

Supplementary Materials

Calcium-bound S100P Protein is a Promiscuous Binding Partner of the Four-Helical Cytokines

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Table S1. The four-helical cytokine samples that did not reveal specificity to S100P, according to SPR spectroscopy (cytokine immobilization on the sensor chip surface by amine coupling).

<i>Full name</i>	<i>Abbreviation</i>	<i>UniProt ID</i>	<i>Manufacturer</i>	<i>Cat. number</i>	<i>Source</i>
<i>Short-chain cytokines</i>					
Macrophage colony-stimulating factor 1	M-CSF	P09603	PeproTech	300-25	<i>E.coli</i>
Interleukin-2	IL-2	P60568	PeproTech	AF-200-02	<i>E.coli</i>
Interleukin-4	IL-4	P05112	PeproTech	AF-200-04	<i>E.coli</i>
<i>Long-chain cytokines</i>					
Interleukin-7	IL-7	P13232	SCI-Store (Russia)	PSG240-10	CHO
Thymic stromal lymphopoietin	TSLP	Q969D9	PeproTech	300-62	<i>E.coli</i>
Chorionic somatomammotropin hormone 1	PL	P0DML2	R&D Systems	5757-PL/CF	CHO
Interleukin-6 [#]	IL-6	P05231	PeproTech	200-06	<i>E.coli</i>
Leukemia inhibitory factor [#]	LIF	P15018	PeproTech	300-05	<i>E.coli</i>
Interleukin-12	IL-12	P29459* & P29460	PeproTech	200-12H	HEK293
Interleukin-23	IL-23	Q9NPF7* & P29460	PeproTech	200-23	Hi-5
<i>Interferons/IL-10</i>					
Interferon α -2	IFN- α 2	P01563	Vector-Medica (Russia)	n/a	<i>E.coli</i>
Interferon γ	IFN- γ	P01579	Pharmaclon (Russia)	n/a	<i>E.coli</i>

[#] ref. [1]

* denotes the chain used for SCOP 2 [2] family assignment

n/a, not applicable

Table S2. The concentrations of four-helical cytokines under normal and pathological conditions.

Cytokine	Condition	Liquid	Detected level				Reference
			Disease		Healthy control		
			pg/ml	pM	pg/ml	pM	
Short-chain cytokines							
GM-CSF	Axial spondyloarthritis	Serum	150	10.36	62	4.28	[3]
	Systemic sclerosis	Serum	120.9±125.5	8.29±8.67	20.1±12.3	1.39±0.85	[4]
	Chronic myelogenous leukemia	Serum	3.9-55	0.27-3.8	-	-	[5]
	Rheumatoid arthritis	Plasma	366±61 (severe) 376±44 (moderate)	25.27±4.22 (severe) 25.97±3.04 (moderate)	174 ± 18	12.02±1.24	[6]
	Systemic lupus erythematosus	Plasma	256±41	17.67±2.83			
	Spondyloarthropathy	Plasma	190±32	13.02±2.21			
	Relapsing-remitting multiple sclerosis	Serum	27.8±18.4 (relapse) 19.4±13.8 (remission)	1.92±1.27 (relapse) 1.34±0.95 (remission)	17.9±13.3	1.24±0.91	[7]
	Healthy	Serum	-	-			
IL-3	Homozygous beta-thalassemia (children)	Plasma	6.9±17.1	0.46±1.13	0.2±0.5	0.013±0.033	[9]
	Healthy	Serum	-	-	< 12	< 0.8	[8]
	Healthy	Serum	-	-	5.8 men 8.0 women	0.38 men 0.53 women	[10]
	Chronic schizophrenia	Serum	27.0±19.7	1.79±1.31	14.6±10.4	0.97±0.69	[11]
IL-5	Healthy	Serum	-	-	< 3.1	< 0.2	[8]
	Hepatocellular carcinoma	Serum	10.97 (0.29–17042.32)	0.83 (0.02-1.30)	-	-	[12]

	Acute asthmatic attack	Serum	4.84±1.68	0.37±0.13	0.32±0.26	0.024±0.02 0	[13]
	Asthma	Serum	9.5 (atopic)	0.72 (atopic)	4.4	0.33	[14]
			8.1 (non-atopic)	0.62 (non-atopic)			
		Serum	0–46.75	0-3.56	0–5.20	0-0.40	[15]
	Chronic obstructive pulmonary disease	Serum	6.4±3.2	0.49±0.24	-	-	[16]
IL-9	Hodgkin's lymphoma	Serum	up to 3350	up to 237	-	-	[17]
	Healthy	Serum	-	-	113.6 men 573.3 women	8.1 men 40.6 women	[10]
	Rheumatoid arthritis	Serum	4.77±3.618	0.34±0.26	1.22±0.706	0.09±0.05	[18]
	Systemic lupus erythematosus	Serum	12.26±25.235	0.87±1.79			
	Colon cancer	Plasma	1.29	0.09	2.53	0.18	[19]
	Inflammatory bowel disease	Serum	40±5	2.83±0.35	< 6	< 0.4	[20]
	Diffuse large B-cell lymphoma	Serum	1.43±0.64	0.10±0.05	0.82±0.15	0.06±0.01	[21]
	Allergic rhinitis	Serum	12.6 (5.03–24.11) (exposed to allergen)	0.9 (0.3-1.7)	-	-	[22]
			4.83 (1.97–14.01) (not exposed to allergen)	0.3 (0.1-1.0)			
	Systemic sclerosis	Serum	84.6±76.0	5.99±5.39	40.4±41.7	2.86±2.95	[23]
	Systemic lupus erythematosus		50.7±52.0	3.59±3.68			
	Dermatomyositis		50.6±55.8	3.58±3.95			
	Atopic dermatitis		41.8±38.8	2.96±2.75			
IL-13	Asthma	Serum	0–157.10	0–9.93	0–5.40	0–0.38	[15]
	Healthy	Serum	-	-	11.2 men	0.8 men	[10]

					14.1 women	1.0 women	
	Insulin resistance	Serum	37.69±17.82	2.38±1.13	15.88±6.71	1.13±0.47	[24]
	Chronic rhinosinusitis with nasal polyps	Serum	0.98±1.56	0.06±0.10	0.34±0.16	0.024±0.01 ₁	[25]
	Acute asthmatic attack	Serum	50.85±27.30	3.22±1.73	8.10±5.40	0.57±0.38	[13]
	Ocular Behcet's disease	Serum	38.7±59.6 (active ocular BD) 9.21±2.03 (ocular BD in remission) 10.3±1.65 (nonocular BD in remission)	2.45±3.77 0.58±0.13 0.65±0.10	7.83±1.85	0.56±0.13	[26]
	Hepatocellular carcinoma	Serum	38.425 (7.73–539.93)	2.43 (0.49–34.14)	-	-	[12]
	Psoriatic arthritis	Serum	2 (2–2)	0.13 (0.13–0.13)	2 (2–6.2)	0.14 (0.14–0.44)	[27]
	Rheumatoid arthritis		10.2 (2–28.3)	0.64 (0.13–1.79)			
	Osteoarthritis		2 (2–5.8)	0.13 (0.13–0.37)			
	Systemic sclerosis	Serum	0.84±0.65	0.05±0.04	0.35±0.18	0.025±0.01 ₂	[28]
IL-15	Polymyositis/dermatomyositis	Serum	47.6±170 (active)	3.73±13.31	28.5±28.89	2.5±2.3	[29]
			25.15±240 (inactive)	1.97±18.79			
	Healthy	Serum	-	-	< 2.1	< 0.16	[8]
	Essential hypertension	Serum	88.7±18.7 (severe organ damage) 55.2±6.9 (mild organ damage)	6.94±1.46 4.32±0.54 3.99±0.65	-	-	[30]

			51.0±8.3 (no organ damage)				
	Kawasaki disease	Serum	11.5±5.8 (acute stage) 1.3±0.9 (subacute stage)	0.91±0.45 0.10±0.07	0.9 (1.0)	0.07 (0.08)	[31]
	Prostate cancer	Serum	208.07±48.50 (early stage prostate cancer) 50.51±14.34 (benign prostatic hyperplasia)	16.28±3.79 3.95±1.12	-	-	[32]
	Multiple sclerosis	Serum	4.2±1.36 5.56±3.6 (PPMS) 4.13±0.61 (RRMS) 4.26±0.73 (SPMS) 4.13±0.45 (IDS)	0.33±0.10 0.44±0.28 0.33±0.05 0.34±0.06 0.33±0.04	-	-	[33]
	Inflammatory neurological diseases		1.95±0.41	0.16±0.03			
	Non-inflammatory neurological diseases		2.96±1.13	0.23±0.09			
	Ulcerative colitis (moderate to severe)	Serum	0-490	0-38	-	-	[34]
	Hepatocellular carcinoma	Serum	77.4±78	6.06±6.11	-	-	
	Bacteremic melioidosis	Serum	49.4 (12.4-338.8)	3.87 (0.98-26.52)	12.8 (< 8.2-122.2)	1.00 (< 0.64-9.57)	[35]
	Non-bacteremic melioidosis	Serum	31.3 (11.6-2743)	2.45			

				(0.91-214.74)			
IL-21	Psoriasis	Serum	68.86±32.13	4.31±2.01	50.04±23.56	3.13±1.47	[36]
	Systemic lupus erythematosus	Serum	24.64 (21.15–28.46)	1.54 (1.32-1.78)	27.74 (23.28–34.64)	1.73 (1.46-2.17)	[37]
	Atopic dermatitis	Serum	454 (up to 6 293)	28.39 (up to 394)	50.6	3.16	[38]
	Chronic hepatitis B	Serum	303.54±152.77	18.98±9.55	68.24±9.06	4.27±0.57	[39]
	Coronary artery disease	Serum	187.0±6.0	11.7±0.4	120.5±5.0	7.5±0.3	[40]
THPO	Cirrhosis	Serum	69±12	1.82±0.32	49±9	1.3±0.24	[41]
	Myelosuppression after intensification chemotherapy of acute leukemia in complete remission	Serum	-	18.46±9.70	-	0.84±0.40	[42]
	Aplastic anemia		-	16.03±9.44			
	Acute lymphoblastic leukemia		-	10.36±5.57			
	Malignant lymphoma		-	2.79±2.27			
	Multiple myeloma		-	3.34±0.20			
	Chronic lymphocytic leukemia		-	1.71±3.91			
	Myeloproliferative disorders		-	1.99±1.47			
	Acute myelogenous leukemia		-	2.27±1.25			
	Hypoplastic leukemia		-	2.76±2.23			
	Myelodysplastic syndrome		-	0.42±0.60			
	Liver cirrhosis		-	1.50±0.92			
	Idiopathic thrombocytopenic purpura		-	2.08±1.41			
	Thrombocytopenia	Serum	>500	>14.1	<100	<2.8	[43]
	Ovarian cancer	Serum	114 (25–435)	3.2 (0.7-12.3)	-	-	[44]

	Benign ovarian disease		74 (34–189)	2.1 (1.0-5.3)			
	Consumptive thrombocytopenia	Serum	63 (48–98)	1.8 (1.4-2.8)	7–99	0.2-2.8	[45]
	Hypoproliferative thrombocytopenia		706 (358–1546)	19.9 (10.1-43.6)			
Long-chain cytokines							
IL-31	Paediatric atopic dermatitis	Serum	1600 (1457.8±770.4) (flare) 1040 (958.7±419.5) (quiescence)	101 (92±49) 66 (61±26)	220 (197.3±91.9)	14 (12±6)	[46]
	Osteoporosis	Serum	43.12±6.97	2.72±0.44	29.58±6.09	1.86±0.38	[47]
	Early axial spondyloarthritis	Serum	12.6±15.4	0.79±0.98	1.8±4.0	0.11±0.25	[48]
	Chronic kidney disease-associated pruritus	Serum	679.9±1112.3	42.9±70.2	57.3±65.1	3.6±4.1	[49]
	Atopic dermatitis	Serum	up to 10 000	up to 631	up to 1 200	up to 76	[50]
	Endometrial cancer	Serum	165.80±39.03 (94.43–240.65) (before operation) 128.91±29.48 (53.54–187.54) (after operation)	10.47±2.46 (5.97-15.20) 8.14±1.86 (3.38-11.84)	77.24±25.85 (32.50–142.82)	4.87±1.63 (2.05-9.02)	[51]
IL-27	Systemic sclerosis	Serum	302.8 (101.6-1034.4) 385 (109-826.3)	6.33 (2.12-21.62) 8.05 (2.28-17.27)	104.2 (51-184.2)	2.18 (1.06-3.85)	[52]
	Chronic HIV-1 Infection	Serum	2 008.0±274.8 (50 copies/ml group)	42.0±5.7 30.7±3.6			[53]

			1 468.7±172.3 (51–10 000 copies group) 1 237.9±127.3 (10 001–100 000 copies/ml group) 1 590.1±223.7 (>100 000 copies/ml group)	25.9±2.7 33.2±4.7	2 990.7±682. 1	62.5±14.3	
	Childhood immune thrombocytopenia	Serum	770.6	16.1	373.8	7.8	[54]
	Ocular Behcet's disease	Serum	320±57.5 (active ocular BD) 316±47.3 (ocular BD in remission) 305±32.4 (nonocular BD in remission)	6.69±1.20 6.60±0.98 6.38±0.67	347±50.1	7.25±1.05	[26]
	Ischemic heart disease	Serum	38.00±14.38 (acute myocardial infarction) 35.77±18.93 (unstable angina)	0.80±0.30 0.75±0.40	24.91±14.9 6	0.52±0.31	[55]
	Diabetic retinopathy	Serum	240.900 (42.224– 617.810)	5.0 (0.9-12.9)	2 712.310 (1 005.375– 5 786.877)	56.68 (21-120)	[56]
	Type 1 diabetes mellitus	Serum	22.06	0.46	14.5	0.30	[57]
	Type 1 diabetes mellitus + Hashimoto's disease		27.82	0.59			
	Healthy	Serum	-	-	Most 100-1 000 Minority >2 000	Most 2.1- 20.9 Minority > 41.8	[58]

					4.4% > 6 000	4.4% > 125.4	
IL-35	Pre-eclampsia	Serum	729±335	15.90±7.31	483.9±242	10.55±5.28	[59]
	Gastric cancer	Serum	17.559±13.266	0.38±0.29	8.077±3.80 1	0.18±0.08	[60]
	Prostate cancer	Serum	20.01±7.03	0.44±0.15	11.60±2.49	0.25±0.05	[61]
	Rheumatoid arthritis	Serum	12.9 (6.4-16.9)	0.28 (0.14-0.37)	6.7 (4.3-12.2)	0.15 (0.09-0.27)	[62]
	Multiple sclerosis	Serum	49.3±3.7	1.08±0.08	69.5±7.8	1.52±0.17	[63]
	Systemic sclerosis	Serum	83.9 (45.1–146.1)	1.83 (0.98-3.19)	36.2 (17.2–49.4)	0.79 (0.38-1.08)	[64]
	Systemic sclerosis	Serum	5.08±0.76 7.75±1.36 (fibrosis) 3.08±0.70 (without fibrosis)	0.111±0.01 7 0.169±0.03 0 (fibrosis) 0.067±0.01 5 (without fibrosis)	1.89±0.69	0.041±0.01 5	[65]
G-CSF	Healthy	Serum	-	-	45.5 (34–53.6)	2.4 (1.8-2.80)	[8]
	Healthy	Serum	-	-	70.3 men 93.7 women	3.7 men 4.9 women	[10]
	Acute stage of infection	Serum	731.8±895.0 (30-3 199)	38.6±47.1 (1.6-168.5)	25.3±19.7 < 100 in all cases	1.33±1.03 < 5.27 in all cases	[66]
	Breast cancer	Serum	92.81±594.54	4.88±31.31	0.00	0.00	[67]
	Acute bacterial infection	Serum	799±1 501	42±79	-	-	[68]
	Viral infection		58±34	3.1±1.8			
	Atypical pneumonia		60±33	3.2±1.7			
	Chronic myelogenous leukemia	Serum	150-2 830	7.9-149.1	-	-	[5]
	Urothelial carcinoma	Serum	147	7.74	< 37	1.95	[69]
	Various disorders	Serum	46 to > 2 000	2.4 to >105.3	< 30 to 163	<1.6 to 8.6	[70]

	Septic shock after surgery	Serum	up to 20 000	up to 1050	<100	< 5.27	[71]
GH	Gastric cancer	Serum	3 140±3 120 (200-10 900)	142±141 (9-493)	690±1 600 (100-9 000)	31±72 (4.5-406.7)	[72]
	Colorectal cancer		3 010±2 910 (200-9 900)	136±132 (9-447)			
	Healthy	Serum	-	-	400-10 000 (adult males) 1 000-14 000 (adult females) 10 000-50 000 (children)	18-452 45-633 452-2 260	[73]
	Acromegaly	Serum	≥ 1 000	≥45	<1 000	< 45	[74]
	Healthy	Serum	-	-	2 400±2 800 (boys) 2 500±3 100 (girls)	108±127 113±140	[75]
GH-V	Down syndrome pregnancy	Maternal serum	-	-	531 (8 th week) 935 (9 th week) 962 (10 th week) 1 103 (11 th week) 1 204 (12 th week) 1 169 (13 th week)	23.79 (8 th week) 41.89 (9 th week) 43.10 (10 th week) 49.42 (11 th week) 53.94 (12 th week) 52.37 (13 th week)	[76]
	Pre-eclampsia	Maternal serum	23 076 (3 473-94 256)	1 030 (156-4 220)	12 157 (2 617-34 016)	545 (117-1 520)	[77]
PRL	Healthy	Serum	-	-	< 20 000	< 870	[27]

					(men) < 25 000 (nonpregnant women) 80 000-40 000 (pregnant women)	(men) < 1 090 (nonpregnant women) 3 490-17 470 (pregnant women)	
	Phenylketonuria	Serum	12 000 (3 000–75 000)	524 (131-3 280)	1 400–24 000 (females) 1 600–10 700 (males)	61-1 050 (females) 70-467 (males)	[78]
	Systemic lupus erythematosus	Serum	17 400±15 100	760±660	6 300±3 200	275±140	[79]
	Rheumatic autoimmune diseases		13 100±10 300	572±450			
	Psoriasis	Serum	11 290±8 050 (3 800-39 600)	493±352 (166-1 730)	7 900±3 930 (2 800-18 600)	345±172 (122-812)	[80]
	Breast cancer	Serum	5 000–77 900	218-3 400	<20 000	<873	[81]
	Type 2 diabetes mellitus	Serum	36 840±6 290	1 610±275	10 660±2 450	466±107	[82]
LEP	Asthma	Serum	13 810±10 560	862±659	6 320±5 200	394±324	[83]
	Multiple sclerosis	Serum	-	50-6250	-	-	[84]
	Multiple sclerosis	Serum	11 135±6 453 (RRMS) 30 258±14 435 (SPMS) 30 301±12 709 (PPMS)	695±403 1 890±901 1 890±793	-	-	[85]
	Non-small cell lung cancer		8 500±1 600 10 700±2 500 (without weight loss) 7 200±2 100 (weight loss)	530±100 668±156 449±131	12 800±2 400	799±150	[86]

	Obesity	Serum	44 920±26 490 (women) 15 150±9 500 (men)	2 800±1 650 (women) 945±593 (men)	21 810±17 110 (women) 7310±5080 (men)	1 360±1 070 (women) 456±317 (men)	[87]
	Obesity	Serum	11 390±8 790 (boys) 12 640±9 330 (girls)	711±549 (boys) 789±582 (girls)	4 800±5 250 (boys) 4 810±4 430 (girls)	300±328 (boys) 300±276 (girls)	[88]
<i>Interferons/IL-10</i>							
IL-10	Healthy	Serum	-	-	12.6 (8.5–16.7)	0.68 (0.46-0.90)	[8]
	Healthy	Serum	-	-	2.7	0.14	[10]
	Melanoma	Serum	15–480	0.80-25.74	<3.0	<0.16	[89]
			8.75	0.47	<3.0	<0.16	
	Gastric cancer		27.52	1.48	<12	<0.64	
			>21.0	>1.13	<3.0	<0.16	
	Pancreatic cancer		>10.0	>0.54	N/D	<0.16	
			>9.8	>0.53	3.0	0.16	
	Colorectal cancer		97.36	5.22	24.53	1.32	
			16.09	0.86	5.1	0.27	
	Hepatic cancer		12	0.64	6.3	0.34	
	Hodgkin lymphoma		>10	>0.54	7.1	0.38	
	Non-Hodgkin lymphoma		>7.98	>0.43	<5.0	<0.28	
	Lung cancer		>38.16	>2.05	32.55	1.75	
			21.4	1.15	9.2	0.49	
	B-cell lymphoma		26.0	1.39	18.0	0.97	
	Chronic lymphocytic leukemia		74	3.97	<13.68	<0.73	
	Psoriasis	Serum	89.5±18.7	4.8±1	117.2±23.4	6.29±1.25	[90]
IL-20	Rheumatoid arthritis	Serum	30.2 (19.1–58.5)	1.72 (1.09-3.34)	13.1 (11–15.1)	0.75 (0.63-0.86)	[91]
	Psoriasis	Serum	20.418±20.587	1.16±1.17	2.703±3.04 3	0.15±0.17	[92]
	Non–small cell lung cancer	Serum	40.35	2.30	37.73	2.15	[93]

			(29.86-63.81)	(1.70-3.64)	(32.49-50.80)	(1.85-2.90)	
	Rheumatoid arthritis	Plasma	282 (134-438)	16.09 (7.65-24.99)	-	-	[94]
	Osteoarthritis		124 (110-147)	7.07 (6.28-8.39)			
	Rheumatoid arthritis	Plasma	89 (45-643)	5.08 (2.57-36.69)	71 (40-80)	4.05 (2.28-4.56)	[95]
	Systemic sclerosis	Serum	56.89±11.6	3.25±0.66	79.11±18.2	4.51±1.04	[96]
	Primary Raynaud's phenomenon		71.42±11.8	4.07±0.67			
IL-22	Psoriasis	Serum	71.600±150.75 9	4.27±9.00	2.358±2.48 6	0.14±0.15	[92]
	Non-small cell lung cancer	Serum	10.66 (1.44-70.34)	0.64 (0.09-4.20)	4.69 (0.35-12.29)	0.28 (0.02-0.73)	[93]
	Systemic sclerosis	Serum	68.3±44.4	4.09±2.65	59.52±16.7	3.55±1.00	[96]
	Primary Raynaud's phenomenon		63.1±11.8	3.77±0.70			
	Epithelial ovarian cancer	Plasma	34.19±4.58	2.04±0.27	22.1±1.71	1.32±0.10	[97]
	Benign ovarian epithelial neoplasm		23.1±1.78	1.38±0.11			
	Hepatocellular carcinoma	Serum	299.675 (5.99-1963.32)	17.89 (0.36-117.2)	-	-	[12]
	Multiple myeloma	Serum	75.5±63.3	4.51±3.78	8.1±5.7	0.48±0.34	[98]
	Low-grade squamous intraepithelial lesion	Serum	168.2	10.0	36.91	2.20	[99]
	High-grade squamous intraepithelial lesion		61.48	3.67			
	Breast cancer	Serum	317.53±14.33	18.96±0.86	62.67±19.1 1	3.74±1.14	[100]
	Type 2 autoimmune hepatitis	Serum	55.26	3.3	0.1	0.006	[101]

IL-24	Rheumatoid arthritis	Plasma	2 210 (310–7290)	122 (17-401)	80 (0–3630)	4.4 (0-200)	[94]
	Spondyloarthritis		2 020 (0–6830)	111 (0-376)			
	Breast cancer	Serum	160.65±55	8.84±3.03	27.4±8.5	1.51±0.47	[102]
	Gastric cancer + H. Pylori infection		76.2±16.27	4.2±0.9			
	Gastric cancer		72.5±17.84	3.99±0.98			
	H. Pylori infection		32.78±12.96	1.8±0.71			
	Systemic lupus erythematosus	Serum	1 375.70 (812.92–2 096.54)	75.76 (44.76-115.45)	334.70 (129.13–634.91)	18.43 (7.11-34.96)	[103]
IL-26	Systemic lupus erythematosus	Serum	4 040±11 660	230±663	740±2 020	42±115	[104]
	Neurosyphilis	Serum	6870	391	1670	95	[105]
	Severe asthma	Serum	1 100±390	63±22	550±250	31±14	[106]
	Behçet's disease	Serum	4 800±1 320 (active) 2 770±1 026 (inactive)	273±75 158±58	310±140	18±8	[107]
	Rheumatoid arthritis	Serum	2 430±3 800	138±216	30±40	1.71±2.27	[108]
	Other inflammatory arthritis	Serum	8 820±16 320	502±928	30±40	1.71±2.27	
IFN-ω1	Dermatomyositis	Serum	0-120	0-5.95	0-60	0-2.98	[109]

Table S3. The structures (PDB [110] entries or AlphaFold2 [111] predictions) of the human cytokines used for structural modelling of their complexes with Ca²⁺-loaded human S100P dimer (chains B, D of PDB entry 2MJW) using ClusPro docking server [112].

<i>Cytokine</i>	<i>PDB entry</i>	<i>Chain</i>	<i>Method</i>	<i>Comments</i>
<i>Short-chain cytokines</i>				
GM-CSF	1CSG	A	X-ray	
IL-3	6NMY	I	X-ray	W6Y substitution; complex with the receptor chains
IL-5	1HUL	A	X-ray	dimeric structure
IL-9	-	-	AlphaFold2	
IL-13	1GA3	A	NMR	
IL-15	4GS7	A	X-ray	complex with the receptor chains
IL-21	2OQP	A	NMR	
THPO	1V7M	V	X-ray	complex with a neutralizing antibody fragment; only structured fragment of the protein 22-184 was used for docking
<i>Long-chain cytokines</i>				
IL-31	-	-	AlphaFold2	
G-CSF	1GNC	A	NMR	
GH	-	-	AlphaFold2	
GH-V	-	-	AlphaFold2	
PRL	1RW5	A	NMR	
LEP	1AX8	A	X-ray	W100A substitution
<i>Interferons/IL-10</i>				
IL-10	2ILK	A	X-ray	
IL-20	4DOH	A	X-ray	complex with the receptor chains
IL-22	1M4R	A	X-ray	

IL-24	6DF3	C	X-ray	N34Q, N48Q, Y73H, N75Q substitutions; complex with the receptor chains
IL-26	-	-	AlphaFold2	
IFN- ω 1	3SE4	B	X-ray	N83Q substitution; complex with the receptor chains

Table S4. The residues of the binding sites for the S100P-cytokine complexes predicted using ClusPro docking server [112]. The contact residues included into 5 or more docking models were considered as the most probable residues of the binding site. The numbering of the residues is according to the PDB entries. The residues of receptor-binding sites of the cytokines are shown in bold. The following receptors are taken into account: GM-CSF receptor subunit α (PDB entry 4RS1), IL-3 receptor subunit α (PDB ID: 5UV8), IL-5 receptor subunit α (PDB ID: 3VA2), IL-15 receptor subunits α , β and γ (PDB ID: 4GS7), IL-21 receptor (PDB ID: 3TGX), G-CSF receptor (PDB ID: 2D9Q), GH receptor (PDB ID: 3HHR), IL-20 receptor subunits α and β (PDB ID: 4DOH), IFN- α/β receptors 1 and 2 (PDB ID: 3SE4).

<i>Short-chain cytokines</i>		
S100P dimer		GM-CSF
Chain B	Chain D	
P42,G43,F44,Y88,F89	M1,T2,E5,G9,D13,R17	
S100P dimer		IL-3
Chain B	Chain D	
G43,Y88,F89,A92	M1,E5	
S100P dimer		IL-5
Chain B	Chain D	
E40, P42,G43,C85,Y88,F89,A92	M1,T2,E5	
S100P dimer		IL-9
Chain B	Chain D	
E3,C85,Y88,F89	M1,E5,G9,I12,D13,S16,R17	
S100P dimer		IL-13
Chain B	Chain D	
G43,F44,C85,F89	E5	
S100P dimer		IL-15
Chain B	Chain D	
M1,E5,P42,F44,Y88,F89	M1,T2,E5,F44,Y88,F89,A92	
S100P dimer		IL-21
Chain B	Chain D	

M1,T2,E3,E5,T6,D13,R17,E40,Y88,G93	M1,T2,E3,E5,T6,M10,D13,S16,R17,E40,F89	M5,Q6,G7,Q8,D9, R10 ,H11, R14 ,N46,W51, R81,P84,S85 ,R90,R91,H94,R95,H127,L128,S129,R131
S100P dimer		THPO
Chain B	Chain D	
E3,R17,Y88,F89,A92,G93,L94	M1,E5,D13,S16,R17,T25,Q26	S7,R11,H14,H17,V38,F40,S41,L42,H115,L123,R130,R134,F135,L138
<i>Long-chain cytokines</i>		
S100P dimer		IL-31
Chain B	Chain D	
F44,Q46,C85,Y88,F89	E5	S1,H2,L4,P5,V6,R7,L9,R10,P11,D53,Q55,P56,N58,F93,Q94,D95
S100P dimer		G-CSF
Chain B	Chain D	
G43,F44,C85,Y88,F89,A92	M1,E5,I12,G43,F44,F89	Q71,L72,A73, Q120 ,Q121,E123, E124 ,L169
S100P dimer		GH
Chain B	Chain D	
M1,E5,G43,F44,C85,Y88,F89	M1,E5,P42,G43,Y88,F89	D11, L15,H18,Q22,R64 ,Q68, R178 ,I179,C182,R183,E184,G187,S188, C189,G190 ,F191
S100P dimer		GH-V
Chain B	Chain D	
D13,F44,Y88	F44	F1,P2,T3,I4,R8,N12,R16,R112,D116,E119,Q122,T123,W126,R127,D130,Q137
S100P dimer		PRL
Chain B	Chain D	
L41,F44,I81,C85,Y88,F89	E5	L1,I3,C4,G6,G7,A9,R10,C11,Q12,V13,T14,R16,D17,D20,R21,R125,E128,K190,I194,H195
S100P dimer		LEP
Chain B	Chain D	
C85,Y88,F89	M1,E5,D13	V1,I3,D85,H88,F92,S93,K94,S95,C96,H97,L98,C146
<i>Interferons/IL-10</i>		
S100P dimer		IL-10
Chain B	Chain D	

E5,Y88,F89,G93,L94	D13,Y88,F89	Q70,K117,S118,A120,V121,K125,M140,F143,F146,Y149,I150,Y153,M154,I158
S100P dimer		IL-20
Chain B	Chain D	
E5,M8,Y88,F89	E5,F44,C85,Y88,F89	S9,V11,R60,R64, K97 ,D98,R100,H103,A104,H105,M106,T107,C108,H109,C110
S100P dimer		IL-22
Chain B	Chain D	
P42,G43,F44,C85,Y88,F89	M1,T2,E5	H6,F47,H48,G49,M52,S53,E54,R55,D104,N143,A144,I146
S100P dimer		IL-24
Chain B	Chain D	
F44,I81,C85,Y88,F89	M1,T2,E5,D13	Y56,H59,T60,P102,Q104,N106,F109,S110,R112,D113,H116,R117,L120,R124,K127,Q128
S100P dimer		IL-26
Chain B	Chain D	
P42,G43,C85,Y88,F89	M1,T2,E5,G9,D13	Y12,S102
S100P dimer		IFN-ω1
Chain B	Chain D	
E5,M8,Y88,F89	E5,G43,F44,C85,Y88,F89	R14,H21 ,Q22,R24,R25,I26,S27, P28,F29 ,L30,K33, R35 ,D140,R147, M148,M151,F155

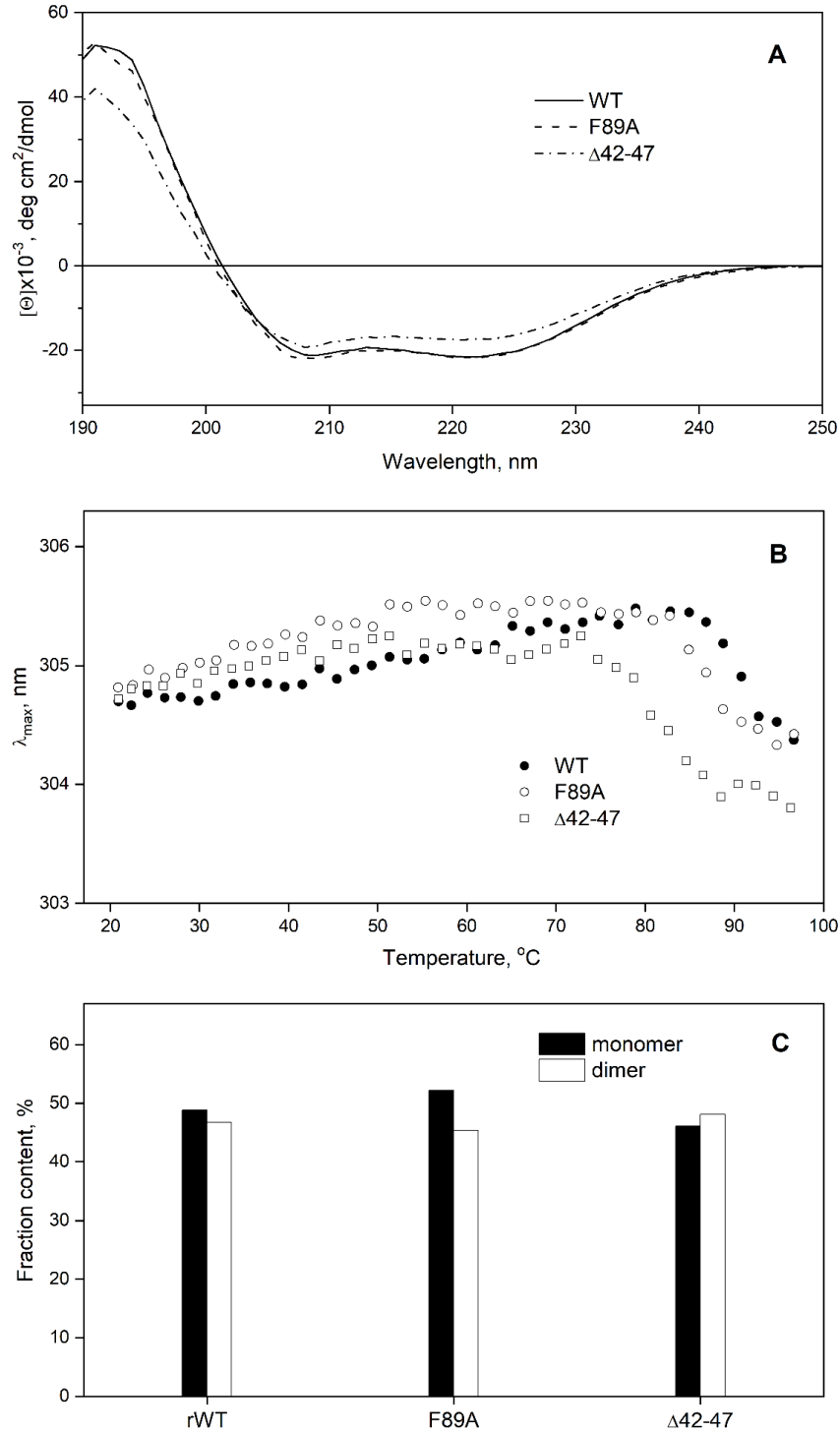


Figure S1. Comparison of structural properties of apo-forms of WT S100P and its F89A, $\Delta 42-47$ mutants, using far-UV CD spectroscopy at 20°C (panel **A**), intrinsic fluorescence (**B**) and chemical crosslinking at 20°C by 0.02% glutaraldehyde for 16 h (**C**) (10 mM tricine-KOH, 1 mM EDTA-KOH, pH 7.4). Protein concentration was 10 μ M (**A**, **B**) or 67 μ M (**C**). Calcium depletion was performed according to ref. [113].

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