA

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<220>

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<222> (1)..(38)

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<222> (1)..(1)

<223> 30 kDa-PEG

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<210> 140

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<222> (1)..(38)

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<222> (1)..(1)

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<210> 141

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<222> (1)..(1)

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<210> 142

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<222> (1)..(48)

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<210> 143

<211> 49

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<210> 144

<211> 49

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<222> (1)..(49)

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<210> 145

<211> 38

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<400> 145
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gcugugaaag uaacauguca augaaaggua accacagc 38

<210> 147

<211> 38

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<400> 147
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<400> 152
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<400> 154
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<400> 155
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<212> RNA

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<400> 156
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<210> 158

<211> 39

<212> RNA

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<210> 159

<211> 36

<212> RNA

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<220>

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<400> 159
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<210> 160

<211> 34

<212> RNA

<213> Artificial sequence

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<400> 160
ugugaaagca acaugucaau gaaagguagc cgca 34

<210> 161

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<400> 161
gugaaagcaa caugucaaug aaagguagcc gc 32

<210> 162

<211> 30

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<400> 162
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<210> 163

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<400> 163
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