

Table S2: Individual performances of biomarkers classification of frailty groups (fitter older patients: G8>14 and frailer older patients: G8≤14). The table reports the number of patients (N) for which the biomarkers could be measured, as well as the area under the curve (AUC) via receiver operating characteristics (ROC), P-value (Wilcoxon rank-sum test) and log fold change (FC) for each biomarker. The log FC compared case vs. control. A positive log FC indicates that the measurement is higher than its reference while a negative measurement indicates that is smaller. Based on these statistics AUC, P-value, log FC scores were computed. The final score combines the 3 scores, where AUC weighted double. The biomarkers are ranked based on their final score.

	Blood markers	N	AUC	P-value	log FC	AUC score	P-value score	log FC score	Final score
1	NK-like T-cells	25	0.941	< 0.001	-1.623	1	1	6	2.25
2	TEMRA CD8 ⁺ CD57 ⁺ cells	25	0.860	0.003	-0.980	2	2	14	5.00
3	T-cell P16 ^{INK4a}	20	0.798	0.041	-1.937	7	8	4	6.50
4	TEMRA CD8 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.816	0.011	-0.897	5	5	17	8.00
5	CD8 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.816	0.011	-0.754	4	4	30	10.50
6	CD8 ⁺ CD57 ⁺ cells	25	0.846	0.005	-0.671	3	3	36	11.25
7	EM CD4 ⁺ CD57 ⁺ cells	25	0.743	0.057	-1.070	11	13	13	12.00
8	TEMRA CD8 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.243	0.044	0.771	10	9	26	13.75
9	TEMRA CD4 ⁺ CD57 ⁺ cells	25	0.728	0.076	-1.198	14	19	9	14.00
10	CD8 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.221	0.027	0.710	8	7	33	14.00
11	CD8 ⁺ CD28 ⁺ cells	25	0.191	0.013	0.629	6	6	43	15.25
12	CD4 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.721	0.086	-1.171	16	20	10	15.50
13	CD8 ⁺ CD27 ⁺ cells	25	0.243	0.044	0.652	9	10	38	16.50
14	CM CD8 ⁺ cells	25	0.279	0.086	0.902	17	21	16	17.75
15	CM CD8 ⁺ CD27 ⁺ cells	25	0.287	0.097	0.910	20	24	15	19.75
16	Gal-9	29	0.716	0.062	-0.656	18	15	37	22.00
17	CD4 ⁺ CD57 ⁺ cells	25	0.706	0.110	-1.077	25	28	12	22.50
18	TEMRA CD8 ⁺ CD27 ⁺ cells	25	0.257	0.057	0.512	12	14	53	22.75
19	Naive CD8 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.713	0.097	-0.756	21	22	28	23.00
20	CD4 ⁺ Tregs	25	0.287	0.097	0.735	19	23	32	23.25
21	CM CD8 ⁺ CD28 ⁺ cells	25	0.294	0.109	0.887	27	27	18	24.75
22	miR-9	29	0.342	0.056		45	12	1	25.75
23	EM CD4 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.684	0.153	-1.247	33	35	8	27.25
24	CM CD8 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.301	0.124	0.882	29	32	19	27.25
25	miR-20a	29	0.721	0.056	-0.359	15	11	69	27.50
26	TEMRA CD4 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.684	0.157	-1.086	34	36	11	28.75
27	CM CD4 ⁺ CD27 ⁺ cells	25	0.301	0.124	0.756	28	31	29	29.00
28	CD56 ^{bright} CD16 ⁻ NK-cells	25	0.301	0.123	0.693	30	30	34	31.00
29	TEMRA CD8 ⁺ cells	25	0.713	0.097	-0.503	22	25	55	31.00
30	sCD25	29	0.711	0.069	-0.448	23	17	61	31.00
31	CM CD4 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.309	0.140	0.753	31	34	31	31.75
32	miR-195	29	0.711	0.069	-0.426	24	18	62	32.00
33	CM CD4 ⁺ CD28 ⁺ cells	25	0.331	0.194	0.809	41	46	21	37.25
34	CM CD4 ⁺ cells	25	0.338	0.215	0.796	42	47	23	38.50
35	Naive CD8 ⁺ CD27 ⁺ cells	25	0.324	0.175	0.592	36	38	46	39.00
36	Naive CD8 ⁺ CD28 ⁺ cells	25	0.324	0.175	0.633	38	40	41	39.25
37	Naive CD8 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.324	0.175	0.606	37	39	44	39.25

38	CD4 ⁺ CD28 ⁺ cells	25	0.294	0.109	0.209	26	26	85	40.75
39	CD56 ^{dim} CD16 ⁺ NK-cells	25	0.735	0.066	-0.034	13	16	122	41.00
40	miR-92a	29	0.684	0.113	-0.313	32	29	72	41.25
41	TEMRA CD8 ⁺ CD28 ⁺ cells	25	0.324	0.175	0.542	39	41	49	42.00
42	miR-17	29	0.676	0.130	-0.490	40	33	57	42.50
43	Class-switched memory B-cells	25	0.676	0.175	-0.405	35	37	66	43.25
44	EM CD8 ⁺ CD28 ⁺ cells	25	0.338	0.215	0.582	44	49	47	46.00
45	Plasmacytoid dendritic cells	25	0.357	0.268	0.757	53	55	27	47.00
46	miR-223	29	0.658	0.176	-0.513	47	42	52	47.00
47	miR-126	29	0.653	0.191	-0.508	49	44	54	49.00
48	Naive CD4 ⁺ CD57 ⁺ cells	25	0.640	0.288	-0.801	58	59	22	49.25
49	Hematopoietic stem cells	25	0.357	0.262	0.636	52	53	40	49.25
50	miR-424	29	0.347	0.191	0.502	50	45	56	50.25
51	let-7e	29	0.358	0.224	0.597	55	50	45	51.25
52	CM CD4 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.621	0.323	-0.827	64	64	20	53.00
53	EM CD4 ⁺ cells	25	0.662	0.215	-0.247	43	48	80	53.50
54	Tregs	25	0.357	0.268	0.537	54	56	51	53.75
55	IP-10	29	0.658	0.179	-0.218	46	43	83	54.50
56	CD8 ⁺ cells	25	0.647	0.262	-0.416	51	54	64	55.00
57	EM CD8 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.371	0.322	0.677	62	63	35	55.50
58	TEMRA CD4 ⁺ cells	25	0.640	0.288	-0.449	56	57	60	57.25
59	Naive CD8 ⁺ cells	25	0.368	0.315	0.483	60	61	58	59.75
60	CD3 ⁺ cells	25	0.654	0.238	-0.147	48	52	91	59.75
61	miR-18a	29	0.379	0.302	0.538	65	60	50	60.00
62	IL-17A	29	0.613	0.335	-0.565	66	65	48	61.25
63	TIM-3	29	0.611	0.353	-0.630	69	69	42	62.25
64	B-cells	25	0.368	0.315	0.403	61	62	67	62.75
65	EM CD8 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.640	0.288	-0.249	57	58	79	62.75
66	EM CD8 ⁺ CD27 ⁺ cells	25	0.397	0.440	0.648	73	76	39	65.25
67	NK-cells	25	0.625	0.344	-0.306	63	66	73	66.25
68	miR-155	29	0.639	0.233	-0.105	59	51	102	67.75
69	CM CD8 ⁺ CD57 ⁺ cells	25	0.426	0.580	0.791	82	84	24	68.00
70	CRP	29	0.389	0.353	0.292	67	67	74	68.75
71	CM CD8 ⁺ CD27 ⁺ CD28 ⁻ cells	25	0.434	0.620	0.776	83	85	25	69.00
72	EM CD8 ⁺ cells	25	0.390	0.406	0.358	70	70	70	70.00
73	LAG-3	29	0.611	0.353	-0.285	68	68	76	70.00
74	CD4/CD8 Ratio	25	0.390	0.406	0.286	71	71	75	72.00
75	IL-17F	29	0.474	0.514		109	80	2	75.00
76	miR-150	29	0.592	0.435	-0.314	78	73	71	75.00
77	CD4 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.397	0.440	0.210	72	75	84	75.75
78	IL-1 α	29	0.592	0.435	-0.284	77	74	77	76.25
79	CD86	29	0.595	0.429	-0.239	76	72	81	76.25
80	4-1BB	29	0.542	0.566	-0.474	93	83	59	82.00
81	Naive Tregs	25	0.596	0.475	-0.108	75	78	100	82.00
82	Naive CD8 ⁺ CD57 ⁺ cells	25	0.581	0.549	-0.154	80	82	89	82.75

83	miR-21	29	0.576	0.520	-0.140	81	81	92	83.75
84	PD-1	29	0.524	0.854	1.433	110	110	7	84.25
85	miR-181a	29	0.582	0.491	0.095	79	79	108	86.25
86	Non-classical monocytes	25	0.559	0.669	-0.181	85	89	87	86.50
87	EM CD8 ⁺ CD57 ⁺ cells	25	0.603	0.440	-0.009	74	77	126	87.75
88	CD4 ⁺ cells	25	0.434	0.628	0.107	84	86	101	88.75
89	CTLA-4	29	0.492	0.931	2.020	122	121	3	92.00
90	miR-19a	29	0.458	0.731	0.147	94	92	90	92.50
91	CM CD4 ⁺ CD57 ⁺ cells	25	0.551	0.705	-0.098	88	90	107	93.25
92	MCP-1	29	0.447	0.663	0.072	87	88	113	93.75
93	sCD27	29	0.558	0.636	0.060	86	87	116	93.75
94	IGF-1	29	0.542	0.735	-0.113	92	93	99	94.00
95	Naive CD4 ⁺ CD27 ⁻ CD28 ⁻ cells	25	0.507	0.977	-1.714	125	123	5	94.50
96	IL-1 β	29	0.545	0.713	0.092	89	91	109	94.50
97	IL12p70	29	0.532	0.801	0.401	104	104	68	95.00
98	EM CD4 ⁺ CD27 ⁺ cells	25	0.544	0.754	-0.101	90	96	104	95.00
99	CD4 ⁺ CD27 ⁺ cells	25	0.463	0.798	0.126	98	99	96	97.75
100	TNF- α	29	0.539	0.747	0.099	96	94	105	97.75
101	TEMRA CD4 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.537	0.798	-0.130	100	101	93	98.50
102	let-7i	29	0.524	0.854	-0.405	111	111	65	99.50
103	Naive CD4 ⁺ CD27 ⁺ cells	25	0.544	0.754	-0.037	91	97	121	100.00
104	EM CD4 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.537	0.798	-0.103	99	100	103	100.25
105	Non-switched memory B-cells	25	0.529	0.842	0.228	106	109	82	100.75
106	PD-L2	29	0.463	0.769	0.083	97	98	111	100.75
107	Naive B-cells	25	0.463	0.798	0.117	102	103	97	101.00
108	TEMRA CD4 ⁺ CD27 ⁺ cells	25	0.533	0.816	-0.127	103	105	94	101.25
109	IL-8	29	0.461	0.748	0.010	95	95	124	102.25
110	IL-10	29	0.518	0.890	0.425	116	116	63	102.75
111	TEMRA CD4 ⁺ CD28 ⁺ cells	25	0.478	0.887	0.256	114	114	78	105.00
112	Monocytes	25	0.537	0.798	0.041	101	102	120	106.00
113	Memory Tregs	25	0.478	0.887	0.114	113	113	98	109.25
114	miR-19b	29	0.471	0.818	-0.067	108	107	114	109.25
115	miR-326	29	0.471	0.817	-0.054	107	106	118	109.50
116	Classical monocytes	25	0.471	0.842	0.012	105	108	123	110.25
117	IL-6	29	0.487	0.927	0.179	121	119	88	112.25
118	EM CD4 ⁺ CD28 ⁺ cells	25	0.522	0.887	-0.058	112	112	117	113.25
119	PD-L1	29	0.516	0.909	0.099	118	118	106	115.00
120	IL-27	29	0.505	0.982	0.196	126	127	86	116.25
121	Naive CD4 ⁺ CD27 ⁺ CD28 ⁺ cells	25	0.493	0.977	0.127	123	124	95	116.25
122	miR-125b	29	0.484	0.909	0.046	117	117	119	117.50
123	Naive CD4 ⁺ cells	25	0.522	0.887	0.010	115	115	125	117.50
124	Naive CD4 ⁺ CD28 ⁺ cells	25	0.485	0.932	0.079	119	122	112	118.00
125	Intermediate monocytes	25	0.493	0.977	0.062	124	125	115	122.00
126	Myeloid dendritic cells	25	0.485	0.930	-0.003	120	120	128	122.00
127	miR-146a	29	0.503	1.000	-0.092	128	128	110	123.50

128		IFN- γ			29		0.505		0.982		0.006		127		126		127		126.75
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