

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).

Full name	Abbreviation	UniProt ID	Manufacturer	Cat. number	Source
<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	Pharmacia (Russia)	n/a	<i>E.coli</i>
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[#] 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		
<i>Short-chain cytokines</i>								
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±4.2 2 (severe) 25.97±3.0 4 (moderate)	174 ± 18	12.02±1.24	[6]	
	Systemic lupus erythematosus	Plasma	256±41	17.67±2.8 3				
	Spondyloarthropathy	Plasma	190±32	13.02±2.2 1				
	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	-	-	38.3 (26.3-63.8)	2.64 (1.82-4.41)	[8]	
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	[10]	

						0.53 women	
	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±0.020	[13]
	Asthma	Serum	9.5 (atopic)	0.72 (atopic)	4.4	0.33	[14]
			8.1 (non-atopic)	0.62 (non- atopic)			
	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	0.3			

			(1.97–14.01) (not exposed to allergen)	(0.1-1.0)			
IL-13	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			
	Asthma	Serum	0–157.10	0–9.93	0–5.40	0–0.38	[15]
	Healthy	Serum	-	-	11.2 men 14.1 women	0.8 men 1.0 women	[10]
	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±0.011	[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±0.012	[28]
IL-15	Polymyositis/dermatomyositis	Serum	47.6±170 (active)	3.73±13.3 1	28.5±28.89	2.5±2.3	[29]
			25.15±240 (inactive)	1.97±18.7 9			
	Healthy	Serum	-	-	< 2.1	< 0.16	[8]
	Essential hypertension	Serum	88.7±18.7 (severe organ damage)	6.94±1.46	-	-	[30]
			55.2±6.9 (mild organ damage)	4.32±0.54			
			51.0±8.3 (no organ damage)	3.99±0.65			
	Kawasaki disease	Serum	11.5±5.8 (acute stage)	0.91±0.45	0.9 (1.0)	0.07 (0.08)	[31]
	Prostate cancer	Serum	208.07±48.50 (early stage prostate cancer)	16.28±3.7 9	-	-	[32]
			50.51±14.34 (benign prostatic hyperplasia)	3.95±1.12			

	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±152.7 7	18.98±9.5 5	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)			
<i>Long-chain cytokines</i>							
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±2.4 6 (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	42.0±5.7			[53]

			(<50 copies/ml group) 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 copies/ml group)	30.7±3.6 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±14.96	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 4.4% > 6 000	Most 2.1- 20.9 Minority > 41.8 4.4% > 125.4	[58]
IL-35	Pre-eclampsia	Serum	729±335	15.90±7.3 1	483.9±242	10.55±5.28	[59]
	Gastric cancer	Serum	17.559±13.26 6	0.38±0.29	8.077±3.801	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±0.0 17 0.169±0.0 30 (fibrosis) 0.067±0.0 15 (without fibrosis)	1.89±0.69	0.041±0.015	[65]
G-CSF	Healthy	Serum	-	-	45.5	2.4	[8]

					(34–53.6)	(1.8–2.80)	
	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±31.3 1	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)	23.79 (8 th week)	[76]
					935 (9 th week)	41.89 (9 th week)	
					962 (10 th week)	43.10 (10 th week)	
					1 103 (11 th week)	49.42 (11 th week)	
					1 204 (12 th week)	53.94 (12 th week)	
					1 169 (13 th week)	52.37 (13 th week)	
	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 (men)	< 870 (men)	[27]
					< 25 000 (nonpregnant women)	< 1 090 (nonpregnant women)	
					80 000-40 000 (pregnant women)	3 490-17 470 (pregnant women)	
	Phenylketonuria	Serum	12 000 (3 000-75 000)	524 (131-3 280)	1 400-24 000 (females)	61-1 050 (females)	[78]
					1 600-10 700 (males)	70-467 (males)	

					(males)		
LEP	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	Serum	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]

Interferons/IL-10							
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]
	Gastric cancer		8.75	0.47	<3.0	<0.16	
	Pancreatic cancer		27.52	1.48	<12	<0.64	
	Colorectal cancer		>21.0	>1.13	<3.0	<0.16	
	Hepatic cancer		>10.0	>0.54	N/D	<0.16	
	Hodgkin lymphoma		>9.8	>0.53	3.0	0.16	
	Non-Hodgkin lymphoma		97.36	5.22	24.53	1.32	
	Lung cancer		16.09	0.86	5.1	0.27	
	B-cell lymphoma		12	0.64	6.3	0.34	
	Chronic lymphocytic leukemia		>10	>0.54	7.1	0.38	
	Psoriasis		>7.98	>0.43	<5.0	<0.28	
			>38.16	>2.05	32.55	1.75	
			21.4	1.15	9.2	0.49	
IL-20	Rheumatoid arthritis	Serum	26.0	1.39	18.0	0.97	[91]
	Psoriasis	Serum	74	3.97	<13.68	<0.73	[92]
	Non-small cell lung cancer	Serum	89.5±18.7	4.8±1	117.2±23.4	6.29±1.25	[93]
	Rheumatoid arthritis	Plasma	30.2 (19.1–58.5)	1.72 (1.09-3.34)	13.1 (11–15.1)	0.75 (0.63-0.86)	[94]

				(7.65-24.99)			
	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±150.7 59	4.27±9.00	2.358±2.486	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±19.11	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]
	Neurosypilis	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- ω 1	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].

Cytokine	PDB entry	Chain	Method	Comments
<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	IL-3	
P42,G43,F44,Y88,F89	M1,T2,E5,G9,D13,R17	Q11,W13,E14,V16,N17,Q20,E21,R23,R24,L28,K72, L115,F119	
S100P dimer		IL-5	
Chain B	Chain D	IL-5	
G43,Y88,F89,A92	M1,E5	Y13, S17,R43 ,L82,P83,C84,L85,P86,L87,A88,T89, N120	
S100P dimer		IL-9	
Chain B	Chain D	IL-9	
E40, P42,G43,C85,Y88,F89,A92	M1,T2,E5	T19, L20 ,A23,N24,Q54,V56,Q57	
S100P dimer		IL-13	
Chain B	Chain D	IL-13	
E3,C85,Y88,F89	M1,E5,G9,I12,D13,S16,R17	C3,Q115,K118,M122,R123,K125,I126	
S100P dimer		IL-15	
Chain B	Chain D	IL-15	
G43,F44,C85,F89	E5	P15,S16,T17,R74,G78,S90,N126	
S100P dimer			
Chain B	Chain D		

M1,E5,P42,F44,Y88,F89	M1,T2,E5,F44,Y88,F89,A92	N1,W2,V3,K10, D30,H32,P33,K36,S76,N77,N79,V80,T81,H105,Q108,M109,I111,N112,T113,S114
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
Interferons/IL-10		
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,A14 4,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,D11 3,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,R3 5,D140,R147,M148,M151,F155

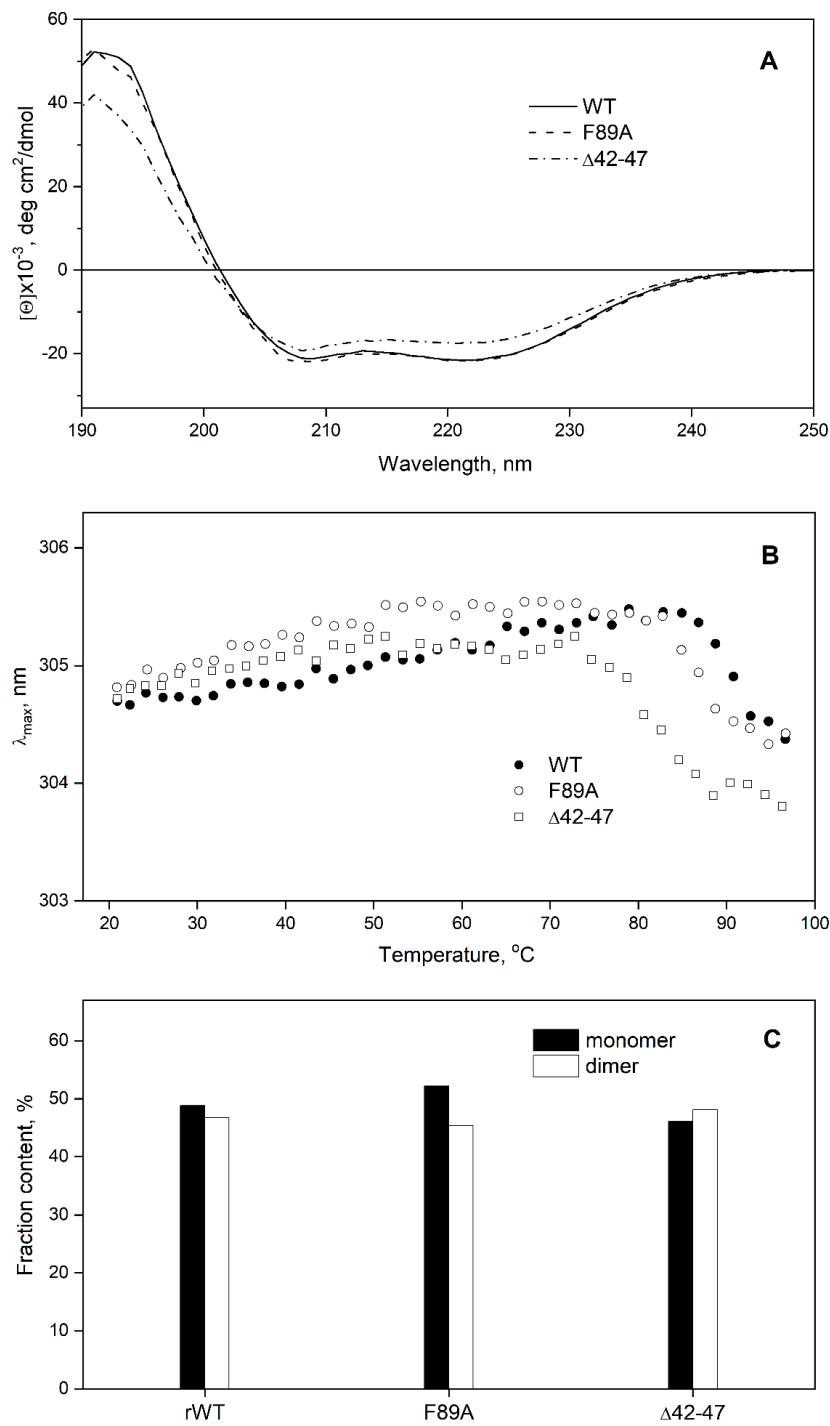


Figure S1. Comparison of structural properties of apo-forms of WT S100P and its F89A, Δ 42-47 mutants, using far-UV CD spectroscopy at 20°C (panel A), intrinsic fluorescence (B) and chemical crosslinking at 20 °C by 0.02% glutaraldehyde for 16 h (C) (10 mM

tricine-KOH, 1 mM EDTA-KOH, pH 7.4). Protein concentration was 10 µM (**A**, **B**) or 67 µM (**C**). Calcium depletion was performed according to ref. [113].

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