Alignment of the SorCS1 protein from different species

Sequence 1: gi|61743975|ref|NP_001013049.1	1198 aa	Human (homo sapiens)
Sequence 2: gi|114632730|ref|XP_508026.2|	1361 aa	Chimpanzee (Pan troglodytes)
Sequence 3: gi|119917739|ref|XP_001253082.	1196 aa	Cow (Bos Taurus)
Sequence 4: gi|12025518|ref|NP_067352.1|	1167 aa	Mouse (Mus musculus)
Sequence 5: gi|109460253|ref|XP_220080.4|	1369 aa	Rat (Rattus norvegicus)
Sequence 6: gi|73998824|ref|XP_535010.2|	997 aa	Dog (Canis lupus familiaris)
Sequence 7: gi|118093020|ref|XP_421750.2|	1258 aa	Chicken (Gallus gallus)

```
Human (homo sapiens)          --------------------------------------------------
Chimpanzee (Pan troglodytes)  --------MTGRFPPRNRKLPTHRPLREPGVDRPRGQGARTQRWDPRPRG 42
Cow (Bos taurus)              --------------------------------------------------
Mouse (Mus musculus)          --------------------------------------------------
Rat (Rattus norvegicus)       MRAQVFLQQSGLSEKKHTDGIPTVPSINVIPERSKELLVPRGRVLWLLAG 50
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       --------------------------------------------------

Human (homo sapiens)          --------------------------------------------------
Chimpanzee (Pan troglodytes)  RRVGGGERRGEAAAAPARPRGSRRRRLQRPETRARARSASDFSSAPPPRG 92
Cow (Bos taurus)              --------------------------------------------------
Mouse (Mus musculus)          --------------------------------------------------
Rat (Rattus norvegicus)       TLRSLGRVGDSTARARLPVHSAARRRDAAPGALAEPALPPASPRRRRRRW 100
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       --------------------------------------------------

Human (homo sapiens)          --------------------------------------------------
Chimpanzee (Pan troglodytes)  GGSLRPDPRSAQAQPGRAAATCPAPPPPAPTAAQLGWSWGPERRPPTAAS 142
Cow (Bos taurus)              --------------------------------------------------
Mouse (Mus musculus)          --------------------------------------------------
Rat (Rattus norvegicus)       LAAPSQPARSSQAQPGRAAGTCPAPPPRAPPPPNLDGVVVLSAHPAAVSP 150
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       ----------------------------------------------MEKV 4
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Fig. 1

```
Human (homo sapiens)          ----------MGKVGAGGGSQARLSALLAGAGLLILCAP 29
Chimpanzee (Pan troglodytes)  AELRAATFVLGPLSPLLFAPAMGKVGAGGGSQARLSALLAGAGLLVLCAP 192
Cow (Bos taurus)              ----------MGKVGAGGVSPAGLSALLAGAGLLVLCAP 29
Mouse (Mus musculus)          ----------MGKVGAGDGSSAGLSALLAGAGLLMLLAP 29
Rat (Rattus norvegicus)       VPRSAACLRFGTPSPLLSAPEMGKVGAGDGSSAALSALLTGAGLLMLLAP 200
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       AGWYPAWHVALLYWTWLFLFTFGFTGAEITCRSCHSQVNPQQQHPQQGLP 54


Human (homo sapiens)          GVCGGGSCCPSPHPSSAPRSASTPRGFSHQGRPGRAPATPLPLVVRPLFS 79
Chimpanzee (Pan troglodytes)  GVCGGGSCCPPPHPSSAPRSASTPRGFSHQGRPGRAPATPLPLVVRPLFS 242
Cow (Bos taurus)              GSCGGGSCCPPRHPSAAPRWAPTPGGLPHQGPRGRAPATPLPQLGRPLFA 79
Mouse (Mus musculus)          GVCSSLSCCPPQHPSSTPRRTLTPRGFPHPGPLGRAPATPPPLFMRPLFA 79
Rat (Rattus norvegicus)       GICSSLSCCPPQHPSSTPRWTLTPRGFSYPGPLGRAPATPPPLFMRPLFA 250
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       MHLKTDRGEKERWRIPGEQGGERGRGAGMDTEDAELQAPFDPALAGTKFS 104


Human (homo sapiens)          -VAPGDRALSLERARGTGASMAVAARSGRR-RRSGADQEKAERGEGASRS 127
Chimpanzee (Pan troglodytes)  -VAPGDRALSLERARGTGASMAVAARSGRR-RRSGADQEKAERGEGASRS 290
Cow (Bos taurus)              -VAPGDRALSLERAPGTGASVAVAPRSGRK-RRSGEDQEKAERGEGTSRS 127
Mouse (Mus musculus)          -VAPGDRALFLERAGGSRVSVATAARSGRR-RRSGTEPEKIEPGEGASRS 127
Rat (Rattus norvegicus)       -VAPGDRALFLERAGGSRVSVATASRSGRR-RRSGMDPEKTEPGEGTSRS 298
Dog (Canis lupus familiaris)  --------------------------------------------------
Chicken (Gallus gallus)       GWETRSWASEPEKAPGDSRPGAAAAPTGEYPQRGQAGGRRNSARRRRGRS 154


Human (homo sapiens)          PRGVLRDGGQQEPGTRERDPDKATRFRMEELRLTSTTFALTGDSAHNQAM 177
Chimpanzee (Pan troglodytes)  PRGVLRDGGQQEPGTLERDPDKATRFRMEELRLTSTTFALTGDSAHNQAM 340
Cow (Bos taurus)              PRGVLRDRGQLEPGTLERDPDKATRFRLEELKLTSTTFALTGDSAHNQAM 177
Mouse (Mus musculus)          RRDMLKDGGQQGLGTGARDPGKATRFRMEELRLTSTTFALTGDSAHNQAM 177
Rat (Rattus norvegicus)       RRDMLRDGGQQGPGTGARDPDKATRFRMEELRLTSTTFALTGDSAHNQAM 348
Dog (Canis lupus familiaris)  ------------------------------MRKVS-----------EIM 8
Chicken (Gallus gallus)       PRGTAGPGGAAG---REPGGSGAARFGLEELRLGSTTFALTGDSAHNQAM 201
                                                              ::  *           : *
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Fig. 1, continued

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Human (homo sapiens)           VHWSGHNSSVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 227
Chimpanzee (Pan troglodytes)   VHWSGHNSSVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 390
Cow (Bos taurus)               VHWSGHNSSVILILTKLFDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 227
Mouse (Mus musculus)           VHWSGHNSSVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 227
Rat (Rattus norvegicus)        VHWSGHNSSVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 398
Dog (Canis lupus familiaris)   VLRSWH--SVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKVGLK 56
Chicken (Gallus gallus)        VHWSGQNSSVILILTKLYDYNLGSITESSLWRSTDYGTTYEKLNDKIGLK 251
                               *  * :  *********:*****************************:***

Human (homo sapiens)           TILSYLYVCPTNKRKIMLLTDPEIESSLLISSDEGATYQKYRLNFYIQSL 277
Chimpanzee (Pan troglodytes)   TILSYLYVCPTNKRKIMLLTDPEIESSLLISSDEGATYQKYRLNFYIQSL 440
Cow (Bos taurus)               TILSYLYVCPTNKRKIMLLTDPEIESSLLISSDEGATYQKYRLNFYIQSL 277
Mouse (Mus musculus)           TILSYLYVCPTNKCKIMLLTDPEIESSLLISSDEGATYQKYRLNFYLQSL 277
Rat (Rattus norvegicus)        TILSYLYVCPTNKRKIMLLTDPEIESSLLISSDEGATYQKYRLNFYIQSL 448
Dog (Canis lupus familiaris)   TILSYLYVCPTNKRKIMLLTDPEIESSLLISSDEGATYQKYRLNFYIQSL 106
Chicken (Gallus gallus)        TILSYLYVCPTNKRKIMLLTDPEVESSLLISTDEGATYQKYRLNFYIHSL 301
                               ************* *********:*******:**************::**

Human (homo sapiens)           LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQEGVVPNRFYWSVMGSNK 327
Chimpanzee (Pan troglodytes)   LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQEGVVPNRFYWSVMGSNK 490
Cow (Bos taurus)               LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQEAVVPNRFYWSVMGSNK 327
Mouse (Mus musculus)           LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQESVVPNRFYWSVMGSSK 327
Rat (Rattus norvegicus)        LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQEAVVPNRFYWSVLGSNK 498
Dog (Canis lupus familiaris)   LFHPKQEDWILAYSQDQKLYSSAEFGRRWQLIQEGVVPNRFYWSVMGSNK 156
Chicken (Gallus gallus)        LFHPKQEDWILAYSQDQKLFSSVEFGRRWLLLHEGVAPNRFYWSMMVSGR 351
                               *******************:**.****** *::*.*.*******:: *.:

Human (homo sapiens)           EPDLVHLEARTVDGHSHYLTCRMQNCTEANRNQPFPGYIDPDSLIVQDHY 377
Chimpanzee (Pan troglodytes)   EPDLVHLEARTVDGHSHYLTCRMQNCTEANRNQPFPGYIDPDSLIVQDHY 540
Cow (Bos taurus)               EPDLVHLEARTVDGHSQYLTCRMQNCTEANRNKPFPGYIDPDSLIVQDDY 377
Mouse (Mus musculus)           EPDLVHLEARTVDGHSIYLTCRMQNCTEANRNKPFPGYIDPDSLIVQDDY 377
Rat (Rattus norvegicus)        EPDLVHLEARTVDGHSIYLTCRMQNCTEANRNKPFPGYIDPDSLIVQDDY 548
Dog (Canis lupus familiaris)   EPDLVHLEARTVDGHSQYLTCRMQNCTEANRNKPFPGYIDPDSLIVQDDY 206
Chicken (Gallus gallus)        EPDLVHLEAKTVDGHAQYITCKMQNCSEASQNKPFPGYIDHNSLIVQDDY 401
                               *********:*****: *:**:****:**.:*:******* :******.*
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Fig. 1, continued

```
Human (homo sapiens)          VFVQLTSGGRPHYYVSYRRNAFAQMKLPKYALPKDMHVISTDENQVFAAV 427
Chimpanzee (Pan troglodytes)  VFVQLTSGGRPHYYVSYRRNAFAQMKLPKYALPKDMHVISTDENQVFAAV 590
Cow (Bos taurus)              VFVQLTSGGRPHYYVSYRRNAFAQMKLPKYALPKDMHVISTDENQVFAAV 427
Mouse (Mus musculus)          VFVQLTSGGRPHYYVSYRRSPFAQMKLPKYALPKDMHVISTDENQVFAAV 427
Rat (Rattus norvegicus)       VFVQLTSGGRPHYYVSYRRNPFAQMKLPKYALPKDMHVISTDENQVFAAV 598
Dog (Canis lupus familiaris)  VFVQLTSGGRPHYYVSYRRNAFAQMKLPKYALPKDMHVISTDENQVFAAV 256
Chicken (Gallus gallus)       VFVQLTSGGRPHYYVSYRRNAFTPIKLPKYSLPKDMHVISTDESQVFAAV 451
                              ********************..*: :*****:************.******

Human (homo sapiens)          QEWNQNDTYNLYISDTRGVYFTLALENVQSSRGPEGNIMIDLYEVAGIKG 477
Chimpanzee (Pan troglodytes)  QEWNQNDTYNLYISDTRGVYFTLALENVQSSRGPEGNIMIDLYEVAGIKG 640
Cow (Bos taurus)              QEWNQNDTYNLYISDTRGVYFTLALENVQSSRGPEGNVMIDLYEVAGIKG 477
Mouse (Mus musculus)          QEWNQNDTYNLYISDTRGVYFTLALENVRSSRGPEGNVMIDLYEVAGIKG 477
Rat (Rattus norvegicus)       QEWNQNDTYNLYISDTRGVYFTLALENVQSSRGPEGNVMIDLYEVAGIKG 648
Dog (Canis lupus familiaris)  QEWNQNDTYNLYISDTRGVYFTLALENVQSSRGPEGNIMIDLYEVAGIKG 306
Chicken (Gallus gallus)       QEWNQNDTYNLYISDTRGVYFTLALENVKSSQGLDGNVMIDLYEVAGIKG 501
                              ****************************:**:* :**:************

Human (homo sapiens)          MFLANKKIDNQVKTFITYNKGRDWRLLQAPDTDLRGDPVHCLLPYCSLHL 527
Chimpanzee (Pan troglodytes)  MFLANKKIDNQVKTFITYNKGRDWRLLQAPDTDLRGDPVHCLLPYCSLHL 690
Cow (Bos taurus)              MFLANKKIDNQVKTFITYNKGRDWRLLQAPDTDLRGDPVHCVLPYCSLHL 527
Mouse (Mus musculus)          MFLANKKIDNQVKTFITYNKGRDWRLLQAPDADLRGDPVHCLLPYCSLHL 527
Rat (Rattus norvegicus)       MFLANKKIDNQVKTFITYNKGRDWRLLQAPDADLRGDPVHCLLPYCSLHL 698
Dog (Canis lupus familiaris)  MFLANKKIDNQVKTFITYNKGRDWRLLQAPDTDLRGDPVHCLLPYCSLHL 356
Chicken (Gallus gallus)       MFLANKKIDNQVKTFITYNKGRDWNLLQAPDTDLKGNPVHCLLPYCSLHL 551
                              ************************.******:**:*:****:********

Human (homo sapiens)          HLKVSENPYTSGIIASKDTAPSIIVASGNIGSELSDTDISMFVSSDAGNT 577
Chimpanzee (Pan troglodytes)  HLKVSENPYTSGIIASKDTAPSIIVASGNIGSELSDTDISMFVSSDAGNT 740
Cow (Bos taurus)              HLKVSENPYTSGIIASRDTAPSIIVASGNIGSELSDSDISMFVSSDAGNT 577
Mouse (Mus musculus)          HLKVSENPYTSGIIASRDTAPSIIVASGNIGSELSDSDISMFVSSDAGNT 577
Rat (Rattus norvegicus)       HLKVSENPYTSGIIASRDTAPSIIVASGNIGSELSDSDISMFVSSDAGNT 748
Dog (Canis lupus familiaris)  HLKVSENPYTSGIIASRDTAPSIIVASGNIGSELSDSDISMFVSSDAGNT 406
Chicken (Gallus gallus)       HLKVSENPYTSGNIASRDTAPSIIVASGNIGPELSDNDISMFVSSDAGNT 601
                              ************ ***:**************.****.*************
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Fig. 1, continued

```
Human (homo sapiens)          WRQIFEEEHSVLYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 627
Chimpanzee (Pan troglodytes)  WRQIFEEEHSVLYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 790
Cow (Bos taurus)              WRQIFEEEHSVLYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 627
Mouse (Mus musculus)          WRQIFEEEHSILYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 627
Rat (Rattus norvegicus)       WRQIFEEEHSILYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 798
Dog (Canis lupus familiaris)  WRQIFEEEHSVLYLDQGGVLVAMKHTSLPIRHLWLSFDEGRSWSKYSFTS 456
Chicken (Gallus gallus)       WRQIFEEEHSVLYLDQGGVLVAIKHTSLPIRHLWLSFDEGKSWSKYSFTS 651
                              **********:**********:**********:**********:********* 

Human (homo sapiens)          IPLFVDGVLGEPGEETLIMTVFGHFSHRSEWQLVKVDYKSIFDRRCAEED 677
Chimpanzee (Pan troglodytes)  IPLFVDGVLGEPGEETLIMTVFGHFSHRSEWQLVKVDYKSIFDRRCAEED 840
Cow (Bos taurus)              IPLFVDGVLGEPGEETLIMTLLDHS--HSDWLVTALQPCCLFLLGNEWED 675
Mouse (Mus musculus)          IPLFVDGVLGEPGEETLIMTVFGHFSHRSEWQLVKVDYKSIFDRRCAEED 677
Rat (Rattus norvegicus)       IPLFVDGVLGEPGEETLIMTVFGHFSHRSEWQLVKVDYKSIFDRRCAEED 848
Dog (Canis lupus familiaris)  IPLFVDGVLGEPGEETLIMTVFGHFSHRSEWQLVKVDYKSIFDRRCAEED 506
Chicken (Gallus gallus)       LPLFVDGILGEPGEETLIMTVFGHFSHRSEWQLVKIDYKSIFDRRCAEED 701
                              :******:**************::.*   :*:* :. ::  .:*      ** 

Human (homo sapiens)          YRPWQLHSQGEACIMGAKRIYKKRKSERKCMQGKYAGAMESEPCVCTEAD 727
Chimpanzee (Pan troglodytes)  YRPWQLHSQGEACIMGAKRIYKKRKSERKCMQGKYAGAMESEPCVCTEAD 890
Cow (Bos taurus)              KIAWKPQDQGEACIMGAKRIYKKRKSERKCMQGKYAGAMESEPCVCTEAD 725
Mouse (Mus musculus)          YRPWQLHSQGEACIMGAKRIYKKRKSERKCMQ-KYAGAMESEPCVCTEAD 726
Rat (Rattus norvegicus)       YRPWQLHSQGEACIMGAKRIYKKRKSERKCMQGTYAGAMESEPCVCTEAD 898
Dog (Canis lupus familiaris)  YRPWQLHSQGEACIMGAKRIYKKRKSERKCMQGKYAGAMESEPCVCTEAD 556
Chicken (Gallus gallus)       YWTWQLHSQGEACIMGAKRIYRKRKSEKKCMQGKYAGAMTSEPCVCTDAD 751
                               .*: :.**************:*****:***** .***** ********:** 

Human (homo sapiens)          FDCDYGYERHSNGQCLPAFWFNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 777
Chimpanzee (Pan troglodytes)  FDCDYGYERHSNGQCLPAFWFNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 940
Cow (Bos taurus)              FDCDYGYERHSNGQCLPAFWFNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 775
Mouse (Mus musculus)          FDCDYGYERHSNGQCLPAFWFNPSSLSKDCSLGQSYLNSAGYRKVVSNNC 776
Rat (Rattus norvegicus)       FDCDYGYERHSSGQCLPAFWFNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 948
Dog (Canis lupus familiaris)  FDCDYGYERHSNGQCLPAFWFNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 606
Chicken (Gallus gallus)       FDCDYGYERHRNGQCLPAFWYNPSSLSKDCSLGQSYLNSTGYRKVVSNNC 801
                              ********** .*********:**********:**********:********** 
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Fig. 1, continued

```
Human (homo sapiens)           TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 827
Chimpanzee (Pan troglodytes)   TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 990
Cow (Bos taurus)               TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 825
Mouse (Mus musculus)           TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 826
Rat (Rattus norvegicus)        TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 998
Dog (Canis lupus familiaris)   TDGVREQYTAKPQKCPGKAPRGLRIVTADGKLTAEQGHNVTLMVQLEEGD 656
Chicken (Gallus gallus)        TDGVREQYTAKPQQCPGKAPQGLRIITSDGKLTAEQGHNVTFLVQLEEGD 851
                               *************:******:****:*:*************::*******

Human (homo sapiens)           VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYQNVGIFRVTVQVDNSLGS 877
Chimpanzee (Pan troglodytes)   VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYQNVGIFRVTVQVDNSLGS 1040
Cow (Bos taurus)               VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYHNVGIFRVTVQVDNSLGS 875
Mouse (Mus musculus)           VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYQNVGIFRVTVQVDNSLGS 876
Rat (Rattus norvegicus)        VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYQNVGIFRVTVQVDNSLGS 1048
Dog (Canis lupus familiaris)   VQRTLIQVDFGDGIAVSYVNLSSMEDGIKHVYHNVGIFRVTVQVDNSLGS 706
Chicken (Gallus gallus)        LQRSLIQVDFGDGTAVSYANLSSTEDGIKHTYQNVGIFRVTVLVENSLGS 901
                               :**:********* ****.**** ******.*:********* *:*****

Human (homo sapiens)           DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 927
Chimpanzee (Pan troglodytes)   DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 1090
Cow (Bos taurus)               DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 925
Mouse (Mus musculus)           DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 926
Rat (Rattus norvegicus)        DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 1098
Dog (Canis lupus familiaris)   DSAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWY 756
Chicken (Gallus gallus)        DNAVLYLHVTCPLEHVHLSLPFVTTKNKEVNATAVLWPSQVGTLTYVWWF 951
                               *.*******************************************:

Human (homo sapiens)           GNNTEPLITLEGSISFRFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 977
Chimpanzee (Pan troglodytes)   GNNTEPLITLEGSISFRFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 1140
Cow (Bos taurus)               GNNTEPLITLEGSIAFKFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 975
Mouse (Mus musculus)           GNNTEPLITLEGSISFKFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 976
Rat (Rattus norvegicus)        GNNTEPLITLEGSISFKFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 1148
Dog (Canis lupus familiaris)   GNNTEPLITLEGSISFKFTSEGMNTITVQVSAGNAILQDTKTIAVYEEFR 806
Chicken (Gallus gallus)        GNNTEPLITLEGSITFTFSVEGMNTITVQVSAGNTILQDTKTIAVYEQFR 1001
                               **************:* *: **************:************:**
```

Fig. 1, continued

```
Human (homo sapiens)          SLRLSFSPNLDDYNPDIPEWRRDIGRVIKKSLVEATGVPGQHILVAVLPG 1027
Chimpanzee (Pan troglodytes)  SLRLSFSPNLDDYNPDIPEWRRDIGRVIKKSLVEATGVPGQHILVAVLPG 1190
Cow (Bos taurus)              SLRLSFSPNLDDYNPDIPEWRRDVSRVIKKALVEATGVPGQHILVAVLPG 1025
Mouse (Mus musculus)          SLRLAFSPNLDDYNPDIPEWRRDISRVIKKSLVEATGIPSQHILVAVLPG 1026
Rat (Rattus norvegicus)       SLRLAFSPNLDDYNPDIPEWRRDISRVIKKSLVEATGIPSQHILVAVLPG 1198
Dog (Canis lupus familiaris)  SLRLSFSPNLDDYNPDIPEWRRDISRVIKKSLVEATGVPGQHILVAVLPG 856
Chicken (Gallus gallus)       SLRLSFSPNLDDYNPDIPEWRRDISRVVKRALVEATGISSKHILVAVLPG 1051
                              ****:******************:.**:*::******:..:*********

Human (homo sapiens)          LPTTAELFVLPYQDPAGENKRSTDDLEQISELLIHTLNQNSVHFELKPGV 1077
Chimpanzee (Pan troglodytes)  LPTTAELFVLPYQDPAGENKRSTDDLEQISELLIHTLNQNSVHFELKPGV 1240
Cow (Bos taurus)              LPTAAELFVLPHQDPTGENKRPAEDLEQISELMIHKLNQNSVHFELKPGV 1075
Mouse (Mus musculus)          LPTAAELFVLPYQDGTRENKRSPEDLEQISEVLIHKLNQNLVHFELKPGV 1076
Rat (Rattus norvegicus)       LPTAAELFVLPYQDGARENKRSPEDLEQISEVLIHKLNQNLVHFELKPGV 1248
Dog (Canis lupus familiaris)  LPTAAELFVLPYQDPTGENKRSAEDLEQISELLIHKLNQNSVHFELKPGV 906
Chicken (Gallus gallus)       LPTSAELFILPYQDATGGNKR-TEDLEQISEILIQKLNQNFVHFELKPGV 1100
                              ***:****:**:** :  *** .:*******::*:.**** *********

Human (homo sapiens)          RVLVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRKIP 1127
Chimpanzee (Pan troglodytes)  RVLVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRKIP 1290
Cow (Bos taurus)              QVLVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRKIP 1125
Mouse (Mus musculus)          QVLVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRRVA 1126
Rat (Rattus norvegicus)       QVLVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRKIP 1298
Dog (Canis lupus familiaris)  QILVHAAHLTAAPLVDLTPTHSGSAMLMLLSVVFVGLAVFVIYKFKRRVA 956
Chicken (Gallus gallus)       RVLVHAAHLTAAPLVDLTPSHSGSAMLMLLSVVFVGLAVFVIYKFKRKIP 1150
                              ::*****************:*****************************::.

Human (homo sapiens)          GINVYAQMQNEKEQEMISPVSHSESRPNVPQTELRRPGQLIDEKVESQLI 1177
Chimpanzee (Pan troglodytes)  GINVYAQMQNEKEQEMISPVSHFESRPSVPQTELRRPGQLIDEKVESQLI 1340
Cow (Bos taurus)              GINVYAQMQNEKEQEMVSRVSHPESRPYVPQTELRRPGQLIDEKVESQLI 1175
Mouse (Mus musculus)          LPSPPSPSAQPGDSSLR----LQRPRPATPPSSPKRGSAGAQFAI----- 1167
Rat (Rattus norvegicus)       GINVYAQMQNEKEQELINPVSHTESRPTAPHPDLRRPGQLVDEKVESHLL 1348
Dog (Canis lupus familiaris)  LPSPPSPSTQPGDSSLR----LQRARHATPPSTPKRGSAGAQFAI----- 997
Chicken (Gallus gallus)       GLNIYAQMQNEKDQEMVSPVSQRESIPNVPQSELMSPEQLVDEKLDVQPI 1200
                                     .  :   :  :..:       ..   .* .         :  :
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Fig. 1, continued

```
Human (homo sapiens)          GSISIVAENQSTKEIPTYVNV---------------------------------- 1198
Chimpanzee (Pan troglodytes)  GSISIVAENQSTKEIPTYVNV---------------------------------- 1361
Cow (Bos taurus)              GSISIVAENQSTKEIPTYVNV---------------------------------- 1196
Mouse (Mus musculus)          ---------------------------------------------------------
Rat (Rattus norvegicus)       GSISIVAENQSTKEIPTYVNV---------------------------------- 1369
Dog (Canis lupus familiaris)  ---------------------------------------------------------
Chicken (Gallus gallus)       EQPQATVQNPRKGNAAKVVWTEDFQKACGSPRGFKPRPGAEVFPQLLSPR 1250

Human (homo sapiens)          --------
Chimpanzee (Pan troglodytes)  --------
Cow (Bos taurus)              --------
Mouse (Mus musculus)          --------
Rat (Rattus norvegicus)       --------
Dog (Canis lupus familiaris)  --------
Chicken (Gallus gallus)       AQKKSLPM 1258
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Fig. 1, continued

Insulin signalling

(adipose tissue SorCS1 KO >< wildtype)

Gene	Fold regulation	p-value
Aebp1 (AE binding protein 1)	-5.93	0.406
Dok1(docking protein 1)	7.24	0.188
Igf1r (insulin-like growth factor 1 receptor)	3.30	0.00008
Irs2 (Insulin receptor substrate 2)	-2.95	0.100
Pik3cb (phosphoinositide-3-kinase, catalytic, beta polypeptide)	-5.65	0.196
Ucp1 (uncoupling protein 1)	-25.35	0.085

Gene	Function
Aebp1	A transcriptional repressor with carboxypeptidase activity. Binds promotor of adipose P2 gene.
Dok1	A member of the IRS family. Function as a scaffolding protein that recruits signalling molecules (ras-GTP, Nck)
Igf1r	Binds IGF1 with high affinity. Has tyrosine kinase activity. Plays a critical role in transformation events.
Irs2	A cytoplasmic signaling molecule that mediates effects of insulin, insulin-like growth factor 1, and other cytokines by acting as a molecular adaptor between diverse receptor tyrosine kinases and downstream effectors.
Pik3cb	PI3k phosphorylate the inositol ring in inositol lipids. Is a participant in signalling pathways regulating cell growth
Ucp1	Plays a role in heat production by uncoupling oxidative phosphorylation from the respiratory chain

Fig. 2A

Lipoprotein signalling and Cholesterol metabolism
(Adipose tissue SorCS1 KO >< wildtype)

Gene	Fold reg.	p-value
Akr1d1(aldo-keto reductase family1, member D1)	8.06	0.042
Colec12 (collectin sub-family member 12)	3.12	0.046
Dhcr7 (7-dehydrocholestrol reductase)	3.82	0.040
Hmgcs2 (3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2)	6.01	0.013
Lcat (Lecithin cholesterol acyltransferase)	3.37	0.008
Ldlr (Low density protein receptor)	3.44	0.014
Mvd (mevalonate (diphospho) decarboxylase)	3.48	0.039
Nr1h4 (Nuclear receptor subfamily 1, group H, member 4)	3.49	0.041
Osbpl5 (Oxysterol binding protein-like 5)	3.61	0.048
Prkag2 (Protein kinase, AMP-activated, gamma 2 non-catalytic)	5.27	0.007
Soat1 (Sterol O-acyltransferase 1)	11.75	0.020
Vldlr (very low density lipoprotein receptor)	4.53	0.018

Gene	Function
Akr1d1	Catalysis of the 5-beta-reduction of bile acid intermediates and steroid hormones.
Colec12	A scavenger receptor binding to carbohydrate antigens on microorganisms and oxidized phospholipids of oxidatively damaged or apoptotic cells.
Dhcr7	A penultimate enzyme of sterol biosynthesis that converts 7-dehydro cholesterol to cholesterol
Hmgcs2	Mediates the first reaction in ketogenesis, a metabolic pathway that provides lipid-derived energy during carbohydrate deprivation
Lcat	An extracellular cholesterol esterifying enzyme. The esterification of cholesterol is required for cholesterol transport.
Ldlr	A cell surface protein involved in receptor mediated endocytosis of specific ligands eg. LDL
Mvd	Catalyzes the conversion of mevalonate pyrophosphate into isopentyl pyrophosphate – one of the early steps in cholesterol biosynthesis
Nr1h4	Regulates the expression of various transport proteins and biosynthetic enzymes crucial to the physiological maintenance of cholesterol and bile acid homeostasis.
Osbpl5	An intracellular lipid receptor – a member of the oxysterol-binding protein family.
Prkag2	Subunit of AMPK an important energy-sensing enzyme that monitors cellular energy status and functions by inactivating key enzymes involved in regulating de novo biosynthesis of fatty acid and cholesterol
Soat1	Forms cholesterol esters from cholesterol. Accumulation of cholesterol esters as cytoplasmic lipid droplets is a characteristic feature of early stages of atherosclerotic plaques
Vldlr	Mediates cholesterol uptake possible in collaboration with ldl

Fig. 2B

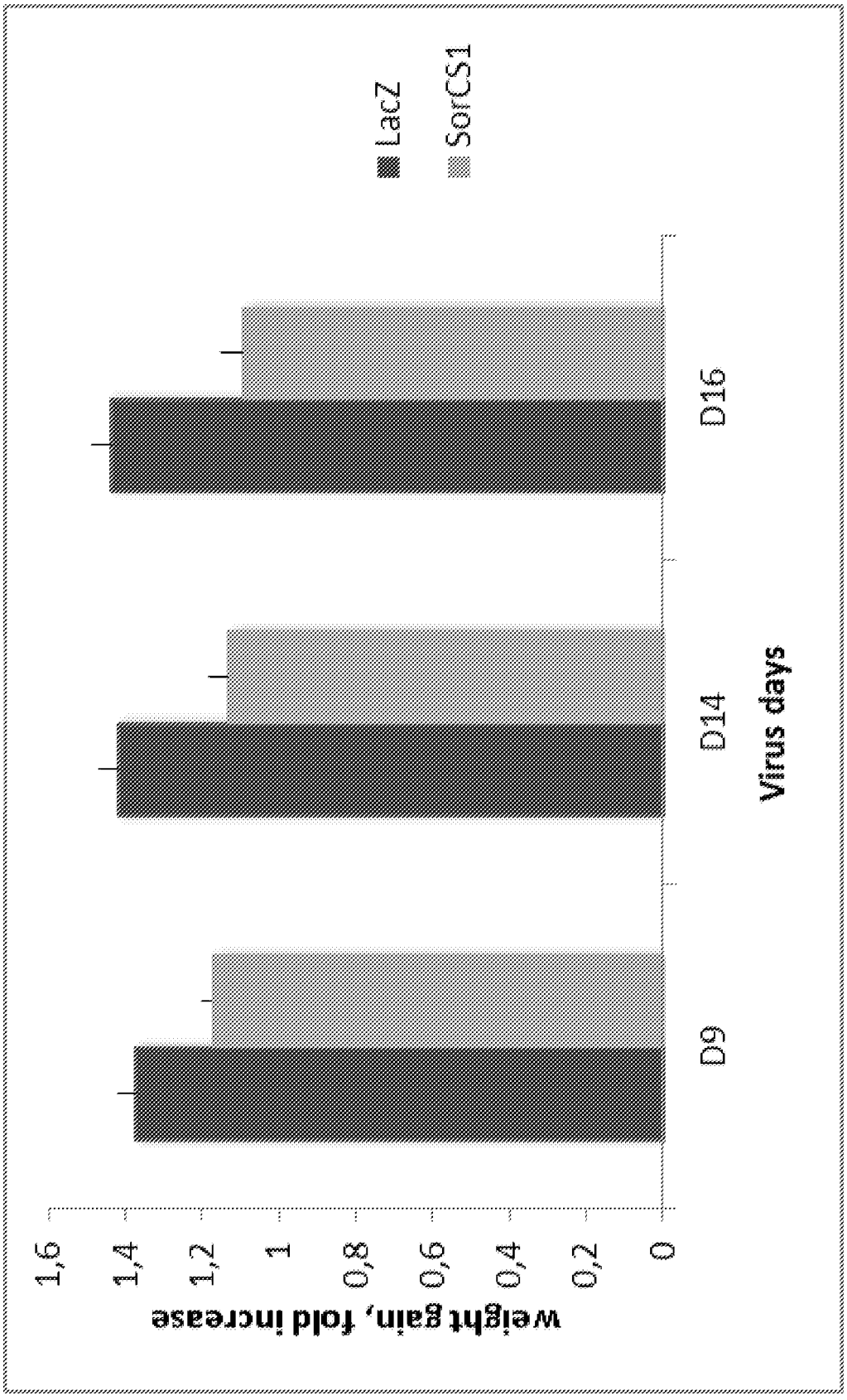
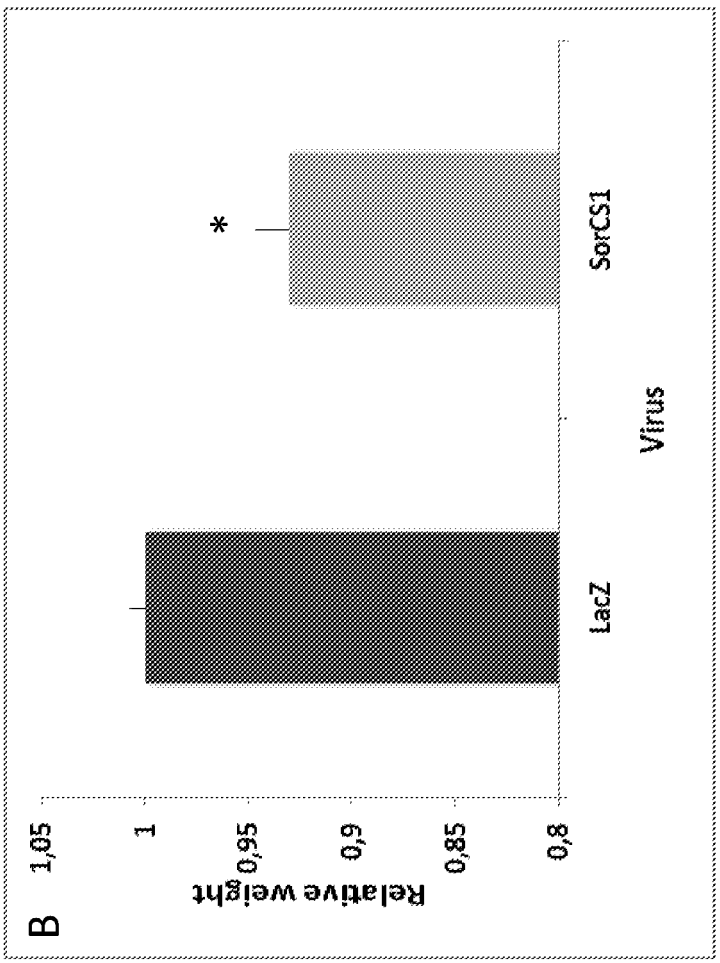

weight gain, fold increase
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
D9
D14
D16
Virus days
LacZ
SorCS1

Fig. 3


B
Relative weight
1,05
1
0,95
0,9
0,85
0,8
*
LacZ
SorCS1
Virus
* P < 0.05 SorCS1 vs LacZ

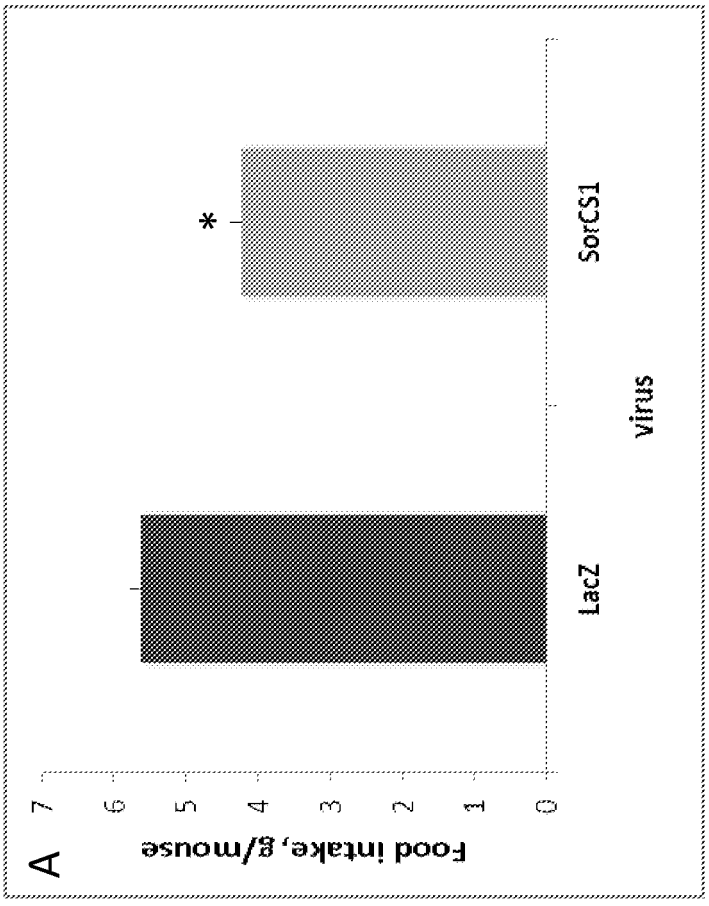

A
Food intake, g/mouse
7
6
5
4
3
2
1
0
*
LacZ
SorCS1
virus
* P < 0.05 SorCS1 vs LacZ

Fig. 4

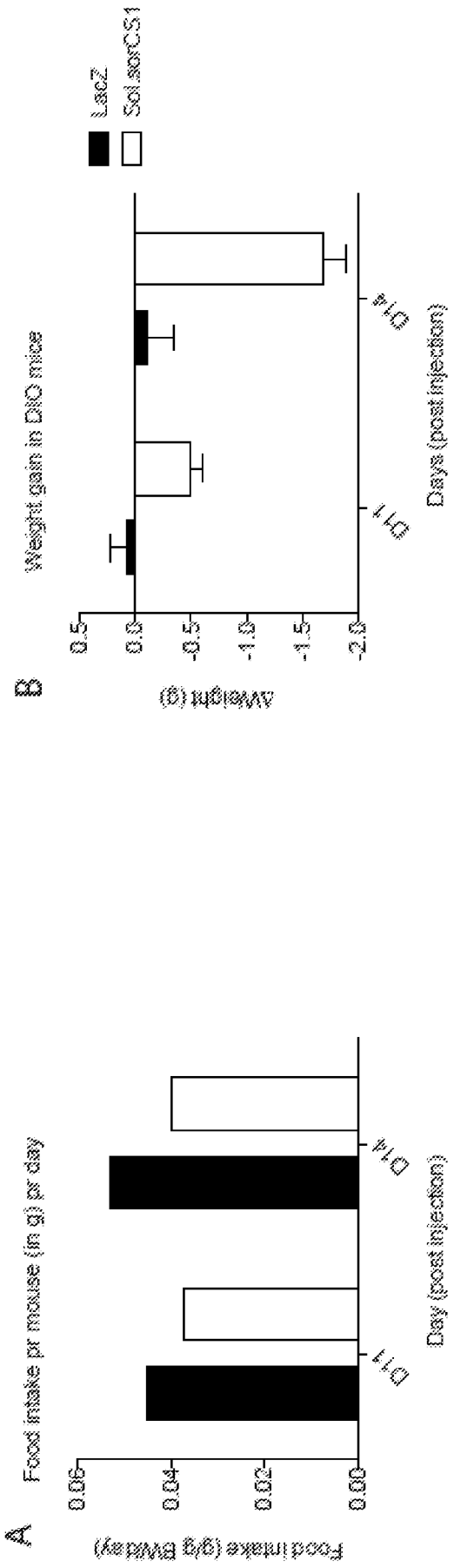

A
Food intake pr mouse (in g) pr day
Food intake (g/g BW/day)
0.06
0.04
0.02
0.00
D1
D4
Day (post injection)
B
Weight gain in DIO mice
Δweight (g)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
D1
D4
Days (post injection)
LacZ
Sol:sorCS1

Fig. 5

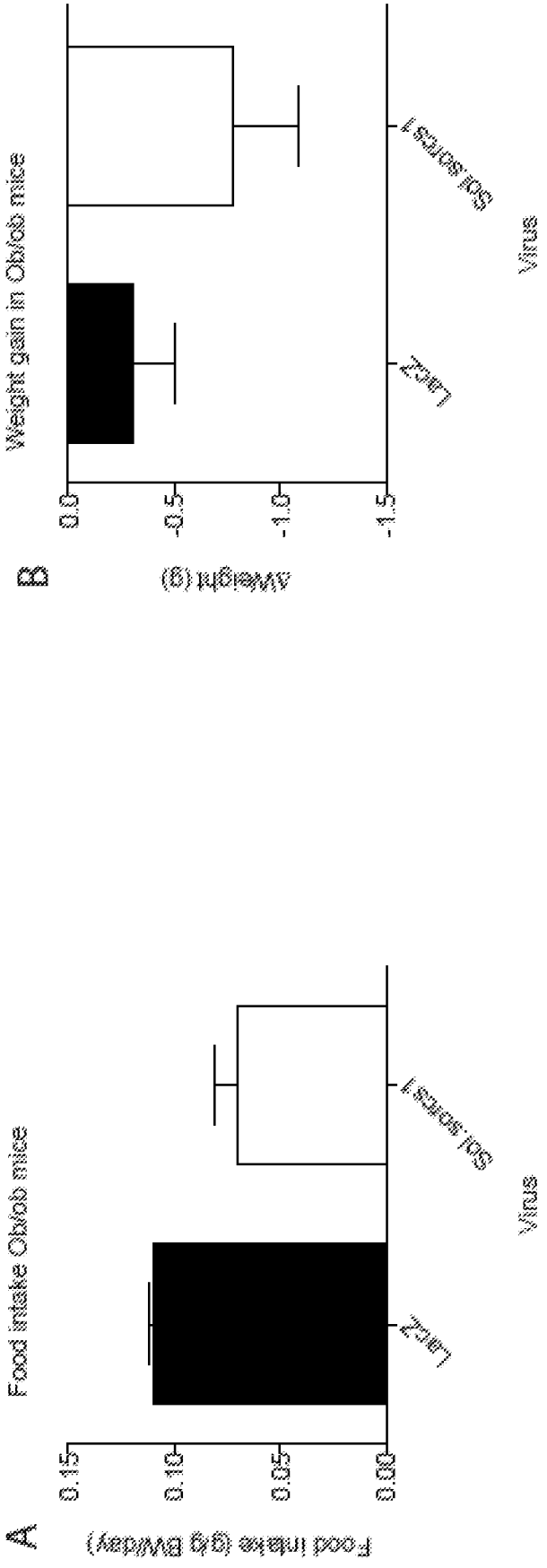

A
Food intake Obob mice
Food intake (g/g BW/day)
0.15
0.10
0.05
0.00
LacZ
Sol scrips 1
Virus
B
Weight gain in Obob mice
Δweight (g)
0.0
-0.5
-1.0
-1.5
LacZ
Sol scrips 1
Virus

Fig. 6

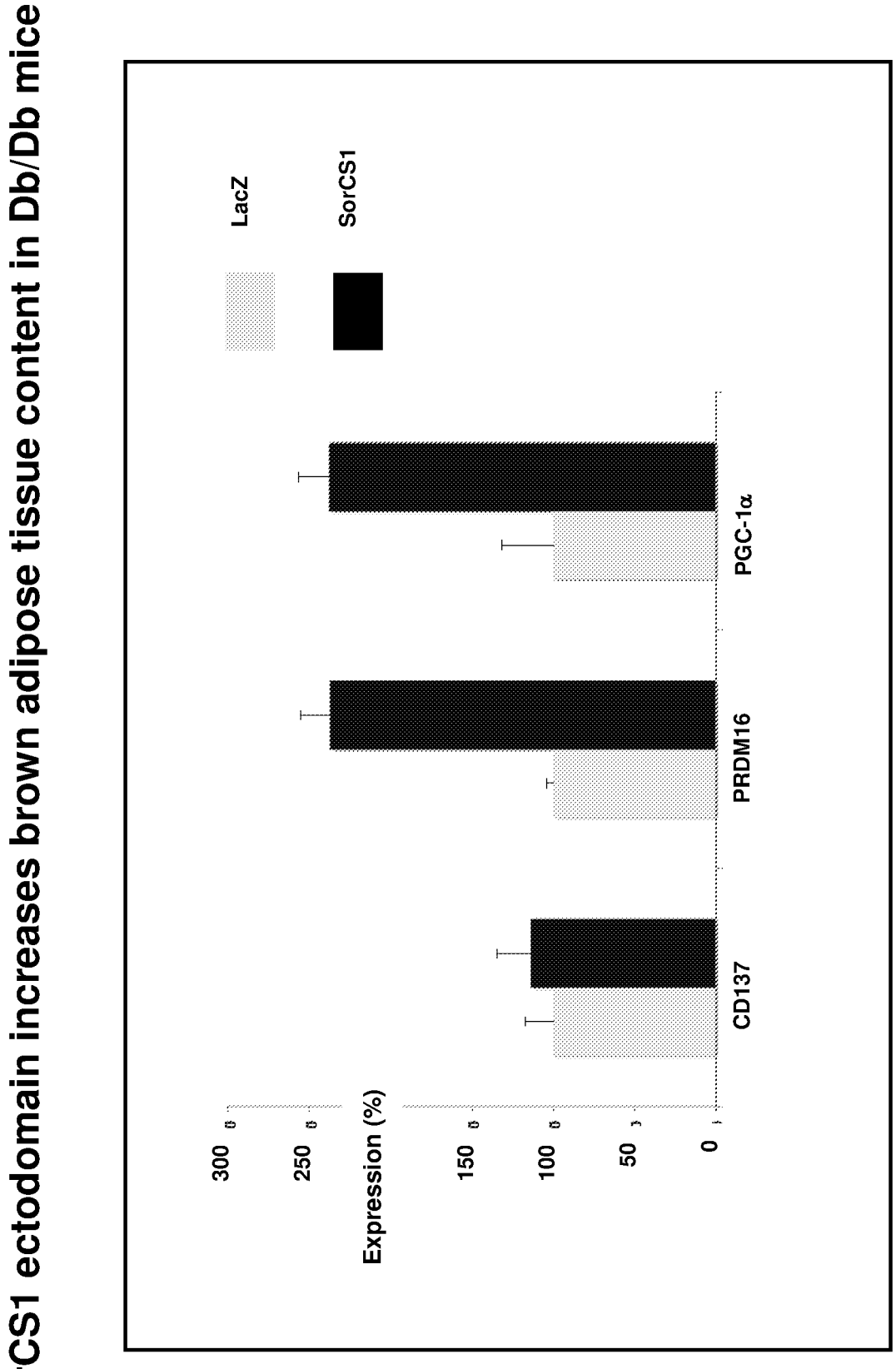

SorCS1 ectodomain increases brown adipose tissue content in Db/Db mice
LacZ
SorCS1
Expression (%)
300
250
150
100
50
0
CD137
PRDM16
PGC-1α

Fig. 7

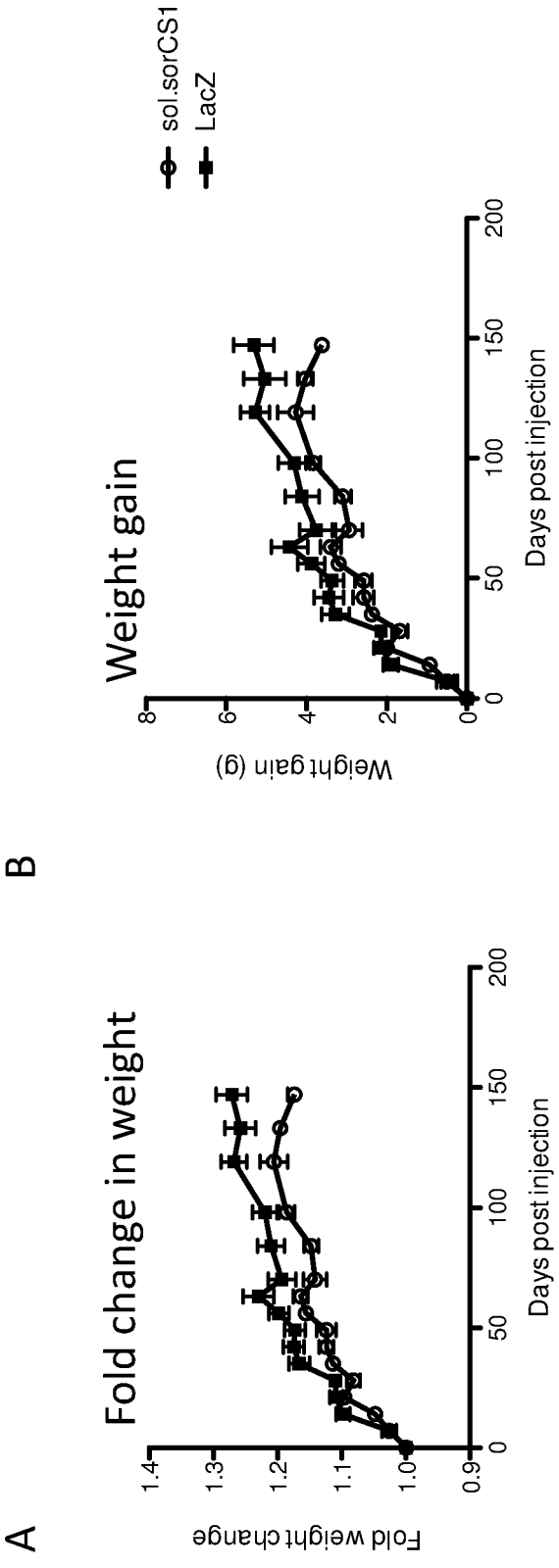

A
Fold change in weight
Fold weight change
1.4
1.3
1.2
1.1
1.0
0.9
0
50
100
150
200
Days post injection
B
Weight gain
Weight gain (g)
8
6
4
2
0
0
50
100
150
200
Days post injection
sol.sorCS1
LacZ

Fig. 8