Supplementary materials

Article information

Interleukin-22 deficiency contributes to the dextran sulfate sodium (DSS)induced inflammation in Japanese medaka, *Oryzias latipes*

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01_1L-22	<u>M</u>	AAAAHASSLRL	ASTAAATLLLLV	LIGWSETATA	HPFHRPLSGPLR	NLKTSQAVLEVAQHAQKK
Sc_IL-22	Mr	LFAAKVVSFLR	PAAAMLVLLPLL		LPVDRPLSQPLR	NPETYQAVREVSQHAQSV
Sm_IL-22	<u>Mr</u>	LHVSTVTPSLC	PAMLVLLPLL	LIGWAQLIAA	HPVDRALSHPLR	SPDTYQAVREVSQHAQTS
Om_1L-22	<u>Mr</u>	ESTVQLVA	AVVVVMSVC	LLRESVA	HSIHRPLSAPLH	SADTDTMVQQVAQHAQSS
Tt_1L-22		<u>-MLG</u>	KMKF AQLAVLLV	WCCCCCALSAD	ARPARLESEPLD	NSDTWNNIMVMAKHAQ
1p_1L-22			-MNCAVLAVLVV	LCCCCALSVD	ARPARLESEPLD	NPDTWNNVMVMAKHAQ
Dr_IL-22	MGDYAKGEKTTTVTYRHDIKAPEPQDALQVSTSRNNG	VHKRTDTRIHS	STCOMACETLIA	LCSCFLSGC	ARPT <mark>PL</mark> D	SSATWNDLAAMTDTAR
HS_IL-22	MP	ALQKSVSSFLM	GTLATSCLLLLA	LLVQGGAAAP.	DIEDOKLOK-SN	FOOPLITNETFMLAKEAS
Mm_IL-22		IVLQKSMSFSLM	GTLAASCLLLIA	D	I Cuc40	FQQPIIVNRTFMLAREAS
	110 4 - D 1 20 4		150 4	<u> </u>		190 200
		1 1			Cvg133	
01 TL-22	ELEEDTNVRL -PRVSSNODHLKTCCLHANTLDFYLN	INT <mark>T.</mark> HHR	DDAH <mark>P</mark> STHRLKT	DLHRTSEDLOS	SYG <mark>C</mark> NVTHYHDH	RHAVEFBRKIEKM
Sc IL-22	OTEDDSSTRLL-PRVNANODHLKICCLHANILDFYLN	NILHHH	DNOH <mark>P</mark> KMHRLKT	DLTRVSEDLO	rog <mark>c</mark> nvthyhdh	HHAVEFRRKLTKM
Sm IL-22	LTEDDSSTRLF-PRVSGDODHMKICCLHANILDFYLN	NILIHS	ADTH <mark>P</mark> KMLRLKT	DLSRVSADLO	rog <mark>c</mark> svthyhdh	LHAVEFRRRLNRM
Om IL-22	DTDTDTKLM-PDIDTKKNHRDICCLHANILDFYLS	NILTTKEKO	DKHH <mark>P</mark> KLPALKE	DLARVSRDLKI	EHGCAIKHYNDH	HHSIAFRKKLSEM
Tf_IL-22	AQDRDHETRLIPVISSDKLKDGDVCCVTIQILDYYLK	HILDGQSREGG	ERQY <mark>P</mark> RLHLVKP	DLHRVARDLOI	PH-CN-STQIDL	EHLNT <mark>F</mark> TONLKRAGEMYK
Ip_IL-22	AQDRDHETRLIPVISSDKLKDGDVCCANVKILDYYLF	AHILDGKAHEGR	EDNY <mark>P</mark> RIHLVKP	D <mark>LNR</mark> VARDLEI	PH-CN-AKQIDL	EHLOTFKONLNRAGEMYK
Dr_IL-22	NED-DHETRLLPYFSHDMLQEEGSCCINARILKYYVN	IHV <mark>L</mark> ESDEHT	DMKY <mark>P</mark> MIRNVRE	G <mark>LHR</mark> VEQE <mark>L</mark> QI	NH- <mark>C</mark> K-HDYSSH	PLVKQFKRNYHASAIM
Hs_IL-22	LADNNTDVRLIGEKLFHGVSMSERCYLMKQVLNFTLE	EV <mark>L</mark> FPQS	DRFQ <mark>P</mark> YMQEVVP	F <mark>LAR</mark> LSNR <mark>L</mark> S'	CHIEGDDLHIQ	RNVQKLKDTVKKL
Mm_IL-22	LADNNTDV <mark>RL</mark> IGEKLFRGVSAKDQ <mark>C</mark> YLMKQV <mark>L</mark> NFT <mark>L</mark> E	DV <mark>L</mark> LPQS	DRFQ <mark>P</mark> YMQEVVP	F <mark>L</mark> TKLSNQ <mark>L</mark> S:	SCHISGDDQNIQ	KNVRRLKETVKKL
	F Cys89			C	/s132	
	210 220 Cyssy 230				D ¹ (1) (1) (1) (1)	_
	· • [] • • [• • • • •] • • • •] • • • <u> </u> • • • [<u>•</u>] • • • •] • • • • • • •] • •	Amino acids (aa)	Similarities (%)	Identities (%)	Disulfide bond	S
01_IL-22	EGERGLNKAVGEIDILFTYLQDHCVQPTPTPGPAL-	189			Human	
Sc_IL-22	GGERGIN <mark>KAVGEIDILF</mark> TY <mark>L</mark> QDF <mark>C</mark> LQPKNSTAAAAH	190	87.8	00.8	Cys40-132	
Sm_IL-22	EAKRGLNKAVGEIDILFTYLQDYCVQPRNSSDATE-	18/	83.9	59.7	Cys89-178	
Om_1L-22	EEGKGIKKAIGEIDILFTFLKDFCVHA	1/3	72.7	41.0	Madalas	(Zobrofich)
Tt_1L-22	NKTKAQNKAIGETDILFHYLYESCRATSAS	181	74.9	28.7	медака	
1p_1L-22	NNTKAQNKAIGETDILFHYLYESCSATSTS	1//	70.7	27.6	Cys89-133	(Cys117-163)
Dr_1L-22	C ECCETTA TOPI DI TEMOT DUADA	213	/3.0	21.5	Cys90-178	(Cys118-210)
HS_1L-22	G-ESGEINAIGELDLLEMSLKNACI	179	11.3	24.4		
Pm_11-22	G-ESGETRATGELDLLEMSLKNAUV	1/9	/0.0	23.0		
	Cys178					
	0,01/0					

Fig. S1. Multiple alignments of the deduced protein sequences of IL-22 (**A**), IL-22RA1 (**B**), and IL-22BP (**C**) in Japanese medaka and other vertebrates. Identities and similarities of each IL-22, IL-22RA1, and IL-22BP protein with Japanese medaka IL-22, IL-22RA1, and IL-22BP peptide, indicated on the right side of the alignment. The amino acid residues highlighted in yellow represent matches of more than 75% among the aligned species. The letters (**A to F**) in the alignment of IL-22 show each range of alpha helix structures. Cysteine residues forming disulfide bonds are surrounded by red boxes (mammal) and blue boxes (teleost). In IL-22RA1 and IL-22BP, the ranges of functional domains (FNIII) and transmembrane regions predicted using SMART7 are shown by arrows. The species for the sequences used in these alignments are as follows; *Oryzias latipes* (Ol), *Siniperca chuatsi* (Sc), *Scophthalmus maximus* (Sm), *Oncorhnchus mykiss* (Om), *Tachysurus fulvidraco* (Tf), *Ictalurus punctatus* (Ip), *Danio rerio* (Dr), *Takifugu rubripes* (Tr), *Cynoglossus joyneri* (Cj), *Salmo salar* (Ss), *Esox lucius* (El), *Astyanax mexicanus* (Am), *Tachysurus fulvidraco* (Tf), *Cyprinus carpio* (Cc), *Homo sapiens* (Hs), and *Mus musculus* (Mm). Full names, abbreviations, and GenBank accession numbers of the sequences shown in this alignment are listed in **Table S2**.

Image: Description Image:	R	L.		ENT domain 1	
<pre>cliptic-liptic liptic lip</pre>	D	10 20 30	40 50	60 70 80	90 100
01 1.1.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2	01 77 00731	·····	· · · · · · · · · · · · · · · · · ·	.Cvs69 .	Cys77
	01_1L-22RA1 Tr 1122RA1	MWNMDVMKLFLLCYACLPAGNGQVYFV MMWTINAVIISIFCSAVCISTE-NESVYFT	SKNFYNVLHWEPVKPSFPGEEVL SKNFNNTLHWIAVDPABPGENIT	YEYSVEYKKHADGEEYBKKAGONI	TALLCOLTEETPAIRDCHY
sin_1_228.1	Cj_IL-22RA1	MNVWSLDIIVLLFCYARLSTATANGTVTF	SKNFTNVLHWDAAEPKYPEEKLL	YSVQYYSHGRDTDGHLQIKKEC2NI	TALSCOLTAETPSLPHVTY
T1_12288.1 M012MPLIVIL_UNR_SSEQUESTS. M012MPLIVIL_UNR	Ss_IL-22RA1	<u>MNL<mark>W</mark>PRKVVV<mark>L</mark>LLYCYGCSA</u> IGEGKPY <mark>F</mark> I	<mark>SRNF</mark> NTV <mark>L</mark> HWNKVDS <mark>P</mark> DEGVF	<mark>YSV</mark> HYKRYGEPYKLNMAC2NI	TTLS <mark>C</mark> DLTAETPYIYQNS <mark>Y</mark>
14 1.1.2.2.2.1.1.2.2.2.1.2.2.2.1.2.2.2.2.2	Tf_IL-22RA1	MDLDMWPLRVLLLLVWCSGSWCESCNMTKVYFE	SRNFHSTIRWDEVKIPGREVR	YSVKYNIYGERPRMMNGC2NI	SEPFCDLSSVMTDVR-SKY
Im	IP_IL-22RA1	MDLDMWLLRALILLVWCSGSWCNNCSMTKVYFE	SRNFHSRLHWDEVKMPGRKVR	YSTEVKYQVYGEQLKLMTGCHNI	
Image: Second	Mm_IL-22RA1	MKTLLTILTVGSLAAHTTVDTSGLLQH <mark>VKF</mark> Q	SSNFENILTWDGGP-ASTSDTV	YSVEYKKYGERKWLAKAGCORI	TQKFCNLTMETRNHTEFYY
110 120 130 140 130 140 170 180 <th></th> <th></th> <th></th> <th> FNII domin 2^{Cys71}</th> <th><u>Cys79</u></th>				FNII domin 2 ^{Cys71}	<u>Cys79</u>
0.1 1.1 2210 220 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20			140 150	160 170 180	
T_1_228A1 WARVENG-ELRIGTENE TLANTEGETALITICSTICIENES LEVIES L	01_11-22RA1	RAKVF <mark>V</mark> NG-STIGIT-TKFMPLRDTVLGPPIL		TGDIITQSKTGF-SRVTVLYILKI	HPEW-AAREMKNTTREFKI
C_11-22A1 HAVV3NG<-RELIGHTANKON/VGENV VALUETUS LLAVTLAGENOVSUD LIKESSIGE-LIVUTLATERNA ATLANEETISTATUTES LLAVTLAGENOM STREETISTATUT TUTTER ATLANEETISTATUTE ATLANEETI	Tr_IL-22RA1	WARVF <mark>V</mark> NGELH <mark>G</mark> CTKTR <mark>F</mark> T <mark>PL</mark> AH <mark>T</mark> TFG <mark>PP</mark> TL	<mark>S</mark> INSTA <mark>S</mark> ALHVHAIP <mark>P</mark> L <mark>GP</mark> NGES	IRDIVARSTEGL-VETQLLYTLEIT	DPQS- <mark>A</mark> VQVKTNTTGQFIL
91 1.228.1 UNKNOWS-CLEAR - LARGE AND UNKNOWS CLEAR - LARGE STILL	Cj_IL-22RA1	HAVVSVNGRELGRTRTRFNPMAHTILGPPTL	SKRTTGSTLIVNVTLPLGPNGVS	VADIIKESKDGP-LKTIIVYTLKIT	EPKW-ATLVHETHTAHFVI
10.1.1.228.1 YVW WODE - CLIED - NEW INSCREDUNG ITAGE STILLTPROOPHINE IS INSCREDUNG YUM THE ISSUE SCHERE CYCLERE STRUCTURE UNDER YOUR CONSTRUCTURE STATUSED THAT CONSTRUCTURE INFORMATION INSCREDUNG TO THE INSCREDUNG TO T	SS_IL-22RAI Tf TL-22RA1	CAQVFANSHSLGHT-ALFKPLRDTVLGPPNV YGKTMADGTCLGEF-MOFVPLEKTVLEAPKL	SVNLTTSSLKVTVTLPLGPDNKT SVITDRSTLTVTITTPMGPONRS	TREISCHERCOESGKSSVNYTVHL	HPEFEAGKVYRNTSGIVTI.
He_LI-228A1 AVYAR SAGGRAFTMEND SECURT TROPOND CENTRES IGNUTURETTE TRADEGIBLIZED FM Display and the security of the se	Ip_IL-22RA1	YVKVM <mark>V</mark> DELCIGEF-RNFIPSEQTSLEAPRL	SGITAG <mark>S</mark> SFTIILTT <mark>PMGP</mark> QKHT	IREISCWERCQYSGESPVN <mark>Y</mark> IVTL <mark>I</mark>	RPESEAGKVFQNTSGMITL
Mm_TL-22AA ARVXAQSAGOPVTINDRESS_DAT_TIDEDVICE/KVR5100L/UETTTVISED060L/LEETFM 1 210 220 200 </th <th>Hs_IL-22RA1</th> <th>ARVTA<mark>V</mark>SAGGRSATKMTDR<mark>F</mark>SSLQH<mark>T</mark>TLKPPDV</th> <th>TCISKVRSIQMIVHPTPT<mark>P</mark>IRAG</th> <th>DGHRLTLEDIFHDLF<mark>Y</mark>H<mark>L</mark>ELQ</th> <th>VNRT-YQMHLGGKQREYEF</th>	Hs_IL-22RA1	ARVTA <mark>V</mark> SAGGRSATKMTDR <mark>F</mark> SSLQH <mark>T</mark> TLKPPDV	TCISKVRSIQMIVHPTPT <mark>P</mark> IRAG	DGHRLTLEDIFHDLF <mark>Y</mark> H <mark>L</mark> ELQ	VNRT-YQMHLGGKQREYEF
210 220 230 240 111250111120111111111111111111111111111	Mm_IL-22RA1	AKVTA <mark>V</mark> SAGGPPVTKMTDR <mark>F</mark> SSLQH <mark>T</mark> TIK PP DV	TCIPKVRSIQMLVHPTLTPVLSE	DGHQLTLEEIFHDLF <mark>Y</mark> R <mark>L</mark> ELH a ragion	IVNHT-YQMHLEGKQREYEF
01.11-228.1 FLUNKTYCKYWYNESSE I HAGANTY CYNLER PERFURANCE 01.11-228.1 N-LINKTYCKYWYNESSE I HAGANTY CYNLER PERFURANCE 02.11-228.1 N-LINKTYCKYWYNESSE I HAGANTY CYNLER PERFURANCE 15.11-228.1 N-LINKTYCKYWYNESSE I HAGANTY CYNLER PERFURANCE 17.11-228.1 NILWSWYL CYNVYNESSE I HAGANTY CYNLER PERFURANCE 17.11-228.1 NILWSWYL CYNVYNESSE I HAGANTY CYNLER PERFURANCE 17.11-228.1 SILWWYL CHARTY HILGARTYS CO'NARCH STRING AND		210 220 230	240	260 270 280	290 300
0. LT-228.1 X-LINNITTC32VV MISPELG-IA&QNATGVTLPDPVUMPHLLSVAVVSOVATLLASVCVKVKVKVLDSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSSTSVEJVLISTC7-VNJSOTGVTNMSGTSTSVEJVLISTC7-VNJSOTGV		Cys195 Cys21	^{L6}	· · · · · · · · · · <u>·</u> · · · · · · · <u>·</u> · · <u> </u> ·	· · · · · · · · · · · · · · · <u> </u>
11 -2200. Phonesci and the tabulation and the tabulation and table for the tabulation and table for the table for table for table for the table for table for table for table for the table for t	01_11-22RA1	K-LKNNITYCGYVVYNKSPEIG-HASONATFCV	TLPEDPVVLWPWLLLSVAVVSGV	AIILAVSMCNYVKGGKTKTMPQTLV	HSSTPQ-KVQHYPDKNLI
ss_1-281 INLINSING CUTVY LPTREKYRANGESING OLDVILLEP WILLIGCLILGS LLEYVORMEYRK-KENNEDAKUTTS SUPPLATE st_1-281 SHIDNING CUVIE FILLING BENERGY CUTVALABANKWI EVITUSU VILLIILULLIUCQUVK-REKKILERAL ONLINGAL (INTERNET EVITUSU VILLIILULLIUCQUVK-REKKILERAL ONLINGAL (INTERNET EVITUSU VILLIILULLIUCQUVK-REKKILERAL ONLINGAL (INTERNET EVITUSU VILLIILULLIUCQUVK-REKKILERAL (INTERNET EVITUSU VILLIILULUCQUVK-REKKILERAL (INTERNET) m_1L-22RA1 SELVEVINE 310 320 330 340 350 360 370 380 390 440 01_1L-22RA1 SELVEVINE	Ci IL-22RAI	N-LKKOTKYCGHVIYAPSSEWGRPESESAPFCV	TLPANPLDF LPWLLF TAVF LLAL TLPDHPLGMLPWLSSVVAFLVIS	ITVTVALTCNYVKGVKKVRLPDSIA	RIFKDP-GPVLOADSSII
Tf_L-22RA1 SHIDMATESCGVULPELINEYTIKUQENTERGYTEVARKWEISTETCSALVULPLLITLEVUCQUVPT-REKKLEPTT-MESKTEPTT, TEYTREPENKEI Hg_LL-22RA1 SHIDMATESCGVULPELINEVTIKUQENTERGENTERGYTUVSUKAPTUVSUKUPGUVERKENLEPTTICHSKAPTUPGUKTEGENTER Mg_LL-22RA1 SGUTPDTEFLGTINICV TAKESAPYKEVKUPDENKTISTEGGVULPELINEKSUKUPCUVERKENKERVUCLUSSKAVTREPPAPHSINORVUTPGOLAFIGENUL Mg_LL-22RA1 SGUTPDTEFLGTINICV LISS 200 340 350 360 370 380 390 400 Ol_LIL-22RA1 SKUPVINGE LISS 200 VGCSD 01520-01C0-01C0-01C0-01C0-01C0-01C0-01C0-01	Ss_IL-22RA1	NLKNSNVE <mark>YCG</mark> YVV <mark>Y</mark> IPTREKYRNA <mark>SE</mark> SHT <mark>FC</mark> V	ALPGDTWLLFPWFLLLGCLLLGS	LLLPVVVCRH <mark>Y</mark> VRKKSNM <mark>P</mark> DA <mark>L</mark> K	LTTSNVPP <mark>P</mark> LWYPPEAIT
Tp_11-228.1 SHDENYTQG WALLFLIHGVIKOG BALT FØVALPADREN FPV1V95VAVFPLLTINSVILVAPPLUTINSVILVAPPLUTINSVILVAPPLUTINSVILVAPPLUSENVORVITTEGELAFTOREN. Mm_11-228.1 LGUTPDTELIGS ITTILTPTIAKEGAPY EVKTLEDERWATSFSGAAL ISKET VAULUSESKIVTREPPPENSENVORVITTEGELAFTOREN. Mm_11-228.1 LGUTPDTELIGS ITTILTP	Tf_IL-22RA1	SH <mark>L</mark> DMNTE <mark>YCG</mark> VVL <mark>Y</mark> ELTHPYIKLQ <mark>SE</mark> NTS <mark>FC</mark> Q	T <mark>LP</mark> VADKPWISIFICSALVVLFL	LIILPLIVCHQYVT-RKRKL <mark>P</mark> ET <mark>L</mark> I	-MSKNT-T <mark>P</mark> YFNPDPNVK <mark>I</mark>
m_11-22R1 LGEPTOTEFLGITTITE	Ip_IL-22RA1	SHLDKNTQYCGVALYELTHPGVKRQSENTTFCV	ALPAADKPWIPVIVVSVLVAFFL	LITMSVILCQQHVK-RKGNLPKALQ	NMLMQP-TPNFNPDPKVEI
Close Close <th< th=""><th>Mm_IL-22RA1</th><th>LGLTPDTEFLGSITILTPILSKESAPYVC</th><th>RVKTLPDRTWAYSFSGAVLFSMG</th><th>FLVGLLCYLG<mark>Y</mark>KYITKPPVP<mark>P</mark>NS<mark>L</mark>N</th><th>VQRVLTFQPLRFIQEHVLI</th></th<>	Mm_IL-22RA1	LGLTPDTEFLGSITILTPILSKESAPYVC	RVKTLPDRTWAYSFSGAVLFSMG	FLVGLLCYLG <mark>Y</mark> KYITKPPVP <mark>P</mark> NS <mark>L</mark> N	VQRVLTFQPLRFIQEHVLI
310 320 330 340 350 360 370 380 390 400 01_IL-22RA1 SKUVENNES DOLGAKLEVPS WOGKSDGISS NALPONESALE (AADAQVEPE N		Cys2	17		
01_II-22RA1 SKVEVNIPS			340 350	360 370 380	
Tr_1L-22RA1 SELVVYUS ————————————————————————————————————	01_11-22RA1	SKVEVNHP <mark>S</mark> DCIDQAKLHVPSV	GGYSPQRISSNLFQGSANSS	VGPNLAETTAQ <mark>S</mark> AEI <mark>Y</mark> GA <mark>V</mark> AAQ	VEPEKSDDFYQPS
Ci_II-22RAI StXVWSLPNDOPTYAAIOPKEPAVKSDYSDOIFWIOSKRESTGTNILFPTINGLDVSGSSDTYGAVAAQMPAEBAEDRETCTVS Ss_II-22RAI STXKVFHYVGYSSGUKKTSGSGSSSDOCFSSIAGPRACDTMSQQOPFESHSNSGSGSSDTYGAVAAQMPAEBAEDRETCTVS JL-22RAI TTKKVFNESPWNTIKPELASSDMPEKIKAVHITVGAAQOYHDODMHCHSYSTMDQAVASKOSAE_CTSSMVVGVAPGDERELSSCAAD JL-122RAI NAXVYABSPWNTIKPELASSDMPEKIKAVHITVGAQOYEDODMHCHSYSTMDQAVASKOSAE_CTSSMVVGVAPGPNERELSSCAAD Mm_II-22RAI NAXVYABSPWNTIKPELASSDMPEKIKAVHITVGAQOYEDDVMHCHSYSTMDQAVASKOSAE_CTSSMVVGVAPGPSYAPQVASDAK Mm_II-22RAI NALL-22RAI PVDLSGPSSLQPUQYSQITVSGPREPPGAVR@SLSDLTYVGQSDVSILOPSNVPPQQTLSPLSYAPKAVPEVQPPSYAPQVASDAK 410 420 430 440 450 460 470 480 440 450 500 	Tr_IL-22RA1	SELVVYVG <mark>S</mark> AKRETAAIHLKHSVPSASL			DPTEDOGATKNPGRS
ss_11-22RAI TINKVPNEPWNITKEEIASDDPKKIKANNIYQUSSIAO SJAQVID-UNGQUSPPLINNSJQSIATSSWVVQUARDUVELDLAHMANSKAN Tr_LI-22RAI TINKVPNEPWNITKEEIASDDPKKIKANNIYQUSSIAO SJAQVID-ANGQASCITSSWVVQUAPQNRQQSASCITSSWVVQUAPQNRELISCAND Ip_LI-22RAI NVXVIAEPWNITKEEIASDDPKKIKANNIYQUSPREPAQPQRHSISSTIYLGQPDISILGPNVPPQISISSWVPQFUPNREELSCAND Mm_LI-22RAI PVIDISGPSLQQVIYGGIRVGOFREPAQPGHSISSTIYLGQDISILGPNVPQQUISPSYPPGILSIXANAAPEVGPDSYAQVIPEAQ Mm_LI-22RAI PVIDISGPSLQQVIYGGIRVGOFREPAQPGHSISSLIYVGQSDVSILQPNVPAQQTISPSYAPKAVPEVGPSYAQVASDAK 410 420 430 440 450 660 470 480 490 500 			<u></u>		
1p IL-22RA1 NAVKYARS PNNTSKSELTLEVULKSTRTVINEG-VAP OV DYCEKOWEGENTNODAYPASIOSAESCTS 21MV VXGMEPFNEELTSCAND Ms_LL-22RA1 1p PVFDLSGP SLOPSVQYSQIRVSGPREPEGAPGAPGRISLSE	Cj_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS	GDYSPQDIPWQGSRESFGTN	LFHPTLNGLDVSGQSSDTYGAVAAQ	MPAEEAEDRETCTVS
Hs_IL-22RA1 PVFDLSGPSSLAQPVQYSQIRVSGPREPGAVRQSLSETYLCGPDISILOPSNVPPPQQTLSPLSYAPNAAPEVGPPSYAPQVTPEAQ Mm_IL-22RA1 PVLDLSGPSSLQPVQYSQIRVSGPREPPGAVRQSLSDLTYVGQSDVSILQPTNVPQQTLSPPSYAPRAVEPVQPPSYAPQVASDAK 410 420 430 440 450 460 470 480 490 500 01_IL-22RA1	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPNNTIKPELASSDMPEKIKAVNIT	GDYSPODIPWQGSRESFGTN GSYSPODGPSSIAQPRHCDTYMG VGYAAODYHDODWHCHSYSN	LFHPTLNGLDVSGQSSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVQ ERVAPVRDOSEASCTSYSMVVQV	MPAEEAEDRETCTVS VANEGVKEECHRHANSENN
Mm_IL-22RA1 PVLDLSGPSSLGOF 10YSQVVVSGPREPEAVWRGSLSDTYVVGSDVSILQPTNVPAQQTLSPPSYAPRAPEVQPPSYAPQVASDAK 410 420 430 440 450 460 470 480 490 500 01_IL-22RA1 TEESAPNRSLFSLRSKRSRDKGGALQFTDM-EASGNNQLVDFPVFVDRNDNGQVLPSSLEPFQCDDDAGSLVNPETKPLLSPLIQDTMAQ 1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNE <mark>S</mark> PWNTIKPELASSDMPEKIKAVNIT NAVKVYAE <mark>S</mark> PWNTSKSELTLPKVLKETRTVNIE	GDYSPQDIPWQGSRESFGTN GSYSPQDGPSSIAQPRHCDTYMG VGYAAQDYHDQDWHCHSYSN G-YAPQDYQEKDWHCHSYTN	LFHPTLNGLDVSG <mark>Q</mark> SSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRDQSEASCTSYSMVVGV DQAVPASNQSAE <mark>S</mark> CTSYSMVVVG	MPAEEAEDRETCTVS JVANEGVKEECHRHANSENN VAPQDREELSSCAAD MEPPNREELTSCAND
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$ \begin{array}{r} \mathbf{s}_{1} \mathbf{L} - 22RA1 & \mathbf{INSPWSSESSVHKP} \mathbf{s}_{C} \mathbf{Q} \mathbf{G} \mathbf{V}_{U} \mathbf{S} \mathbf{S} \mathbf{G} \mathbf{A} \mathbf{G} \mathbf{V}_{U} \mathbf{A} \mathbf{S} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{S} \mathbf{S} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{S} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{S} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{G} \mathbf{G} G$	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Hs_IL-22RA1 Mm_IL-22RA1 O1_IL-22RA1 Tr_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTSKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPP 410 420 430 TEESAPNHSLLFSLRRSKRSRDKGGALQ NKLNSSLEECGSDHAITSVIASHTGSPLSV	GDYSPODIPWQGSRESFGTN GSYSPODGPSSIAQPRHCDTYMG VGYAAQDYHDQDWHCHSYSN G-YAPQDYQEKDWHCHSYSN GAVQRDSEITYLGQPDIS GAVWRQSLSDLTYVGQSDVS 440 450 	LFHPTINGLDVSGCSSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRDQSEASCTSYSMVVVQ DQAVPASNQSAESCTSYSMVVVQ ILQPSNVPPPQILSPLSYAPNAAPE ILQPTNVPAQQTLSPPSYAPKAVPE 460 470 480 	MPAE EAEDRETCTVS NPAE
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Mm_IL-22RA1 ALFYSPQQGMKTRPATYDPQDILDSCPASYAVCVEDSGKDSTPGILSTPKYLKTKGQLQEDTLVRSCLPGDLSLQKVTSLGEGETQ 510 520 530 540 550 560 570 580 590 600 01_IL-22RA1 ESLQSIE-SSEGLDSGCEISTVMTPTSPYCNTHTPOLSYFQRCQTTCTIFESRYKQNMME	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Hs_IL-22RA1 Mm_IL-22RA1 O1_IL-22RA1 Tr_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Tb_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTSKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPA PVLDLSGPSSLPQPIQYSQVVVSGPREPP 410 420 430 TEESAPNHSLLFSLRRSKRSRDKGGALQ NKLNSSLEECGSDHAITSVIASHTGSPLSV LVTGRDSRGENGNSPQSMSPRD-APTPH INSPWSSESSVHKPSCFQGVPVLFSHGAPPEPN SGIGDSISPGLSSCTEDLFKVIRHAEPDEDLG	GDYSPODIPWQGSRESFGTN GSYSPODGPSSIAQPRHCDTYMG VGYAAQDYHDQDWHCHSYSN GAPQRHSLSEITYLGQPDIS GAVWRQSLSEITYLGQPDIS GAVWRQSLSDLTYVGQSDVS 440 450 	LFHPTINGLDVSGCSSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRDQSEASCTSYSMVVVQ ILQPSNVPPPQILSPLSYAPNAPE 460 470 480 	MPAE Selection MPAE Selection VANEGVKEECHRHANSENN VAPQ DREELSSCAAD MEPP NREPLISCAND VGPP SYAPQVTPEAQ VQPP SYAPQVTPEAQ VQPP SYAPQVASDAK 0 490 500 I
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Ss_IL-22RA1 EEEEEGEEGGDERGSEFFLGGWVVQILG 608 70.7 31.4 Cys128-217 Tf_IL-22RA1 AEPEEDIEDSPSDLEEIFLGGWVQIQG 579 68.5 23.0 Medaka Ip_IL-22RA1 AEPEEDVDESPSELEAIFLGGWNVQQG 581 67.1 21.8 Cys69-77 Hs_IL-22RA1 SPAPETSDLEQPTELDSLFRGLALTVQWES 574 64.6 16.8 Cys195-216 Mm_IL-22RA1 CPSAAASELEQSTELDSLFKGLALTVQWES 581 65.4 16.2 Cys195-216	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Tr_IL-22RA1 Tr_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Tr_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STARPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTSKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPA PVLDLSGPSSLAQPVQYSQIRVSGPREPA NLDSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA NLNSSLEECGSDHAITSVIASHTGSPLSV TEESAPNHSLLFSLRSKRSRCKGGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV IVTGRDSRGENGNSPQSMSPRD-APTPH INSPWSSESSVHKPSCFQGVPVLFSHGAPPEPN SGIGDSISPGLSSCTEDDLFQILPNAEPEEDLG FPFYAPQAISKVQPSSYAPQATPDSWPPSYGVCI ALFYSPQQGMKTRPATYDPQDILDSCPASYAVC 510 520 530 ESLQSIE-SSEGLDSGCEISTVNTPTSPYCNTH PSLSSFL-ILDGAESECDDGIVTSPTQTYNSH STVQSFD-HSEWSDSGCDDSSVTTPTLEFCNTH LSDLVTTGETEWLDPGTGREERTIYTFISPMCTH AGERTIL-LTNLDSADNSDWTDNELSSDHRNNY EAKSLHQ-PLGICTDRTSDPNVLHSGEEGTPQY RPKSLPS-PLGFCTDRGPDLHTLRSEEPETPRY 610 620 630 AI	GDYSPODIPWQGSRESFGTN GSYSPODGPSSIAQPRHCDTYMG VGYAAQDYHDQDWHCHSYSN G-YAPQDYQEKDWHCHSYSN GAPQRHSLSEITYLGQPDIS GAVWRQSLSDLTYVGQSDVS 440 450 	LFHPTINGLDVSGQSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRDQSEASCTSYSMVVVQ DQAVPASNQSAESCTSYSMVVVQ LQPSNVPPQILSPLSYAPNAPE 460 470 480 	MPAE EAEDRETCTVS MPAE EAEDRETCTVS NATE EAEDRETCTVS WANEGVKEECHRHANSENN VVAPQ VAPQ DREELSSCAND SWGPP SYAPQVTPEAQ VVQPP SYAPQVASDAK 0 490 500
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Ip_ID_22RA1ReferenceSolutionSol	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Tr_IL-22RA1 Tr_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 Tf_IL-22RA1 If_IL-22RA1 If_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPA PVLDLSGPSSLAQPVQYSQIRVSGPREPA NLDSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA SGIGSISPGLSSCTEDLFXIRASFDSGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV TTESAPNHSLLFSLRSKRSROKGGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV IVTGRDSRGENGNSPQSMSPRD-APTPH INSPWSSESSVHKPSCFQGVPVLFSHGAPPEPN SGIGDSISPGLSSCTEDLFXVIRHAEPDEDLGI SGLGGSISPGLSSCTEDDLFQILPNAEPEEDLGI FPFYAPQAISKVQPSSYAPQATPDSWPPSYGVCI ALFYSPQQGMKTRPATYDPQDILDSCPASYAVC 510 520 530 ESLQSIE-SSEGLDSGCEISTVNTPTSPYCNTH STVQSFD-HSEWSDSGCDDSSVTTPTLEFCNTH LSDLVTTGETEWLDPGTGREERTIYTFISPMCTH AGERTIL-LTNLDSADNSDWTDNDSMPEYRKVY VKERTLL-LTDLVSMGDSDWTDNELSSDHRNNY EAKSLHQ-PLGICTDRTSDPNVLHSGEEGTPQY RPKSLPS-PLGFCTDRGPDLHTLRSEPETPRY 610 620 630 AI 	GD YSP OD IPWQGSRESFGTN GS YSP OD GP SSIAQPRHCD TYMG VGYAAQDYHDQDWHCHSYSN G-YAP QD YQEKDWHCHSYSN GAPQRHSLSE	LFHPTINGLDVSGQSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVQ ERVAPVRQSEASCTSYSMVVQ DQAVPASNQSAESCTSYSMVVQ DQAVPASNQSAESCTSYSMVVQ LQPSNVPPQILSPLSYAPNAAPE 460 470 480 470 QUVLPSLSPPYAPKAVPE 460 470 QLVPSVPPQLSPLSYAPNAAPE 1LQPTNVPAQTLSPPSYAPKAVPE 460 470 QLVLPSLEFQFQTDCDDAGSLVMPE NLVLPFPSFQFQSSTATLQR	MPAE EAEDRETCTVS MPAE EAEDRETCTVS NATE EAEDRETCTVS WANEGVKEECHRHANSENN VVAPQ VAPQ DREELSSCAND SWEPP NREELTSCAND WQPP SVAPQVASDAK 0 490 500
Mm_IL-22RA1 CPSAAASELEQSTELDSLFKGLALTVQWES 581 65.4 16.2	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Tr_IL-22RA1 Tr_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Cj_IL-22RA1 Tf_IL-22RA1 If_IL-22RA1 If_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Cj_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTSKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPA PVLDLSGPSSLAQPVQYSQIRVSGPREPA NLDSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA SGIGSISPGLSSCTEDLFXIRASFGSALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV TTESAPNHSLLFSLRSKRSROKGGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV IVTGRDSRGENGNSPQSMSPRD-APTPH INSPWSSESSVHKPSCFQGVPVLFSHGAPPEPN SGIGDSISPGLSSCTEDLFXVIRHAEPDEDLG SGLGGSISPGLSSCTEDLFXVIRHAEPDEDLG SGLGGSISPGLSSCTEDLFXVIRHAEPDEDLG SGLGGSISPGLSSCTEDDLFQILPNAEPEEDLG FPFYAPQAISKVQPSSYAPQATPDSWPPSYGVCI ALFYSPQQGMKTRPATYDPQDILDSCPASYAVC 510 520 530 ESLQSIE-SSEGLDSGCEISTVNTPTSPYCNTH STVQSFD-HSEWSDSGCDDSVTTPTLEFCNTH LSDLVTTGETEWLDPGTGREERTIYTFISPMCTH AGERTIL-LTNLDSADNSDWTDNDSMPEYRKVY VKERTLL-LTDLVSMGDSDWTDNELSSDHRNNY EAKSLHQ-PLGICTDRTSDPNVLHSGEEGTPQY RPKSLPS-PLGFCTDRGPDLHTLRSEPETPRY 610 620 630 	GD YSP OD IPWQGSRESFGTN GS YSP OD GP SSIAQPRHCD TYMG VGYAAQDYHDQDWHCHSYSN G-YAP QD YQE	LFHPTINGLDVSGQSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRQSEASCTSYSMVVVQ DQAVPASNQSAESCTSYSMVVVQ LQPSNVPPQILSPLSYAPNAAPE ILQPTNVPAQQTLSPPSYAPKAVPE 460 470 480 	MPAE EAEDRETCTVS MPAE EAEDRETCTVS NATE EAEDRETCTVS WANEGVKEECHRHANSENN VVAPQ VAPQ DREELSSCAND SWEPP NREELTSCAND WQPP SVAPQVASDAK 0 490 500
	Cj_IL-22RA1 Ss_IL-22RA1 Tf_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Tr_IL-22RA1 Tr_IL-22RA1 Cj_IL-22RA1 Ss_IL-22RA1 Ip_IL-22RA1 Ip_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Cj_IL-22RA1 If_IL-22RA1 If_IL-22RA1 If_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Mm_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1 Ss_IL-22RA1	SKVMVSLPNDQTPYAAIQFKPKEPAVKS STAKPYHYPVGFSYGDLKTGKLQMGSKFTSSGS TTMKVFNESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKPELASSDMPEKIKAVNIT NAVKVYAESPWNTIKSELTLPKVLKETRTVNIE PVFDLSGPSSLAQPVQYSQIRVSGPREPA PVLDLSGPSSLAQPVQYSQIRVSGPREPA NLDSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA VLDLSGPSSLAQPVQYSQIRVSGPREPA SGIGDSISPGLSSCTEDLFXIRASFDSGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV TTESAPNHSLLFSLRSKRSROKGGALQI NKLNSSLEECGSDHAITSVIASHTGSPLSV IVTGRDSRGENGNSPQSMSPRD-APTPH INSPWSSESSVHKPSCFQGVPVLFSHGAPPEPN SGIGDSISPGLSSCTEDLFKVIRHAEFDEDLG SGLGGSISPGLSSCTEDLFKVIRHAEFDEDLG FPFYAPQAISKVQPSSYAPQATPDSWPPSYGVCI ALFYSPQQGMKTRPATYDPQDILDSCPASYAVC 510 520 530 ESLQSIE-SSEGLDSGCEISTVNTPTSPYCNTH STVQSFD-HSEWSDSGCDDSSVTTPTLEFCNTH LSDLVTTGETEWLDPGTGREERTIYTFISPCTH AGERTIL-LTNLDSADNSDWTDNDSMPEYRKVY VKERTLL-LTDLVSMGDSDWTDNELSSDHRNNY EAKSLHQ-PLGICTDRTSDPNVLHSGEEGTPQY RPKSLPS-PLGFCTDRGPDLHTLRSEPETPRY 610 620 630 AI 	GD YSP OD IPWQGSRESFGTN GS YSP OD GP SSIAQPRHCD TYMG VGYAAQDYHDQDWHCHSYSN G-YAP QD YQE	LFHPTINGLDVSGQSDTYGAVAAQ QQGPPPEHSNNSTQSSTNYSMVVVQ ERVAPVRQSEASCTSYSMVVVQ DQAVPASNQSAESCTSYSMVVVQ LQPSNVPPQILSPLSYAPNAPE 1LQPTNVPAQQTLSPPSYAPKAVPE 460 470 480 	MPAE EAEDRETCTVS MPAE EAEDRETCTVS NATE EAEDRETCTVS WANEGVKEECHRHANSENN VVAPQ VAPQ DREELSSCAND SWEPP NREELTSCAND WQPP SVAPQVASDAK 0 490 500

Fig. S1. Continued.

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O1_IL-22BP	<mark>MTPL</mark> LLAAV	LGNLT-ICILO	<u> 9</u> 9ELLAP <mark>P</mark>	TQ <mark>V</mark> RFNS	STDYR <mark>N</mark> V	MI <mark>W</mark> TP-PTNQ	r-slq <mark>y</mark> h <mark>vq</mark> wi	KI <mark>YG</mark> EQE <mark>W</mark> LNV	/AS <mark>C</mark> Q <mark>G</mark> IQEHQ <mark>C</mark>	DLSRVTS
Sc_IL-22BP	<mark>MTRL</mark> LLGAV	<mark>LLGNLG-VCVT</mark> E	EQVPEKLAP <mark>P</mark>	TQ <mark>V</mark> KFDS	SVDYK <mark>N</mark> I	LR <mark>W</mark> TP-PTNS:	r-slq <mark>y</mark> yi <mark>q</mark> wi	KI <mark>YG</mark> EAQ <mark>W</mark> LDV	/DG <mark>C</mark> Q <mark>G</mark> IQKHQ <mark>C</mark>	DLSAVTS
Tr_IL-22BP	<mark>MSRL</mark> LLLLL	<mark>L</mark> PGTLGTLGGTF	RKDLAMLAP <mark>P</mark>	TN <mark>V</mark> RFDS	SVDYK <mark>N</mark> I	LC <mark>W</mark> SP-PANSS	S-SLL <mark>Y</mark> Y <mark>VQ</mark> WI	KI <mark>YG</mark> DPQ <mark>W</mark> LDV	/SS <mark>C</mark> Q <mark>G</mark> TLKLQ <mark>C</mark>	DLSNVTS
Ss_IL-22BP	<mark>MASL</mark> LIHTL	<mark>llcysslsrc</mark> se	ESKEYPLDVFA <mark>P</mark>	HE <mark>V</mark> KFHS	SLDYR <mark>N</mark> V	LH <mark>W</mark> KQ-HANST	INDQQ <mark>Y</mark> F <mark>VQ</mark> WI	KV <mark>YG</mark> EKQ <mark>W</mark> TN#	AKE <mark>C</mark> H <mark>G</mark> ISRLL <mark>C</mark>	DLSKE <mark>TS</mark>
Om_IL-22BP	<mark>MASL</mark> LIPTL	<mark>llcysslsrc</mark> se	ESKEYPLDVFA <mark>P</mark>	QE <mark>V</mark> KFHS	SLDYR <mark>N</mark> V	LH <mark>W</mark> KQ-HANST	INDQQ <mark>Y</mark> F <mark>VQ</mark> WI	KV <mark>YG</mark> EKL <mark>W</mark> TNA	AKE <mark>C</mark> H <mark>G</mark> ISRLL <mark>C</mark>	DLSKE <mark>TS</mark>
E1_IL-22BP	<mark>MEFL</mark> LILAL	<mark>LLFSITRSCC</mark> LE	EGNGTHSDVLA <mark>P</mark>	QE <mark>V</mark> RFVS	SLDYK <mark>N</mark> I	LH <mark>W</mark> KQ-HANS	I'NNQQ <mark>Y</mark> Y <mark>VQ</mark> WI	KV <mark>YG</mark> KKH <mark>W</mark> TKI	AK <mark>C</mark> Q <mark>G</mark> IRRLH <mark>C</mark>	DLSQE <mark>TS</mark>
Am_IL-22BP	<mark>M</mark> FVPATLLL	LCDLVLLSCAN	ISTLPFLDDLA <mark>P</mark>	lk <mark>vef</mark> hs	LNFR <mark>N</mark> V	<mark>L</mark> H <mark>W</mark> RQ-HPGAI	PEDLQ <mark>Y</mark> V <mark>VQ</mark> YI	KV <mark>YG</mark> EKQ <mark>W</mark> SD#	AKL <mark>C</mark> QAIHDFQ <mark>C</mark>	DLSQE <mark>TS</mark>
Tf_IL-22BP	<mark>MCIL</mark> STLL	LLWNVALFCRAF	EGDVQLLDYTA <mark>P</mark>	FQ <mark>VE</mark> FHS	SVNFR <mark>N</mark> V	<mark>L</mark> H <mark>W</mark> KH-HPEAI	PGGLR <mark>Y</mark> F <mark>VQ</mark> YI	KV <mark>YG</mark> DKQ <mark>W</mark> IV(CES <mark>C</mark> QATHKLQ <mark>C</mark>	DLSQE <mark>TS</mark>
Ip_IL-22BP	<mark>M</mark> FVLSTLL	LUNDLALVCGAN	ISTVQLQDDTA <mark>P</mark>	FQ <mark>VE</mark> FHS	SVNFR <mark>N</mark> V	LH <mark>W</mark> KH-HPEA <i>I</i>	ADDLQ <mark>Y</mark> F <mark>VQ</mark> YI	<mark>KVYG</mark> DKE <mark>W</mark> SVO	CEP <mark>C</mark> QAIHEPQ <mark>C</mark>	DLSQE <mark>TS</mark>
Cc_IL-22BP	<mark>MYAL</mark> TGRQSLE	<mark>L</mark> FFAIILLCWAI	DCSPSLQDDLA <mark>P</mark>	LE <mark>V</mark> KFHS	<mark>S</mark> LDFR <mark>N</mark> V	<mark>L</mark> H <mark>W</mark> KH-PQKAV	VKNQT <mark>Y</mark> F <mark>VQ</mark> YI	<mark>KIYG</mark> DKE <mark>W</mark> TNS	SEH <mark>C</mark> Q <mark>G</mark> IRLLE <mark>C</mark>	DLSQA <mark>TS</mark>
Dr_IL-22BP	MPFNMLTLTGHQCLD	IVFAISLLCWAR	<u>EC</u> SPTQQKEMA <mark>P</mark>	TE <mark>VQ</mark> FQS	LDFR <mark>N</mark> V	LH <mark>W</mark> KH-QHKA	FKNLK <mark>Y</mark> F <mark>VQ</mark> HI	<mark>KIH</mark> GDKE <mark>W</mark> SNS	SKH <mark>C</mark> Q <mark>G</mark> IRTLQ <mark>C</mark>	DLTQE <mark>TS</mark>
Hs_IL-22BP	MMPKHCFL	GFLISFFLTGVA	<u>AG</u> TQSTHESLK <mark>P</mark>	QR <mark>VQ</mark> FQS	RNFH <mark>N</mark> I	LQ <mark>W</mark> QPGRALT(GNSSV <mark>Y</mark> F <mark>VQ</mark> YI	<mark>KIYG</mark> QRQ <mark>W</mark> KNH	KED <mark>CWG</mark> TQELS <mark>C</mark>	DLTSE <mark>TS</mark>
Mm_IL-22BP	MMPKHCLL	GLLI-ILLSSA	TEIQPARVSLT <mark>P</mark>	QK <mark>V</mark> RFQS	RNFH <mark>N</mark> I	LH <mark>W</mark> QAGSSLPS	SNNSI <mark>Y</mark> F <mark>VQ</mark> YI	<mark>KMYG</mark> QSQ <mark>W</mark> EDH	(VD <mark>C</mark> WGTTALF <mark>C</mark>	<mark>dl</mark> tne <mark>t</mark> l
				· · · · · ·				FNIII domai	n 2	/\$86
	110	120	130	140	150	160	170	180	190	200
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OI_IL-22BP	DTSEWYYARVHASSA	ASGSRSAWTLS	PRESPREETKIS	APVLKLS	SISKRNH	IQVHVKPPRVI	LLRKMRSN	<mark>L</mark> LF.F	TEVINAGGEE-	REFDMDC
SC_IL-22BP	DPREWYYARVHASSL	PS-SKSAWALS	PRESPRWDTKIS		IVTEQG-		LVRKMHSS	<mark>L</mark> QYF	(IYLIHTSGEE-	EVFEMDC
Tr_IL-22BP		TS-SRSDWSLSP			VTEKR-		HIRKMERR	<mark>L</mark> QYI		ELFIVDC
SS_IL-22BP	DPREWIIARVHAAHS		ARE NPRWETSVS		IVTE-KG		PHRRPNGSWI	SVRRLQRMSF1		ETFEMEG
UM_IL-22BP			ARE NPRWETSVS		IVIE-KG		PHRRSNGSW1	SVRRLQRMSF1	THEMOSDVER-	ETFEMEG
EI_IL-22BP	DDDEWYYADUOATSE						ARKLINGSWI	SMRRLQRMSI		NILLEILS
MM_IL-22BP	DDDOWYYADVOACS			PPQIKLN	NTE-OC		LOGKKÖNKI	AVIALQALIF		TUETNG
11_1L-22BP				DDNTVTN			PUNGQRNSRV	SVIKLLKLIFF		
	DDDEWYYADUDGEGG				₩1 <u>Q</u> -QG		PEQGQKNSKI			EVVETDS
CC_IL-22BP	DDDEWYYADUDGI GD			PPQIAVI			PLRGQRGSRI			EVILIDS
DI_IL-22BP	DTOEDVYCDUDAASA	CCVCFWCMTT				TTUTTUNDNT	DVDVORERNU	STEDVVET I VI	VETTNNGTEK_	FORUVEC
Mm TL=22BP		CPUSAWTPTI				T.P.VT.T.P.D.FT.I	NPNOSCKNA	SMETYVCLUVI	WETINNSLER-	FORAVEC
MM_10 220F	DI IMIII GRUMINCH	isk n <mark>o</mark> a <mark>n</mark> ikii	Te II WWEIKED		INVIA AD		n <mark>n</mark> ngoonna.	5M21116 <mark>0</mark> 711	WEIIMADD <mark>D</mark> A I	LQIAILG
	210	220	230	240						
		vs194	Cvs2	15 . An	nino acids	(aa) Similaritie	es (%) Identitie	s (%) Disu	fide bonds	
O1_IL-22BP	CSNRLTLPKL KHKAK	FCIQAQTIILPO	DIKS <mark>SARS</mark> HEK <mark>C</mark>	ITAP	219			11		
Sc_IL-22BP	C SNKVTLNE <mark>L</mark> KHKGK	YCLQAQTMIPLQ	AKT <mark>SARGSVK</mark> C	VTML	219	72.2	65.6	nur	nan	
Tr_IL-22BP	CPGKLTL-H <mark>L</mark> KHKQK	YCIQ <mark>A</mark> QTRIFLQ	AKI <mark>SARS</mark> PPTC	VTTF	219	74.3	54.9	Cj	/s78-86	
Ss_IL-22BP	CAKQLL <mark>I</mark> SDLSPGTT	YCLTAESRLHLI	LDRR <mark>STRS</mark> PRAC	ITTL	231	75.4	38.7	C	/s206-227	
Om_IL-22BP	CAKQLL <mark>I</mark> SDLSPRTT	YCLTAESRLHLI	LGRR <mark>S</mark> T <mark>RS</mark> PRAC	ITTL	231	75.0	38.4	Me	daka	
E1_IL-22BP	CAKQFLISDLSRRTT	YCLQ <mark>A</mark> ESRLHLI	LDRR <mark>S</mark> PL <mark>S</mark> PKAC	VTTL	231	70.6	34.6	IVIE	-72.00	
Am_IL-22BP	CSKKVL <mark>I</mark> KALSPKTA	YCLQ <mark>A</mark> VTVTPPE	GRT <mark>S</mark> T <mark>RS</mark> PSTC	ITTA	232	72.8	36.8	C)	1572-80	
Tf_IL-22BP	CQRKLL <mark>I</mark> EH <mark>L</mark> YPQTT	YCIQAVTVMPLS	SGIT <mark>S</mark> P <mark>RS</mark> PES <mark>C</mark>	ISTL	229	69.6	34.6	Cj	15194-215	
Ip_IL-22BP	CPKKVL <mark>I</mark> EHLSPQTT	YCVQ <mark>A</mark> VTVKPLS	SGLT <mark>S</mark> S <mark>RS</mark> PKS <mark>C</mark>	ISTL	229	72.6	33.9			
Cc_IL-22BP	C SKELV <mark>I</mark> EG <mark>L</mark> RPKTT	YCLQAMSVTPRS	GHK <mark>SLRS</mark> PSTC	ISTH	233	70.1	36.2			
Dr_IL-22BP	CSKELV <mark>I</mark> EA <mark>L</mark> RPKTT	YCLQALSVTPRS	SGRI <mark>S</mark> S <mark>RS</mark> PRTC	ITTH	238	71.2	36.6			
Hs_IL-22BP	AHRAVE <mark>I</mark> EALTPHSS	YCVV <mark>A</mark> EIYQPMI	LDRR <mark>SQRS</mark> EER <mark>C</mark>	VEIP	231	66.7	29.9			
Mm_IL-22BP	TQRAVE <mark>I</mark> EG <mark>L</mark> IPHSS	YCVVAEMYQPME	DRR <mark>SPRS</mark> KERC	VHIP	230	70.3	28.7			
—	– – c	ys206	Cys2	27						

Fig. S1. Continued.



Fig. S2. 3D structures of IL-22 (**A**), IL-22RA1 (**B**), and IL-22BP (**C**) in human, yellow catfish, and medaka predicted using SWISS-MODEL. In the predicted 3D structures, the alpha helices A to F in IL-22 and the FNIII domain in IL-22RA1 and IL-22BP are shown. GenBank accession numbers of all nucleotide sequences are listed in **Table S2**.



Fig. S3. Schematic representation of synteny for *il22* (**A**), *il22ra1* (**B**), and *il22bp* (**C**) in various species. *il22*, *il22ra1*, and *il22bp* highlighted by the black boxes. The dark gray and light gray boxes represent high and low gene homology, respectively.



Fig. S4. Negative control (sense probe) of *in situ* hybridization (ISH) in medaka *il22* and *il22bp* mRNA localization. *il22* (**A**) and *il22bp* (**B**) expression in adult medaka gill; *il22* (**C**) *and il22bp* (**D**) expression in adult medaka intestine; *il22* (**E**) and *il22bp* (**F**) expression in larval medaka intestine. Scale bar: 100 μ m. After 4% (v/v) paraformaldehyde fixation, the gills and intestines of healthy adult medaka and the whole body of the larvae were embedded in paraffin. DIG-labeled anti-sense RNA-probes were used for detection. After hybridization, color development was performed using AP-labeled anti-DIG IgG (sheep) and NBT/BCIP solution.



Fig. S5. crRNA regions, mutated sequences, and mutation efficiency of medaka *il22*. (**A**) crRNA regions in medaka *il22*. crRNA designed in exon 1 of *il22*. Mutated nucleotide (**B**) and amino acid sequences (**C**) in WT and KO strains. Mutated regions in filial generation zero (F0) founder and F3 homo individuals confirmed by sequencing. The asterisk (*) indicates the stop codon. Mutant strains contained premature stop codons in the amino acid sequences introduced by frameshift mutations. (**D**) Efficiency of mutation determined using crRNA and the heteroduplex mobility assay (HMA). (**E**) HMA for mutated medaka; a 4 bp deletion shown in a 12% agarose gel.



Fig. S6. Morphological comparison of WT and IL-22-KO medaka (-4). No morphological differences were observed between the KO strain (4 bp deletion strain) and WT medaka when 14 days post-fertilization larvae (**A**) and 3-month adult medaka (**B**) were observed.



Fig. S7. Gene expression analyses of *il22* (A), *il22ra1* (B), and *il22bp* (C) in WT and KO medaka. Significant *il22* and *il22bp* downregulation was observed in KO (4 bp-deficient) medaka larvae compared with that in WT. Comparisons were performed on healthy medaka. The expression scale shows relative values when the expression in the WT group was set to 1. ***; P < 0.001, **; P < 0.01, *; P < 0.05 (two-tailed Student's *t*-test). Data shown were obtained from a single experiment (n = 7).



Fig. S8. Histological analysis of dextran sulfate sodium (DSS)-induced inflammation in WT and IL-22-KO medaka larvae. Samples of the anterior intestinal tissue sections from WT and IL-22-KO medaka at 1, 2, and 5 days after DSS stimulation and staining with hematoxylin-eosin (H&E) and Alcian blue (AB). All larval WT and IL-22KO medaka used were at 14 days post-fertilization. Arrows indicate the changes in tissue architecture caused by DSS. The arrowheads (\mathbf{V}) indicate the AB-positive cells.





B

Gene_ID	Gene name	Gene	WT_DSS / WT*1		IL-22-KO (-4)_DSS / WT_DSS* ²	
		Symbol	Fold change	p_value	Fold change	p_value
Up (WT / WT_DSS)						
ENSORLG00000017636	eukaryotic translation initiation factor 4E	eif4e	1.974	0.039	1.071	n.s.
ENSORLG00000018568	Insulin receptor	insr	2.373	0.015	0.920	n.s.
ENSORLG0000003389	Integrin beta-3	itgb3	2.393	0.014	0.947	n.s.
ENSORLG00000022689	laminin subunit gamma-2	lamc2	2.005	0.042	0.938	n.s.
ENSORLG00000023149	oncostatin-M-specific receptor subunit beta	osmr	2.054	0.046	0.638	n.s.
ENSORLG0000001742	5'-AMP-activated protein kinase catalytic subunit alpha-2	prkaa2	2.401	0.015	0.679	n.s.
Down (WT_DSS / IL-22-KO_DSS)						
ENSORLG0000009171	DNA damage inducible transcript 4	ddit4	0.664	n.s.	0.613	0.044
ENSORLG0000009764	DNA damage-inducible transcript 4-like protein	ddit41	4.172	n.s.	0.484	0.018
ENSORLG0000000289	fibroblast growth factor 19	fgf19	0.756	n.s.	0.287	0.015
ENSORLG00000024957	insulin-like growth factor-binding protein 1	igfbp1	1.476	n.s.	0.558	0.029
ENSORLG0000009059	serine/threonine-protein kinase Sgk1	sgk1	1.372	n.s.	0.577	0.034

Fig. S9. The PI3K-Akt signaling pathway maps of differentially expression gene (DEG) hits determined using data from the Kyoto Encyclopedia of Genes and Genomes (KEGG) database. (A) WT medaka stimulated with DSS showed upregulation of genes related to the "PI3K-Akt" pathway (red). IL-22-KO medaka stimulated with DSS showed downregulation of genes related to the "PI3K-Akt" pathway (greenstar). (B) Eleven DEGs showed significant localization in WT and IL-22-KO medaka stimulated with DSS.



B

Gene_ID	Gene name Gen	Gene	ene WT_DSS / WT*1		IL-22-KO (-4)_DSS / WT_DSS* ²	
		Symbol	Fold change	p_value	Fold change	p_value
Up (WT / WT_DSS)						
ENSORLG00000025805	voltage-dependent P/Q-type calcium channel subunit alpha-1A	cacnala	2.523	0.020	0.889	n.s.
ENSORLG0000008618	voltage-dependent T-type calcium channel subunit alpha-1H	cacnalh	2.160	0.032	0.816	n.s.
ENSORLG00000015184	dual specificity phosphatase 5	dusp5	2.423	0.014	0.513	0.022
ENSORLG0000004247	filamin-C	flnc	1.921	0.041	0.868	n.s.
ENSORLG0000000217	interleukin-1 beta	il1b	2.545	0.012	1.056	n.s.
ENSORLG00000011136	mitogen-activated protein kinase kinase kinase 11	map3k11	2.040	0.047	0.974	n.s.
Down (WT_DSS / IL-22-KO_DSS)						
ENSORLG0000009024	MAPK interacting serine/threonine kinase 2	mknk2	1.041	n.s.	0.620	0.048
ENSORLG00000015184	dual specificity phosphatase 5	dusp5	2.423	0.014	0.513	0.022
ENSORLG0000000289	fibroblast growth factor 19	fgf19	0.756	n.s.	0.287	0.015
ENSORLG00000022536	growth arrest and DNA damage-inducible protein GADD45 beta	gadd45b	1.242	n.s.	0.593	0.047
ENSORLG0000030080	growth arrest and DNA damage-inducible protein GADD45 gamma	gadd45g	1.073	n.s.	0.545	0.026
ENSORLG0000006132	oryzias latipes heat shock protein 70 (hsp70-5), mRNA	hsp70-5	0.786	n.s.	0.476	0.038
ENSORLG00000023848	neurotrophic receptor tyrosine kinase 1	ntrk l	0.930	n.s.	0.527	0.026

Fig. S10. MAPK signaling pathway maps of differentially expressed gene (DEG) hits determined using data from the Kyoto Encyclopedia of Genes and Genomes (KEGG) database. (A) WT medaka stimulated with dextran sulfate sodium (DSS) showed upregulation of genes related to the "MAPK" pathway (red). IL-22-KO medaka stimulated with DSS showed downregulation of genes related to the "MAPK" pathway (green-star). (B) Twelve DEGs showed significant localization in WT and IL-22-KO medaka stimulated with DSS.



Fig. S11. Real-time PCR (qPCR) analysis of inflammatory cytokines and multiple genes related to the PI3K-Akt and MAPK signaling pathways. The expression of inflammatory cytokine (*il22, il1b*, and *tnfa*) and PI3K-Akt and MAPK signaling pathway-related genes (*ddit4l* and *fgf19*) in the intestines, gills, and skin of adult medaka was quantified using qPCR. *ddit4l* and *fgf19* were chosen as the target genes based on the qPCR and RNA-seq results in the dextran sulfate sodium (DSS) stimulation experiment using larval medaka. DSS stimulation was performed by the immersion method in the larval experiment. The expression scale shows the relative values obtained when the expression of the naïve WT group was set to 1. Data represent the mean \pm SEM from five individual medaka in each group (n=5). ***; *P* < 0.001, **; *P* < 0.01, *; *P* < 0.05 (two-tailed Student's *t*-test).

Fig. S12.



B

Gene_ID	Gene name	Gene	WT_DSS /	WT* ¹	IL-22-KO (-4)_DSS / WT_DSS* ²	
		Symbol	Fold change	p_value	Fold change	p_value
Up (WT / WT_DSS)						
ENSORLG00000026388	complement C1q subcomponent subunit C	c1qc	2.361	0.014	0.148	n.s.
ENSORLG00000027110	complement C1q-like protein 2	c1ql2	3.038	0.035	0.367	0.038
ENSORLG0000006961	complement C4	c4b	5.141	0.005	0.303	0.019
ENSORLG00000014843	complement C6	c6	2.410	0.013	0.482	0.015
Down (WT_DSS / IL-22-KO_DSS)						
ENSORLG00000027110	complement C1q-like protein 2	c1ql2	3.038	0.035	0.367	0.038
ENSORLG00000012352	complement C1r	c1r	1.694	n.s.	0.482	0.038
ENSORLG0000006961	complement C4	c4b	5.141	0.005	0.303	0.019
ENSORLG0000006939	complement C4	c4b	1.383	n.s.	0.449	0.024
ENSORLG00000017552	complement C5	c5	1.484	n.s.	0.561	0.028
ENSORLG00000014843	complement C6	c6	2.410	0.013	0.482	0.015
ENSORLG00000014812	complement C7	c7	1.394	n.s.	0.594	0.042
ENSORLG00000013399	Coagulation Factor V	f5	1.671	n.s.	0.579	0.033
ENSORLG0000002453	fibrinogen alpha chain	fga	1.717	n.s.	0.614	0.042
ENSORLG0000008257	fibrinogen gamma chain	fgg	1.542	n.s.	0.626	0.047
ENSORLG00000010473	serpin family E member 1	serpine1	1.678	n.s.	0.488	0.038



Fig. S12. Complement cascade maps of differentially expressed gene (DEG) hits determined using data from the Kyoto Encyclopedia of Genes and Genomes (KEGG) database. (**A**) WT medaka stimulated with dextran sulfate sodium (DSS) showed upregulation of genes related to the "complement" cascade (red). IL-22-KO medaka stimulated with DSS showed downregulation of genes related to the "complement" cascade (green-star). (**B**) Twelve DEGs showed significant localization in WT and IL-22-KO medaka stimulated with DSS. (C, D) Of the 12 DEGs, the expression of *clqc* and *c6* was confirmed by qPCR. ***; *P* < 0.001, **; *P* < 0.01, *; *P* < 0.05, +; *P* < 0.1 (two-tailed Student's *t*-test). Data shown were obtained from a single experiment (n=7).



Fig. S13. Real-time PCR (qPCR) analysis of *fgf7* and *muc2* in the anterior and posterior intestines of adult medaka. Dextran sulfate sodium stimulation was performed by the immersion method in the larval experiment. The expression scale shows the relative values obtained when the expression of the naïve WT group was set to one. Data represent the mean \pm SEM from five individual medaka in each group (n=5). ***; *P* < 0.001, **; *P* < 0.01, *; *P* < 0.05 (two-tailed Student's *t*-test).