

# **SUPPLEMENTAL MATERIAL**

**Table S1. Patient characteristics of ACMP cases without heart failure and matched controls.**

<b>Characteristic</b>	<b>Controls (n=21)</b>	<b>ACMP cases (n=20)</b>
Male sex	8 (38.1)	11 (55.0)
Age at cancer diagnosis	7.39 [5.32, 10.40]	8.54 [3.10, 12.83]
Age at blood sampling	39.52 [32.81, 46.97]	34.48 [30.00, 43.41]
Time since cancer diagnosis	28.09 [22.22, 33.21]	21.44 [16.21, 27.06]
Anthracyclines	19 (90.5)	15 (75.0)
Anthracyclines cumulative dose*, mg/m <sup>2</sup>	288.60 [186.00, 400.00]	234.00 [72.00, 472.50]
Mitoxantrone	7 (33.3)	7 (35.0)
Mitoxantrone dose, mg/m <sup>2</sup>	50.00 [40.00, 102.00]	120.00 [50.00, 121.00]
Chest RT	2 (9.5)	1 (5.0)
Chest RT cumulative dose, Gray	20.00 [20.00, 20.00]	50.00 [50.00, 50.00]
Cardiac medication(s)	2 (9.5)	8 (40.0)
Hypercholesterolemia	1 (4.8)	1 (5.0)
Diabetes	0 (0.0)	0 (0.0)
Hypertension	0 (0.0)	1 (5.0)
Systolic blood pressure, mmHg	124.86 (15.92)	121.95 (21.07)
Diastolic blood pressure, mmHg	77.95 (10.26)	75.85 (16.85)
Heart rate, bpm	69.66 (14.93)	74.54 (12.31)
BMI, kg/m <sup>2</sup>	26.36 (4.59)	25.59 (5.24)
Biplane LVEF, %	57.66 (2.42)	41.28 (3.28)
LVIDd, cm	4.59 (0.61)	5.11 (0.68)

Categorical values are presented as number (%). Continuous values are presented as mean  $\pm$  standard deviation (sd) or as median [inter-quartile range]. \*Doxorubicin equivalents (Daunorubicin\*0.6 + epirubicin\*0.8 + idarubicin\*3). BMI=Body mass index, LVEF=left ventricular ejection fraction, LVIDd=left ventricular end diastolic diameter, chest RT=chest-directed radiotherapy.

**Table S2. Results of the multivariable linear regression analyses comparing plasma levels of 221 proteins between anthracycline-related cardiomyopathy (ACMP) cases and anthracycline-treated controls and between ACMP cases and dilated cardiomyopathy patients (DCM). Models were adjusted for sex, time since cancer diagnosis, anthracycline and chest-directed radiotherapy dose.**

Protein	Uniprot ID	ACMP - controls				ACMP - DCM		
		Fold change	p-value	q-value	Selected by elastic net	Fold change	p-value	q-value
NT-proBNP	NA	2.429	0.001	0.036	Forced	1.711	0.054	0.125
CCL19	Q99731	1.550	0.001	0.036	Yes	1.254	0.140	0.239
PTN	P21246	1.543	0.001	0.036	No	1.345	0.079	0.159
PSP-D	P35247	1.637	0.001	0.036	Yes	1.345	0.060	0.130
CCL20	P78556	1.995	0.003	0.086	Yes	1.562	0.105	0.195
JAM-A	Q9Y624	1.466	0.006	0.139	No	1.290	0.162	0.260
CCL16	O15467	1.448	0.008	0.144	Yes	1.427	0.014	0.057
CD40	P25942	1.270	0.009	0.144	No	1.121	0.326	0.433
CCL25	O15444	1.393	0.009	0.144	Yes	1.666	0.001	0.013
CXCL10	P02778	1.479	0.010	0.144	No	1.182	0.386	0.481
RARRES2	Q99969	1.222	0.011	0.144	Yes	1.376	0.000	0.005
CXCL9	Q07325	1.613	0.012	0.146	No	1.336	0.152	0.252
IL-6RA	P08887	1.225	0.015	0.168	Yes	1.190	0.045	0.112
FGF-21	Q9NSA1	2.173	0.016	0.168	Yes	3.666	0.001	0.017
SELP	P16109	1.301	0.018	0.169	Yes	1.352	0.024	0.074
CXCL11	O14625	1.383	0.018	0.169	No	1.230	0.213	0.313
GDF-15	Q99988	1.415	0.020	0.169	No	1.254	0.193	0.297
VEGFA	P15692	1.233	0.021	0.169	No	1.188	0.071	0.150
NUCB2	P80303	1.270	0.026	0.189	No	1.411	0.004	0.024
CHIT1	Q13231	1.689	0.027	0.189	No	1.329	0.114	0.205
CXCL6	P80162	1.282	0.030	0.189	No	1.247	0.074	0.155
CA14	Q9ULX7	0.805	0.030	0.189	Yes	1.528	0.000	0.002
IL-17A	Q16552	1.303	0.031	0.189	Yes	0.979	0.894	0.911
ENTPD2	Q9Y5L3	1.207	0.032	0.189	No	1.127	0.166	0.261
TNFRSF9	Q07011	1.296	0.033	0.189	No	1.428	0.007	0.038
PON2	Q15165	1.179	0.036	0.189	Yes	1.273	0.013	0.057
SIRT2	Q8IXJ6	1.664	0.037	0.189	Yes	1.307	0.325	0.433
NOS3	P29474	1.227	0.038	0.189	Yes	0.974	0.840	0.876
STX8	Q9UNK0	1.293	0.038	0.189	No	1.137	0.382	0.481
AIFM1	O95831	1.584	0.039	0.189	Yes	1.154	0.584	0.672
CSTB	P04080	1.370	0.040	0.189	No	1.284	0.120	0.211
PON3	Q15166	0.754	0.041	0.189	No	1.165	0.250	0.360
IL8	P10145	1.275	0.046	0.189	No	1.285	0.060	0.130
MCP-1	P13500	1.202	0.049	0.189	No	1.330	0.005	0.027
t-PA	P00750	1.240	0.051	0.189	No	1.547	0.001	0.015
FABP4	P15090	1.517	0.051	0.189	No	1.194	0.415	0.503
MMP-1	P03956	1.414	0.052	0.189	Yes	1.223	0.351	0.453
CPB1	P15086	1.310	0.053	0.189	No	1.037	0.825	0.864

SERPINA9	Q86WD7	1.289	0.053	0.189	Yes	1.205	0.329	0.435
CTSD	P07339	1.188	0.053	0.189	Yes	1.345	0.003	0.021
IL-12B	P29460	1.274	0.054	0.189	No	1.027	0.869	0.897
EPO	P01588	1.413	0.055	0.189	Yes	1.176	0.437	0.516
CCL24	O00175	0.721	0.058	0.189	No	1.122	0.603	0.690
HGF	P14210	1.197	0.059	0.189	No	1.400	0.002	0.021
IGFBP-7	Q16270	1.242	0.059	0.189	No	1.560	0.001	0.017
IL6	P05231	1.583	0.062	0.189	No	1.555	0.091	0.174
MEPE	Q9NQ76	1.241	0.063	0.189	Yes	1.355	0.019	0.065
NT-3	P20783	1.226	0.064	0.189	No	1.145	0.246	0.357
4E-BP1	Q13541	1.724	0.065	0.189	No	1.088	0.799	0.841
vWF	P04275	1.385	0.066	0.189	No	1.385	0.047	0.112
CASP-3	P42574	1.467	0.067	0.189	Yes	1.261	0.343	0.445
STAMBP	O95630	1.411	0.067	0.189	No	1.262	0.258	0.368
YES1	P07947	1.457	0.068	0.189	No	0.899	0.652	0.717
CDCP1	Q9H5V8	1.205	0.081	0.220	No	1.602	0.000	0.005
LRP1	Q07954	1.140	0.082	0.220	Yes	1.224	0.021	0.068
TNF	P01375	1.167	0.084	0.220	No	1.143	0.163	0.260
MVK	Q03426	1.313	0.085	0.220	Yes	1.087	0.633	0.709
Flt3L	P49771	1.136	0.087	0.221	Yes	1.275	0.014	0.057
BAMBI	Q13145	1.203	0.094	0.228	No	1.258	0.114	0.205
MAP4K5	Q9Y4K4	1.469	0.095	0.228	No	0.894	0.650	0.717
U-PAR	Q03405	1.170	0.099	0.228	No	1.338	0.004	0.026
GP6	Q9HCN6	1.161	0.102	0.228	No	1.105	0.372	0.471
MAEA	Q7L5Y9	1.199	0.103	0.228	No	1.093	0.636	0.709
MCP-1	P13500	1.159	0.103	0.228	No	1.310	0.006	0.032
ST1A1	P50225	1.340	0.105	0.228	Yes	1.188	0.430	0.514
PTPRJ	Q12913	1.309	0.105	0.228	No	1.375	0.075	0.156
DNER	Q8NFT8	0.906	0.106	0.228	No	1.132	0.106	0.195
uPA	P00749	1.131	0.106	0.228	No	1.358	0.000	0.005
TRANCE	O14788	1.259	0.107	0.228	Yes	1.238	0.146	0.248
PAI	P05121	1.326	0.115	0.238	No	1.794	0.003	0.021
PECAM-1	P16284	1.154	0.118	0.238	No	1.227	0.064	0.137
SCGB3A2	Q96PL1	1.329	0.123	0.238	No	1.291	0.195	0.298
LAP TGF-beta-1	P01137	1.135	0.124	0.238	No	1.351	0.002	0.018
IL2-RA	P01589	1.183	0.125	0.238	No	1.231	0.100	0.188
PRKRA	O75569	1.154	0.127	0.238	No	1.141	0.200	0.302
CCL15	Q16663	1.226	0.127	0.238	No	1.313	0.079	0.159
PD-L1	Q9NZQ7	1.124	0.128	0.238	No	1.192	0.063	0.136
RARRES1	P49788	1.066	0.128	0.238	Yes	1.064	0.211	0.313
PI3	P19957	1.184	0.129	0.238	No	1.321	0.017	0.062
TNFRSF14	Q92956	1.145	0.132	0.238	No	1.290	0.011	0.049
TIGAR	Q9NQ88	1.141	0.132	0.238	No	1.146	0.336	0.441
AXIN1	O15169	1.322	0.142	0.253	No	0.993	0.973	0.973
CASP-8	Q14790	1.236	0.147	0.259	No	1.979	0.000	0.002

IL10	P22301	1.309	0.149	0.260	No	1.423	0.105	0.195
TWEAK	O43508	0.892	0.154	0.265	Yes	1.045	0.609	0.693
LAT2	Q9GZY6	1.245	0.159	0.271	No	0.874	0.437	0.516
CD244	Q9BZW8	1.104	0.164	0.275	No	1.238	0.009	0.044
PTK7	Q13308	1.136	0.174	0.286	No	1.248	0.056	0.129
TNFSF13B	Q9Y275	1.131	0.174	0.286	No	1.235	0.015	0.058
CSF-1	P09603	1.082	0.176	0.286	No	1.146	0.047	0.112
INPPL1	O15357	1.227	0.179	0.288	No	1.082	0.656	0.717
CCL11	P51671	1.125	0.181	0.288	No	1.207	0.080	0.159
FOXO1	Q12778	1.149	0.194	0.305	No	1.105	0.415	0.503
TOP2B	Q02880	1.155	0.199	0.310	No	1.297	0.026	0.078
EGFR	P00533	0.927	0.212	0.326	No	1.175	0.003	0.021
TNFRSF10C	O14798	0.868	0.222	0.331	Yes	1.126	0.310	0.420
PLIN1	O60240	1.220	0.223	0.331	No	1.266	0.165	0.261
FABP9	Q0Z7S8	1.152	0.223	0.331	No	1.214	0.150	0.250
CD163	Q86VB7	1.133	0.224	0.331	No	1.456	0.004	0.025
PVALB	P20472	1.432	0.226	0.331	No	1.178	0.615	0.697
BANK1	Q8NDB2	1.264	0.232	0.331	No	1.023	0.912	0.922
KIM1	Q96D42	1.191	0.234	0.331	No	1.587	0.020	0.065
BID	P55957	1.174	0.236	0.331	No	1.235	0.116	0.208
CX3CL1	P78423	0.896	0.239	0.331	Yes	1.134	0.262	0.371
KLK6	Q92876	1.119	0.240	0.331	No	1.391	0.002	0.018
SLAMF1	Q13291	1.184	0.242	0.331	No	1.400	0.021	0.068
MB	P02144	1.154	0.243	0.331	No	1.237	0.162	0.260
FAS	P25445	1.099	0.244	0.331	No	1.334	0.002	0.018
TNF-R1	P19438	1.134	0.248	0.333	No	1.413	0.005	0.027
CPA1	P15085	1.183	0.253	0.337	No	1.171	0.393	0.485
TFPI	P10646	1.105	0.259	0.342	Yes	1.434	0.000	0.009
CAPG	P40121	1.198	0.268	0.350	No	1.741	0.001	0.013
SCF	P21583	0.906	0.275	0.357	Yes	1.168	0.191	0.296
TR	P02786	0.886	0.284	0.365	Yes	1.225	0.083	0.161
FOSB	P53539	0.824	0.304	0.387	Yes	1.071	0.646	0.717
ST2	Q01638	1.099	0.310	0.391	No	1.595	0.000	0.003
CNTN1	Q12860	0.917	0.314	0.393	No	1.244	0.011	0.050
CA12	O43570	0.923	0.324	0.403	Yes	1.238	0.020	0.065
GRN	P28799	1.081	0.329	0.405	No	1.304	0.002	0.021
HPGDS	O60760	0.933	0.333	0.407	No	1.145	0.096	0.182
IL-17C	Q9P0M4	1.181	0.341	0.409	No	0.809	0.341	0.445
CD5	P06127	1.071	0.342	0.409	No	1.169	0.079	0.159
TFF3	Q07654	1.224	0.343	0.409	No	1.068	0.750	0.800
OPN	P10451	1.141	0.349	0.412	No	1.353	0.060	0.130
NPPC	P23582	1.186	0.353	0.414	No	1.185	0.456	0.535
CXCL1	P09341	1.157	0.356	0.414	No	0.854	0.427	0.512
IL-18BP	O95998	1.083	0.361	0.414	No	1.360	0.003	0.021
CALR	P27797	1.087	0.362	0.414	No	0.891	0.310	0.420

CTSZ	Q9UBR2	1.100	0.364	0.414	No	1.326	0.016	0.060
IFN-gamma	P01579	1.258	0.373	0.420	No	1.997	0.004	0.025
PCSK9	Q8NBP7	1.066	0.380	0.425	No	1.395	0.000	0.003
EGFL7	Q9UHF1	1.080	0.384	0.427	No	1.113	0.304	0.416
Ep-CAM	P16422	0.828	0.396	0.437	No	1.728	0.018	0.064
AMN	Q9BXJ7	1.203	0.405	0.443	No	1.095	0.496	0.576
SELE	P16581	1.115	0.415	0.449	No	1.400	0.036	0.098
CXCL16	Q9H2A7	1.077	0.420	0.449	No	1.338	0.003	0.021
LTBR	P36941	1.079	0.422	0.449	No	1.194	0.121	0.211
AP-N	P15144	1.078	0.423	0.449	No	1.250	0.018	0.064
ITGB2	P05107	1.057	0.434	0.454	No	1.255	0.007	0.038
PLXDC1	Q8IUUK5	0.952	0.434	0.454	No	1.079	0.371	0.471
PDGF subunit A	P04085	1.089	0.437	0.454	No	1.070	0.625	0.704
PLC	P98160	1.071	0.440	0.454	No	1.221	0.040	0.104
LIF-R	P42702	1.051	0.448	0.460	No	1.270	0.003	0.021
IL-10RB	Q08334	1.064	0.459	0.463	No	1.339	0.001	0.017
ADA	P00813	1.070	0.460	0.463	No	0.985	0.879	0.900
TNF-R2	P20333	1.079	0.467	0.463	No	1.290	0.036	0.098
MCP-4	Q99616	0.918	0.470	0.463	No	1.116	0.398	0.489
Gal-4	P56470	1.085	0.477	0.463	No	1.318	0.037	0.099
FGR	P09769	1.071	0.477	0.463	No	0.751	0.009	0.044
PGF	P49763	1.059	0.477	0.463	No	1.217	0.035	0.098
CCL3	P10147	1.127	0.478	0.463	No	1.457	0.008	0.040
CDH5	P33151	1.063	0.480	0.463	No	1.160	0.080	0.159
GALNT10	Q86SR1	1.043	0.492	0.472	No	1.202	0.014	0.057
MCP-2	P80075	1.092	0.503	0.479	No	1.360	0.048	0.112
SHPS-1	P78324	1.063	0.509	0.480	No	1.373	0.001	0.017
DSG4	Q86SJ6	1.099	0.509	0.480	No	1.199	0.157	0.256
TGF-alpha	P01135	1.047	0.523	0.486	No	1.065	0.390	0.484
BLM hydrolase	Q13867	1.052	0.524	0.486	No	1.119	0.198	0.302
PGLYRP1	O75594	1.078	0.526	0.486	No	1.323	0.032	0.092
CLEC1A	Q8NC01	1.064	0.540	0.493	No	1.279	0.029	0.086
MPO	P05164	0.947	0.546	0.493	No	1.148	0.131	0.226
ENAH	Q8N8S7	1.048	0.547	0.493	No	1.089	0.292	0.403
CD6	P30203	1.063	0.552	0.493	No	1.165	0.167	0.261
NCF2	P19878	1.111	0.554	0.493	No	0.930	0.713	0.764
IGFBP-1	P08833	0.872	0.556	0.493	Yes	2.391	0.001	0.017
IL-1RT1	P14778	1.047	0.557	0.493	No	1.307	0.001	0.017
CNTN2	Q02246	1.056	0.561	0.493	No	1.313	0.008	0.041
EN-RAGE	P80511	1.094	0.565	0.494	No	1.447	0.059	0.130
MMP-3	P08254	0.935	0.573	0.498	No	1.381	0.019	0.065
IL18	Q14116	1.067	0.590	0.510	No	1.321	0.054	0.125
ICAM-2	P13598	1.045	0.593	0.510	Yes	1.272	0.003	0.023
Notch 3	Q9UM47	0.950	0.599	0.511	Yes	1.293	0.018	0.065
Gal-3	P17931	1.048	0.612	0.520	No	1.167	0.081	0.160

ALDH3A1	P30838	1.089	0.635	0.531	No	1.297	0.137	0.235
CCL28	Q9NRJ3	0.962	0.636	0.531	No	1.118	0.312	0.420
IL-1RT2	P27930	0.962	0.637	0.531	No	1.263	0.004	0.025
CXCL5	P42830	1.132	0.639	0.531	No	0.915	0.776	0.821
MMP-9	P14780	0.931	0.646	0.534	No	1.142	0.421	0.507
RETN	Q9HD89	0.959	0.651	0.535	Yes	1.155	0.205	0.307
TNFSF14	O43557	1.046	0.661	0.539	No	1.236	0.039	0.102
CST5	P28325	0.954	0.671	0.545	Yes	1.076	0.580	0.671
OSM	P13725	0.933	0.680	0.549	No	1.228	0.276	0.388
FGF-19	O95750	1.066	0.687	0.551	No	0.651	0.031	0.089
MMP-2	P08253	0.966	0.689	0.551	Yes	1.255	0.014	0.057
IL-18R1	Q13478	1.031	0.715	0.566	No	1.110	0.255	0.365
TNNI3	P19429	1.127	0.716	0.566	No	0.890	0.755	0.802
IGFBP-2	P18065	1.049	0.761	0.596	Yes	1.547	0.016	0.060
TMPRSS15	P98073	0.948	0.762	0.596	No	1.024	0.913	0.922
PDCD1	Q15116	1.023	0.772	0.599	No	1.062	0.659	0.717
COL1A1	P02452	1.027	0.777	0.599	No	1.266	0.027	0.080
CCL4	P13236	1.048	0.780	0.599	No	1.516	0.002	0.021
PDGFC	Q9NRA1	0.981	0.782	0.599	No	1.081	0.280	0.391
CD93	Q9NPY3	1.024	0.794	0.605	No	1.279	0.010	0.046
CRH	P06850	0.957	0.804	0.610	No	0.657	0.059	0.130
CD8A	P01732	1.032	0.832	0.625	No	1.138	0.481	0.562
CALCA	P01258	0.961	0.833	0.625	No	1.222	0.367	0.470
EPHB4	P54760	1.016	0.840	0.627	Yes	1.256	0.010	0.047
CCL23	P55773	1.018	0.863	0.634	No	1.153	0.218	0.319
AGR2	O95994	0.971	0.865	0.634	No	1.268	0.207	0.309
ST3GAL1	Q11201	1.017	0.866	0.634	No	1.136	0.282	0.391
TRAIL	P50591	0.989	0.870	0.634	No	0.989	0.874	0.898
TNFB	P01374	1.016	0.871	0.634	No	1.046	0.688	0.742
OPG	O00300	1.013	0.878	0.634	No	1.267	0.020	0.065
DLK-1	P80370	1.023	0.880	0.634	No	1.497	0.026	0.078
AZU1	P20160	0.978	0.885	0.635	No	1.247	0.155	0.254
ALCAM	Q13740	1.011	0.891	0.635	No	1.284	0.001	0.017
TIMP4	Q99727	0.989	0.896	0.635	No	0.962	0.680	0.736
TR-AP	P13686	0.988	0.901	0.635	No	1.177	0.088	0.170
IL-17RA	Q96F46	0.987	0.903	0.635	No	1.272	0.041	0.106
NBN	O60934	0.985	0.907	0.635	No	1.113	0.384	0.481
AXL	P30530	1.008	0.921	0.642	No	1.226	0.035	0.098
LDL receptor	P01130	1.013	0.932	0.647	No	1.438	0.039	0.102
PRTN3	P24158	1.007	0.948	0.655	No	1.225	0.047	0.112
MMP-10	P09238	0.994	0.964	0.661	No	1.258	0.120	0.211
CHI3L1	P36222	0.994	0.966	0.661	Yes	1.468	0.031	0.089
ENTPD6	O75354	1.003	0.970	0.661	No	1.112	0.147	0.248
IL7	P13232	0.996	0.978	0.663	No	1.019	0.862	0.894
TLT-2	Q5T2D2	1.001	0.990	0.664	No	1.211	0.045	0.112

RASSF2	P50749	1.001	0.992	0.664	No	1.007	0.954	0.958
DPP6	P42658	1.000	0.998	0.664	No	1.213	0.046	0.112
OPG	O00300	1.000	0.998	0.664	No	1.312	0.008	0.040



**Table S3. Sensitivity analyses comparing plasma protein expression of ACMP cases with controls.**

<b>Protein</b>	<b>Adjusted for NT-proBNP<sup>1</sup></b>		<b>Analysis in 20 ACMP cases without heart failure<sup>2</sup></b>	
	<b>Fold change</b>	<b>p-value</b>	<b>Fold change</b>	<b>p-value</b>
NT-proBNP	-	-	1.24	0.231
CCL19	1.45	0.010	1.61	0.002
CCL20	1.72	0.037	1.64	0.025
PSPD	1.52	0.012	1.88	<0.001
PTN	1.30	0.047	1.35	0.033

1: Linear regression model adjusted for sex, time since cancer diagnosis, anthracycline dose, chest-directed radiotherapy dose and NT-proBNP. 2: Linear regression in 20 asymptomatic cases compared to their matched controls, adjusted for sex, time since cancer diagnosis, anthracycline dose, chest-directed radiotherapy dose. CCL19=C-C motif chemokine ligand 19, CCL20=C-C motif chemokine ligand 20, NT-proBNP=N-terminal pro-B-type natriuretic peptide, PSPD=Pulmonary surfactant protein D, PTN=Pleiotrophin.