					Extracellular only	
Experiment	**# identified MS/MS spectra**	**# unique peptides with a validated L/H ratio**	**# unique proteins**	**# unique proteins (2 or more peptides)**	**# unique proteins**	**# unique proteins (2 or more peptides)**
Patient 1	9025	1004	310	192	129	106
Patient 2	9870	1722	392	275	190	249
Patient 1 (Met-COFRADIC)	20157	3133	1331	644	309	186

Supporting Information Table S2. Coverage of myofibroblast secretomes following light or heavy SILAC labelling of cancer-derived myofibroblasts (CAMs) and adjacent tissue myofibroblasts (ATMs). Only peptides with validated SILAC ratios were counted. Pairs of CAM/ATMs were analysed from two patients using a shotgun approach; one (Patient 1) was also analysed by Met-COFRADIC.

Uniprot accession	Protein name	Functional Classification	Patient 1	Patient 2	Patient 1 (Met-COFRADIC)
Q6FHJ7	Secreted frizzled-related protein 4	binding protein	2 ATM singletons	1.38	-665.02
O14498	Immunoglobulin superfamily containing leucine-rich repeat protein	binding protein			-620.38
Q6UXB8	Peptidase inhibitor 16	protease inhibitor	5 ATM singletons	4.57	-441.00
Q6WRI0	Immunoglobulin superfamily member 10	binding protein			-378.04
P26927	Hepatocyte growth factor-like protein	ligand			-309.08
P00734	Prothrombin	protease			-187.31
Q8IWU6	Extracellular sulfatase Sulf-1	enzyme			-84.16
Q13361	Microfibrillar-associated protein 5	binding protein		-1.17	-82.21
P39059	Collagen alpha-1(XV) chain	ECM			-81.18
P49747	Cartilage oligomeric matrix protein	binding protein	-23.47	-1.07	-61.29
P21810	Biglycan	binding protein		-3.46	-41.36
Q9NQ30	Endothelial cell-specific molecule 1	receptor			-41.07
P36222	Chitinase-3-like protein 1	binding protein		-1.27	-40.78
P05155	Plasma protease C1 inhibitor	binding protein	-9.14		-29.16
Q8N6G6	ADAMTS-like protein 1	protease			-27.96
Q13753	Laminin subunit gamma-2	ECM			-25.64
P10124	Serglycin	binding protein			-23.88
P17936	Insulin-like growth factor-binding protein 3	binding protein	-6.51	2.28	-19.83
Q86Y38	Xylosyltransferase 1	enzyme		-1.69	-19.59
P00742	Coagulation factor X	protease			-19.34
O75326	Semaphorin-7A	receptor		1.14	-17.92
P26022	Pentraxin-related protein PTX3	binding protein		-2.42	-17.33
P00813	Adenosine deaminase	enzyme			-17.02
P24592	Insulin-like growth factor-binding protein	binding protein	-9.06	-1.53	-14.07

	6				
P02452	Collagen alpha-1(I) chain	ECM	-4.52	-3.38	-13.53
P22105	Tenascin-X	binding protein		-20388.71	-13.53
P49788	Retinoic acid receptor responder protein 1	receptor	-12.92	-1.80	-13.08
Q14767	Latent-transforming growth factor beta-binding protein 2	binding protein	-4.08	-1.84	-10.53
Q96CG8	Collagen triple helix repeat-containing protein 1	ECM			-10.10
P98095	Fibulin-2	ECM			-9.69
P02751	Fibronectin	ECM	-4.32	-1.71	-8.54
P08294	Extracellular superoxide dismutase [Cu-Zn]	enzyme		-1.34	-8.51
Q9UJ72	Annexin A10	immune system			-7.98
P23142	Fibulin-1	ECM	-3.33	1.32	-7.84
Q9UGI8	Testin	binding protein			-7.81
P12821	Angiotensin-converting enzyme	protease			-7.76
P09486	SPARC	binding protein	-7.12	-2.17	-7.76
Q02388	Collagen alpha-1(VII) chain	ECM		-1.09	-7.31
P51884	Lumican	binding protein	-4.31	1.01	-7.25
P20908	Collagen alpha-1(V) chain	ECM		-3.14	-6.74
Q8IUX7	Adipocyte enhancer-binding protein 1	binding protein		-2.90	-6.00
O43852	Calumenin	other	-2.29	-2.13	-5.94
P05121	Plasminogen activator inhibitor 1	protease inhibitor	-9.45	1.43	-5.63
Q9UM47	Neurogenic locus notch homolog protein 3	receptor			-5.48
Q15063	Periostin	ECM		-7.48	-5.25
P55268	Laminin subunit beta-2	ECM		-2.82	-5.19
P09668	Cathepsin H	protease			-5.07
P24821	Tenascin	ligand		-3.18	-5.03
Q99985	Semaphorin-3C	receptor			-4.94
P07093	Glia-derived nexin	protease inhibitor	-5.32	1.21	-4.89
Q14112	Nidogen-2	binding protein		-1.28	-4.85
P08123	Collagen alpha-2(I) chain	ECM	-4.49	-1.73	-4.79
P13611	Versican core protein	ECM	-3.83	-1.60	-4.77

P08603	Complement factor H	immune system		1.80	-4.60
P02461	Collagen alpha-1(III) chain	ECM	-4.39	-2.74	-4.57
Q8N436	Carboxypeptidase-like protein X2	protease			-4.43
Q9UM22	Mammalian ependymin-related protein 1	binding protein			-4.37
Q76M96	Coiled-coil domain-containing protein 80	binding protein	-3.39	-1.52	-4.24
Q08431	Lactadherin	ligand			-4.22
P01891	HLA class I histocompatibility antigen, A-68 alpha chain	immune system			-3.99
P28300	Protein-lysine 6-oxidase	enzyme	-2.67	-1.39	-3.78
P98160	Basement membrane-specific heparan sulfate proteoglycan core protein	ECM	-2.60	1.31	-3.70
Q9NRN5	Olfactomedin-like protein 3	unknown		-1.55	-3.65
Q92520	Protein FAM3C	ligand		1.15	-3.64
A1L4H1	Scavenger receptor cysteine-rich domain-containing protein LOC284297	other			-3.62
P13521	Secretogranin-2	ligand	-2.17	3.17	-3.59
P19022	Cadherin-2	binding protein			-3.59
O95897	Noelin-2	unknown			-3.58
P10909	Clusterin	unknown	-4.24	-1.24	-3.51
Q15828	Cystatin-M	binding protein			-3.49
Q9NS15	Latent-transforming growth factor beta-binding protein 3	binding protein			-3.47
Q5JTB6	Placenta-specific protein 9	unknown			-3.33
P35555	Fibrillin-1	ECM	-3.04	-1.12	-3.25
P08476	Inhibin beta A chain	ligand	-2.56	-2.33	-3.24
P24043	Laminin subunit alpha-2	ECM	-1.38	2.46	-3.21
P01033	Metalloproteinase inhibitor 1	protease inhibitor	-3.06	-1.18	-3.18
Q7Z7M0	Multiple epidermal growth factor-like domains 8	unknown			-3.16
P55058	Phospholipid transfer protein	binding protein		1.16	-3.07
P01034	Cystatin-C	protease inhibitor	-3.17	-1.02	-3.05
P13497	Bone morphogenetic protein 1	protease	-2.33	-1.54	-3.00
P01892	HLA class I histocompatibility antigen,	immune			-2.96

	A-2 alpha chain	system			
Q9BQJ4	Transmembrane protein 47	unknown			-2.94
Q08629	Testican-1	binding protein	-2.56	-1.20	-2.91
Q08380	Galectin-3-binding protein	binding protein	-1.92	-1.27	-2.91
P24593	Insulin-like growth factor-binding protein 5	binding protein	-4.30	1.19	-2.85
Q15389	Angiopoietin-1	ligand			-2.81
O60687	Sushi repeat-containing protein SRPX2	binding protein	-2.06	1.04	-2.76
P00750	Tissue-type plasminogen activator	protease	1.63	2.90	-2.76
Q9BXJ0	Complement C1q tumor necrosis factor-related protein 5	other			-2.69
Q12841	Follistatin-related protein 1	binding protein	-1.09	-1.66	-2.67
P36955	Pigment epithelium-derived factor	binding protein	-1.25	-3.35	-2.65
Q99470	Stromal cell-derived factor 2	ligand			-2.65
P54764	Ephrin type-A receptor 4	receptor			-2.63
P02649	Apolipoprotein E	ligand	4 CAM singletons		-2.60
Q08397	Lysyl oxidase homolog 1	enzyme			-2.59
O15072	A disintegrin and metalloproteinase with thrombospondin motifs 3	protease			-2.56
P12109	Collagen alpha-1(VI) chain	ECM	-2.45	-1.01	-2.53
O00391	Sulfhydryl oxidase 1	enzyme	-1.49	1.27	-2.47
P05997	Collagen alpha-2(V) chain	ECM	-3.34	-2.23	-2.47
P80303	Nucleobindin-2	binding protein	-1.76	-1.05	-2.43
P07711	Cathepsin L1	protease		-2.13	-2.33
P08572	Collagen alpha-2(IV) chain	ECM	-1.80	-2.17	-2.31
P12111	Collagen alpha-3(VI) chain	ECM		-2.36	-2.30
O75718	Cartilage-associated protein	binding protein			-2.29
P06396	Gelsolin	binding protein	1.08	-1.07	-2.27
Q05707	Collagen alpha-1(XIV) chain	ECM	1.83	-1.91	-2.26
P15692	Vascular endothelial growth factor A	ligand			-2.26
P22064	Latent-transforming growth factor beta-binding protein, isoform 1S	binding protein			-2.20
P49908	Selenoprotein P	binding protein			-2.05
Q9Y4K0	Lysyl oxidase homolog 2	enzyme	-1.65	1.00	-2.05
Q6NW40	RGM domain family member B	other			-2.04
Q12884	Seprase	protease			-2.03
Q9NUM4	Transmembrane protein 106B	unknown			-2.00

P51858	Hepatoma-derived growth factor	ligand			-1.98
P69849	Nodal modulator 3	binding protein			-1.93
P07339	Cathepsin D	protease			-1.92
Q13219	Pappalysin-1	protease		-1.31	-1.92
P07996	Thrombospondin-1	ECM	1.25	-3.09	-1.83
P11047	Laminin subunit gamma-1	ECM	-1.25	-1.24	-1.81
O75487	Glypican-4	other			-1.81
Q9HB40	Retinoid-inducible serine carboxypeptidase	protease			-1.79
Q9BRK5	45 kDa calcium-binding protein	ligand	-1.36	-1.44	-1.78
Q96GP6	Scavenger receptor class F member 2	other			-1.77
P07237	Protein disulfide-isomerase	enzyme	1.54	1.31	-1.77
P20073	Annexin A7	immune system			-1.77
Q96RW7	Hemicentin-1	binding protein			-1.76
O94856	Neurofascin	binding protein			-1.75
P57087	Junctional adhesion molecule B	binding protein			-1.74
Q9H4A4	Aminopeptidase B	protease			-1.73
Q16363	Laminin subunit alpha-4	ECM	-1.47	-1.27	-1.73
Q9Y6Z7	Collectin-10	binding protein	-1.43		-1.73
Q92743	Serine protease HTRA1	protease	1.15	-1.50	-1.73
Q9Y2E5	Epididymis-specific alpha-mannosidase	enzyme			-1.73
P10646	Tissue factor pathway inhibitor	protease inhibitor		1.01	-1.72
P28799	Granulins	ligand			-1.68
P08648	Integrin alpha-5	receptor			-1.67
P16035	Metalloproteinase inhibitor 2	protease inhibitor	-1.57	-1.54	-1.66
P40189	Interleukin-6 receptor subunit beta	receptor			-1.66
P07942	Laminin subunit beta-1	ECM	-1.26	-1.01	-1.65
O95980	Reversion-inducing cysteine-rich protein with Kazal motifs	protease inhibitor			-1.62
Q969H8	UPF0556 protein C19orf10	ligand		1.08	-1.61
Q6UXH8	Collagen and calcium-binding EGF domain-containing protein 1	binding protein			-1.60
P53621	Coatomer subunit alpha	binding protein			-1.59
P12110	Collagen alpha-2(VI) chain	ECM	-1.65	-1.01	-1.59

O60330	Protocadherin gamma-A12	binding protein			-1.59
Q13214	Semaphorin-3B	receptor			-1.59
Q8TER0	Sushi, nidogen and EGF-like domain-containing protein 1	unknown			-1.59
P07585	Decorin	ECM	-1.27	1.18	-1.57
Q9Y646	Plasma glutamate carboxypeptidase	protease	1.64	-2.04	-1.57
O75882	Attractin	receptor			-1.57
Q16270	Insulin-like growth factor-binding protein 7	binding protein	-1.41	-1.11	-1.56
P34741	Syndecan-2	receptor			-1.55
P01137	Transforming growth factor beta-1	ligand			-1.53
P15151	Poliovirus receptor	receptor			-1.52
O15031	Plexin-B2	receptor			-1.51
Q16610	Extracellular matrix protein 1	ECM	-1.03	-1.59	-1.49
P00736	Complement C1r subcomponent	protease	-1.15	-1.52	-1.48
O95450	A disintegrin and metalloproteinase with thrombospondin motifs 2	protease			-1.48
P78539	Sushi repeat-containing protein SRPX	other			-1.48
Q9UBX1	Cathepsin F	protease			-1.48
A6NMY6	Putative annexin A2-like protein	immune system	1.22	1.48	-1.46
P30740	Leukocyte elastase inhibitor	protease inhibitor			-1.46
P09871	Complement C1s subcomponent	protease	-1.30	1.34	-1.45
Q9Y625	Glypican-6	other			-1.44
P07858	Cathepsin B	protease	1.70	2.29	-1.43
Q04721	Neurogenic locus notch homolog protein 2	receptor			-1.42
P14174	Macrophage migration inhibitory factor	ligand		1.50	-1.41
Q9P0L0	Vesicle-associated membrane protein-associated protein A	binding protein			-1.39
O95967	EGF-containing fibulin-like extracellular matrix protein 2	binding protein		1.23	-1.38
Q99715	Collagen alpha-1(XII) chain	ECM	-1.90	-1.25	-1.38
P04083	Annexin A1	immune system	2.00	1.50	-1.35
Q9Y240	C-type lectin domain family 11 member A	ligand	-2.02	1.02	-1.33

O75629	Protein CREG1	ligand			-1.32
Q15262	Receptor-type tyrosine-protein phosphatase kappa	receptor		1.45	-1.32
Q9UKU6	Thyrotropin-releasing hormone-degrading ectoenzyme	protease			-1.31
O60888	Protein CutA	binding protein			-1.29
P05556	Integrin beta-1	receptor			-1.29
Q8NB37	Parkinson disease 7 domain-containing protein 1	unknown			-1.29
Q9Y3I0	UPF0027 protein C22orf28	binding protein			-1.27
Q92484	Acid sphingomyelinase-like phosphodiesterase 3a	enzyme			-1.24
Q15113	Procollagen C-endopeptidase enhancer 1	binding protein	1.24	-1.71	-1.23
P20020	Plasma membrane calcium-transporting ATPase 1	enzyme			-1.23
Q9UIQ6	Leucyl-cystinyl aminopeptidase	protease			-1.22
Q8NGA1	Olfactory receptor 1M1	receptor			-1.22
P50995	Annexin A11	immune system			-1.18
P08758	Annexin A5	immune system	1.30	3.16	-1.18
O94919	Endonuclease domain-containing 1 protein	binding protein			-1.17
Q6UXH1	Cysteine-rich with EGF-like domain protein 2	binding protein			-1.16
Q9NUP9	Lin-7 homolog C	binding protein			-1.15
P54289	Voltage-dependent calcium channel subunit alpha-2/delta-1	channel			-1.14
Q9UKP4	A disintegrin and metalloproteinase with thrombospondin motifs 7	protease			-1.14
Q14314	Fibroleukin	binding protein			-1.13
Q15582	Transforming growth factor-beta-induced protein ig-h3	ECM	1.59	-1.90	-1.12
P07225	Vitamin K-dependent protein S	other	2.29		-1.12
P43251	Biotinidase	enzyme		1.01	-1.12
Q9H1J7	Protein Wnt-5b	ligand			-1.10
Q9Y5H3	Protocadherin gamma-A10	binding protein			-1.09
Q9UBR2	Cathepsin Z	protease	1.19	1.97	-1.08

P41222	Prostaglandin-H2 D-isomerase	enzyme	2.45	-16.48	-1.07
P35613	Basigin	other			-1.06
P09382	Galectin-1	ligand		-1.04	-1.05
Q9UHI8	A disintegrin and metalloproteinase with thrombospondin motifs 1	protease	1.01	-1.81	-1.04
P17301	Integrin alpha-2	receptor			-1.03
P43235	Cathepsin K	protease	12.00	-2.31	-1.03
P27487	Dipeptidyl peptidase 4	protease		4.33	-1.03
P16234	Alpha-type platelet-derived growth factor receptor	receptor			-1.02
P50281	Matrix metalloproteinase-14	protease	4.59		-1.02
P21589	5'-nucleotidase	enzyme			-1.01
P09525	Annexin A4	immune system			-1.01
P19634	Sodium/hydrogen exchanger 1	channel			-1.00
P27658	Collagen alpha-1(VIII) chain	ECM			1.00
P07384	Calpain-1 catalytic subunit	protease			1.01
P08962	CD63 antigen	receptor	3.18		1.02
P14210	Hepatocyte growth factor	ligand			1.02
Q9BUD6	Spondin-2	binding protein	1.38	9.97	1.02
Q14517	Protocadherin Fat 1	binding protein			1.03
P08253	72 kDa type IV collagenase	protease	1.61	-1.50	1.04
P23634	Plasma membrane calcium-transporting ATPase 4	enzyme	1.11		1.04
P48745	Protein NOV homolog	ligand	-1.44	-9.26	1.05
Q13018	Secretory phospholipase A2 receptor	receptor			1.07
P35052	Glypican-1	receptor	1.13	1.13	1.07
O43854	EGF-like repeat and discoidin I-like domain-containing protein 3	ligand		-1.20	1.08
P55283	Cadherin-4	binding protein			1.08
Q86WC4	Osteopetrosis-associated transmembrane protein 1	other			1.09
Q13492	Phosphatidylinositol-binding clathrin assembly protein	binding protein	1.30	1.78	1.09
P61769	Beta-2-microglobulin	immune system	1.17	-1.51	1.09
P05067	Amyloid beta A4 protein	receptor			1.10
P14543	Nidogen-1	binding protein	2.11	-1.12	1.11

Q9BUN1	Uncharacterized protein C1orf56	other			1.12
P01023	Alpha-2-macroglobulin	protease inhibitor		-6.42	1.13
Q9HDC9	Adipocyte plasma membrane-associated protein	enzyme			1.13
P01130	Low-density lipoprotein receptor	receptor			1.13
P05023	Sodium/potassium-transporting ATPase subunit alpha-1	enzyme			1.13
P22692	Insulin-like growth factor-binding protein 4	binding protein	1.13	1.12	1.14
Q9BRK3	Matrix-remodeling-associated protein 8	other	2.48	1.24	1.15
P15144	Aminopeptidase N	protease		-1.20	1.18
P55899	IgG receptor FcRn large subunit p51	receptor			1.18
Q07954	Prolow-density lipoprotein receptor-related protein 1	receptor	1.61	-1.11	1.21
Q9UKU9	Angiopoietin-related protein 2	ligand		-1.45	1.21
P84157	Matrix-remodeling-associated protein 7	other			1.22
Q9UBX5	Fibulin-5	ECM	1.16	1.20	1.24
Q8N8Z6	Discoidin, CUB and LCCL domain-containing protein 1	unknown			1.25
O00300	Tumor necrosis factor receptor superfamily member 11B	receptor			1.26
P04222	HLA class I histocompatibility antigen, Cw-3 alpha chain	receptor			1.28
Q4LDE5	Sushi, von Willebrand factor type A, EGF and pentraxin domain-containing protein 1	binding protein		1.31	1.28
Q14956	Transmembrane glycoprotein NMB	enzyme			1.30
Q8NFY4	Semaphorin-6D	receptor			1.31
P35318	ADM	ligand			1.35
P30530	Tyrosine-protein kinase receptor UFO	receptor	1.32	-2.04	1.37
P08172	Muscarinic acetylcholine receptor M2	receptor			1.39
Q6YHK3	CD109 antigen	binding protein	3.23	-1.10	1.41
Q9UBP4	Dickkopf-related protein 3	binding protein	-1.09	-1.10	1.42
O76061	Stanniocalcin-2	ligand		-1.40	1.42
P55285	Cadherin-6	binding protein		18.98	1.45
Q9H6X2	Anthrax toxin receptor 1	receptor		2.92	1.47
P55196	Afadin	binding protein			1.49

P54284	Voltage-dependent L-type calcium channel subunit beta-3	channel			1.49
Q06481	Amyloid-like protein 2	protease inhibitor			1.53
P13500	C-C motif chemokine 2	ligand			1.54
P09603	Macrophage colony-stimulating factor 1	ligand	2.39	1.62	1.54
P48307	Tissue factor pathway inhibitor 2	protease inhibitor	1.46	-1.85	1.59
Q8N3Z0	Inactive serine protease 35	protease			1.60
P02786	Transferrin receptor protein 1	receptor			1.61
P16070	CD44 antigen	receptor	2.42	3.71	1.61
Q13332	Receptor-type tyrosine-protein phosphatase S	receptor			1.63
Q96J84	Kin of IRRE-like protein 1	other			1.66
P28827	Receptor-type tyrosine-protein phosphatase mu	receptor			1.68
O15230	Laminin subunit alpha-5	ECM		1.37	1.68
P21781	Keratinocyte growth factor	ligand			1.68
P27701	CD82 antigen	receptor			1.68
Q13740	CD166 antigen	binding protein	2.66		1.71
P41221	Protein Wnt-5a	ligand			1.71
P35442	Thrombospondin-2	ECM	2.49	-3.10	1.76
Q96PD2	Discoidin, CUB and LCCL domain-containing protein 2	binding protein			1.78
Q92859	Neogenin	receptor		5.58	1.84
Q16787	Laminin subunit alpha-3	ECM			1.97
Q13444	Disintegrin and metalloproteinase domain-containing protein 15	protease		-1.19	2.05
P30411	B2 bradykinin receptor	receptor			2.28
P56199	Integrin alpha-1	receptor			2.34
Q9H5V8	CUB domain-containing protein 1	unknown			2.51
Q9NWQ8	Phosphoprotein associated with glycosphingolipid-enriched microdomains 1	binding protein			2.60
P06756	Integrin alpha-V	receptor			2.65
Q12805	EGF-containing fibulin-like extracellular matrix protein 1	binding protein		2.42	2.76
P14209	CD99 antigen	binding protein	2.08		2.79

Q14563	Semaphorin-3A	receptor			2.82
P05120	Plasminogen activator inhibitor 2	protease			3.01
P04156	Major prion protein	unknown	2.93	2.35	3.14
P00533	Epidermal growth factor receptor	receptor			3.15
P35556	Fibrillin-2	ECM			3.25
P13747	HLA class I histocompatibility antigen, alpha chain E	receptor			3.58
Q6UVK1	Chondroitin sulfate proteoglycan 4	other			3.67
P19320	Vascular cell adhesion protein 1	receptor			3.76
P01893	Putative HLA class I histocompatibility antigen, alpha chain H	receptor			3.79
P01236	Prolactin	ligand			4.37
P52823	Stanniocalcin-1	ligand	1.50	2.69	4.54
Q13822	Ectonucleotide pyrophosphatase/phosphodiesterase family member 2	enzyme			6.52
P10319	HLA class I histocompatibility antigen, B-58 alpha chain	receptor			6.61
Q9NR99	Matrix-remodeling-associated protein 5	binding protein			7.51
Q6UXD5	Seizure 6-like protein 2	receptor			7.67
P03956	Interstitial collagenase	protease	3.53	18.83	8.81
P22352	Glutathione peroxidase 3	enzyme			8.87
P39900	Macrophage metalloelastase	protease			11.57
P00749	Urokinase-type plasminogen activator	protease		3.44	12.66
O00533	Neural cell adhesion molecule L1-like protein	ECM			13.44
P09238	Stromelysin-2	protease	4.70	5.27	30.77
P08254	Stromelysin-1	protease	8.42	11.45	40.00
P05452	Tetranectin	binding protein		27.25	
P08493	Matrix Gla protein	binding protein	-9.90	2.97	
P09228	Cystatin-SA	binding protein	-6.15	2.00	
P55083	Microfibril-associated glycoprotein 4	binding protein		1.74	
O00468	Agrin	binding protein		1.43	
P55001	Microfibrillar-associated protein 2	binding protein		1.32	
Q9BY76	Angiopoietin-related protein 4	binding protein		1.15	
Q6EMK4	Vasorin	binding protein	-1.61	-1.02	
P55287	Cadherin-11	binding protein		-1.17	

Q9HCB6	Spondin-1	binding protein		-1.29	
Q9HCU0	Endosialin	binding protein	1.04	-1.46	
Q14766	Latent-transforming growth factor beta-binding protein 1	binding protein		-1.58	
Q99674	Cell growth regulator with EF hand domain protein 1	binding protein		-2.77	
Q7Z7G0	Target of Nesh-SH3	binding protein		-3.30	
P16112	Aggrecan core protein	binding protein		-5.19	
P55290	Cadherin-13	binding protein		-6.69	
Q08554	Desmocollin-1	binding protein	2 CAM singletons		
P43121	Cell surface glycoprotein MUC18	binding protein	2.26		
P23763	Vesicle-associated membrane protein 1	binding protein	1.49		
P39060	Collagen alpha-1(XVIII) chain	ECM		1.74	
Q9Y6C2	EMILIN-1	ECM	-1.01	-1.77	
Q01955	Collagen alpha-3(IV) chain	ECM		-2.16	
P02462	Collagen alpha-1(IV) chain	ECM		-2.66	
Q06828	Fibromodulin	ECM		-3.52	
Q92626	Peroxidasin homolog	enzyme	1.11	-1.26	
Q9UJJ9	N-acetylglucosamine-1-phosphotransferase subunit gamma	enzyme		-1.77	
P07355	Annexin A2	immune system	1.46	1.36	
P02788	Lactotransferrin	ligand		3 ATM singletons	
P02787	Serotransferrin	ligand		2 ATM singletons	
Q99969	Retinoic acid receptor responder protein 2	ligand	-1.05	1.33	
P01344	Insulin-like growth factor II	ligand	2 CAM singletons	-1.19	
P29279	Connective tissue growth factor	ligand	-1.07	-1.30	
P61278	Somatostatin	ligand	-4.91		
P04216	Thy-1 membrane glycoprotein	other	-1.17	1.87	
P13473	Lysosome-associated membrane glycoprotein 2	other		1.49	
Q99584	Protein S100-A13	other	1.98	1.18	
P0C6K4	Non-structural polyprotein 1A	other		1.13	
P19021	Peptidyl-glycine alpha-amidating monooxygenase	other		-1.76	
Q6UXH9	Inactive serine protease RAMP	protease	1.29	1.03	

O14672	Disintegrin and metalloproteinase domain-containing protein 10	protease		-1.29	
P00751	Complement factor B	protease		-1.77	
P48740	Mannan-binding lectin serine protease 1	protease		-3.48	
P16870	Carboxypeptidase E	protease		-4.37	
P35625	Metalloproteinase inhibitor 3	protease inhibitor	-3.45	-1.20	
P01011	Alpha-1-antichymotrypsin	protease inhibitor		-2.19	
O95274	Ly6/PLAUR domain-containing protein 3	receptor		2.93	
P31431	Syndecan-4	receptor	-2.24	1.68	
Q9UNN8	Endothelial protein C receptor	receptor	-1.82	1.64	
Q9UBG0	C-type mannose receptor 2	receptor		1.21	
O14786	Neuropilin-1	receptor		-1.44	
Q03405	Urokinase plasminogen activator surface receptor	receptor	1.17	-1.55	
O95965	Integrin beta-like protein 1	receptor	-10.55	-2.23	
O75462	Cytokine receptor-like factor 1	receptor	-4.24	-3.29	
Q16378	Proline-rich protein 4	unknown		2 ATM singletons	
Q96FE7	Phosphoinositide-3-kinase-interacting protein 1	unknown		1.14	

Supporting Information Table S3. All quantified extracellular proteins, and their functional classification, based on at least one unique peptide identification using either ‘shotgun’ proteomics in two patients or Met-COFRADIC applied to patient 1. Fold changes expressed as relative abundance in CAM media compared with ATM. Where a peptide was uniquely identified in either the CAM or ATM sample of an experiment, this is denoted as a singleton in the relevant fold change column. Functional classifications were manually annotated using the Uniprot database as a reference.

Uniprot accession	Protein name	Functional Classification	Fold change (1:2)		
			Patient 1 (Met-COFRADIC)	Patient 1 (shotgun)	Patient 2 (shotgun)
O00533	Neural cell adhesion molecule L1-like protein	ECM	13.44		
O14498	Immunoglobulin superfamily containing leucine-rich repeat protein	binding protein	-620.38		
O75326	Semaphorin-7A	receptor	-17.92		
P00533	Epidermal growth factor receptor	receptor	3.15		
P00734	Prothrombin	protease	-187.31		
P00742	Coagulation factor X	protease	-19.34		
P00749	Urokinase-type plasminogen activator	protease	12.66		3.44
P00813	Adenosine deaminase	enzyme	-17.02		
P01236	Prolactin	ligand	4.37		
P01344	Insulin-like growth factor II	ligand		2 CAM singletons	
P01893	Putative HLA class I histocompatibility antigen, alpha chain H	receptor	3.79		
P02452	Collagen alpha-1(I) chain	ECM	-13.53		
P02649	Apolipoprotein E	ligand		4 CAM singletons	
P02787	Serotransferrin	ligand			2 ATM singletons
P02788	Lactotransferrin	ligand			3 ATM singletons
P03956	Interstitial collagenase	protease	8.81	3.53	18.83
P04156	Major prion protein	unknown	3.14		
P05155	Plasma protease C1 inhibitor	binding protein	-29.16		
P05452	Tetranectin	binding protein			27.25
P08254	Stromelysin-1	protease	40	8.42	11.45
P08758	Annexin A5	immune system			3.16
P08962	CD63 antigen	receptor		3.18	
P09238	Stromelysin-2	protease	30.77	4.7	5.27
P10124	Serglycin	binding protein	-23.88		
P10319	HLA class I histocompatibility antigen, B-58 alpha chain	receptor	6.61		
P13521	Secretogranin-2	ligand			3.17

P13747	HLA class I histocompatibility antigen, alpha chain E	receptor	3.58		
P16070	CD44 antigen	receptor			3.71
P17936	Insulin-like growth factor-binding protein 3	binding protein	-19.83		
P19320	Vascular cell adhesion protein 1	receptor	3.76		
P21810	Biglycan	binding protein	-41.36		
P22105	Tenascin-X	binding protein	-13.53		-20388.71
P22352	Glutathione peroxidase 3	enzyme	8.87		
P24592	Insulin-like growth factor-binding protein 6	binding protein	-14.07		
P26022	Pentraxin-related protein PTX3	binding protein	-17.33		
P26927	Hepatocyte growth factor-like protein	ligand	-309.08		
P27487	Dipeptidyl peptidase 4	protease			4.33
P35556	Fibrillin-2	ECM	3.25		
P36222	Chitinase-3-like protein 1	binding protein	-40.78		
P39059	Collagen alpha-1(XV) chain	ECM	-81.18		
P39900	Macrophage metalloelastase	protease	11.57		
P41222	Prostaglandin-H2 D-isomerase	enzyme			-16.48
P43235	Cathepsin K	protease		12	
P49747	Cartilage oligomeric matrix protein	binding protein	-61.29	-23.47	
P49788	Retinoic acid receptor responder protein 1	receptor	-13.08	-12.92	
P50281	Matrix metalloproteinase-14	protease		4.59	
P52823	Stanniocalcin-1	ligand	4.54		
P55285	Cadherin-6	binding protein			18.98
Q08554	Desmocollin-1	binding protein		2 CAM singletons	
Q13361	Microfibrillar-associated protein 5	binding protein	-82.21		
Q13753	Laminin subunit gamma-2	ECM	-25.64		
Q13822	Ectonucleotide pyrophosphatase/phosphodiesterase family member 2	enzyme	6.52		
Q16378	Proline-rich protein 4	unknown			2 ATM singletons
Q6FHJ7	Secreted frizzled-related protein 4	binding protein	-665.02	2 ATM singletons	
Q6UVK1	Chondroitin sulfate proteoglycan 4	other	3.67		
Q6UXB8	Peptidase inhibitor 16	protease inhibitor	-441	5 ATM singletons	4.57
Q6UXD5	Seizure 6-like protein 2	receptor	7.67		

Q6WRI0	Immunoglobulin superfamily member 10	binding protein	-378.04		
Q6YHK3	CD109 antigen	binding protein		3.23	
Q86Y38	Xylosyltransferase 1	enzyme	-19.59		
Q8IWU6	Extracellular sulfatase Sulf-1	enzyme	-84.16		
Q8N6G6	ADAMTS-like protein 1	protease	-27.96		
Q92859	Neogenin	receptor			5.58
Q9BUD6	Spondin-2	binding protein			9.97
Q9NQ30	Endothelial cell-specific molecule 1	receptor	-41.07		
Q9NR99	Matrix-remodeling-associated protein 5	binding protein	7.51		

Supporting Information Table S4. Proteins showing greatest differential abundance in CAM media compared with ATM. The proteins listed are those exhibiting differential abundance beyond 95% confidence limits.

	# quantified identifications	# quantified, AcD3-labelled identifications	# quantified unique peptides	# quantified, AcD3-labelled unique peptides
Patient 1	1593	369	908	251
Patient 2	2119	377	1221	243
Patient 1 (N-terminal COFRADIC)	4821	1839	1235	519

Supporting Information Table S5. Coverage of myofibroblast secretomes following SILAC labelling of cancer-derived myofibroblasts (CAMs) and adjacent tissue myofibroblasts (ATMs), trideutero-acetylation (AcD3) of neo-N-terminal peptides and enrichment for N-terminal peptides. Pairs of CAM/ATMs were analysed from two patients using a strong cation exchange enrichment; one (Patient 1) was also analysed by N-terminal-COFRADIC. N-terminal COFRADIC increased the number of quantified tri-deutero-acetylated peptides approximately two-fold.

	Valid quantification only			Extracellular		
	Identifications	**Unique peptides**	**Unique proteins**	**Identifications**	**Unique peptides**	**Unique proteins**
Patient 1	408	290	121	195	131	61
Patient 2	421	287	116	281	180	65
Patient 1 (N-terminal COFRADIC)	794	244	137	453	105	69

Supporting Information Table S6. Coverage of myofibroblast secretomes using N-terminal peptide enrichment proteomics. The data have been filtered to exclude identifications starting at residues 1 or 2 i.e. immediately following signal peptide cleavage. The dataset therefore correspond to proteolytically cleaved proteins.

Uniprot ID		Start	End	Patient 1		Patient 2		Patient 1 (N-terminal COFRADIC)	
				Mascot score	Ratio	Mascot score	Ratio	Mascot score	Ratio
P08253	**72 kDa type IV collagenase**								
	FFGLPQTGDLDQNTIETMR	80	98					75	11.17
Q9UHI8	**A disintegrin and metalloproteinase with thrombospondin motifs 1**								
	LGRPSEEDEELVVPELER	50	67	110	0.94	87	0.67	137	1.09
	RPSEEDEELVVPELER	52	67			76	0.61	106	1.06
P78536	**ADAM 17**								
	PRPPDDPGFGPHQR	18	31					56	CAM singleton
P35318	**ADM**								
	TDKDKDNVAPR	128	138	52	1.45				
P01011	**Alpha-1-antichymotrypsin**								
	HPNSPLDEENLTQENQDR	24	41			54	0.59		
Q06481	**Amyloid-like protein 2**								
	VPEKCQFFHKER	145	156					56	1.69
P02649	**Apolipoprotein E**								
	KVEQAVETEPEPELR	19	33	81	14.77				
O75882	**Attractin**								
	SAHIVTLKNGR	448	458					57	0.98
P98160	**Basement membrane-specific heparan sulfate proteoglycan core protein**								
	DAPGQYGAYFHDDGFLAFPGHVFSR	4197	4221			48	1.00		
	IAHVELADAGQYR	3542	3554					99	0.36
P61769	**Beta-2-microglobulin**								
	VSGFHPSDIEVDLLKNGER	47	65			55	1.03		
P13497	**Bone morphogenetic protein 1**								
	DDTITKKGFHLR	961	972					59	0.65
P55285	**Cadherin-6**								
	ALELSGNSKNELNR	37	50	69	1.02			94	0.95
	ELSGNSKNELNR	39	50	52	0.39				

O43852	**Calumenin**								
	AKTFDQLTPEESKER	58	72	66	9.21				
	LSKPTEKKDR	18	27	52	0.52				
P07858	**Cathepsin B**								
	IESEVVAGIPR	321	331	54	CAM singleton				
	KGLVSGGLYESHVGCRPY	165	182					123	0.88
P43235	**Cathepsin K**								
	MTGLKVPLSHSR	90	101	69	20.95				
P16070	**CD44 antigen**								
	ESSETPDQFMTADETR	716	731	77	4.40				
	KESSETPDQFMTADETR	715	731	78	1.54	78	4.25		
	LVNKESSETPDQFMTADETR	712	731	57	2.04				
	SETPDQFMTADETR	718	731	69	2.35	79	4.11		
P14209	**CD99 antigen**								
	DADLADGVSGGEGKGGSDGGGSHR	92	115	63	1.91				
	DLADGVSGGEGKGGSDGGGSHR	94	115	107	2.81				
	SFSDADLADGVSGGEGKGGSDGGGSHR	89	115	61	CAM singleton				
	VSGGEGKGGSDGGGSHR	99	115	74	2.20				
P36222	**Chitinase-3-like protein 1**								
	FSKIASNTQSR	106	116			62	1.07		
P10909	**Clusterin**								
	ASSIIDELFQDR	183	194			72	1.09		
	FMETVAEKALQEYR	430	443	52	0.36				
	QIKTLIEKTNEER	55	67	77	0.86				
	TLIEKTNEER	58	67			58	2.11		
P02452	**Collagen alpha-1(I) chain**								
	ADDANVVR	1218	1225	53	0.49	56	0.71		
	AGPAGPVGPVGAR	1072	1084			52	0.32		
	AGPPGFPGAVGAKGEAGPQGPR	340	361			55	0.62		
	AGPPGPIGNVGAPGAKGAR	847	865					53	0.53
	AGPVGPVGAR	1075	1084					57	0.12
	DDANVVR	1219	1225	55	0.25	69	0.45		
	DGEAGAQGPPGPAGPAGER	613	631	109	0.30	104	0.38		
	GADGSPGKDGVR	752	763	50	0.16				

	GEPGKQGPSGASGER	980	994			62	0.34		
	GEPGPVGVQGPPGPAGEEGKR	449	469			51	0.26		
	GPAGPQGPR	1085	1093	59	0.42	50	0.38		
	GSEGPQGVR	362	370			49	0.44		
	GVQGPPGPAGPR	686	697	55	0.29	54	0.39		
	KGAAGEPGKAGER	586	598			54	ATM singleton		
	KGADGSPGKDGVR	751	763			53	0.40		
	MGPPGLAGPPGESGR	1000	1014	90	0.17	54	0.25		
	SGDRGETGPAGPAGPVGPVGAR	1063	1084	102	0.29	83	0.42		
	SGEPGKQGPSGASGER	979	994	61	0.23	62	0.30		
	SLSQQIENIR	1237	1246	51	2.05	62	0.40		
P02461	**Collagen alpha-1(III) chain**								
	GPPGLAGAPGLR	684	695			51	0.44		
	GRPGLPGAAGAR	309	320	49	0.21				
	IAGITGAR	949	956					50	3.36
	LAGAPGLR	688	695					58	4.02
	SGDRGESGPAGPAGAPGPAGSR	1061	1082			84	0.40		
P02462	**Collagen alpha-1(IV) chain**								
	SAPFIECHGR	1610	1619					56	0.58
	SLLYVQGNER	1472	1481			65	0.51	61	
P12109	**Collagen alpha-1(VI) chain**								
	GDPGEAGPQGDQGR	443	456	51	0.41	62	1.12		
	SVAITPDHLEPR	188	199			67	0.96	78	0.54
P27658	**Collagen alpha-1(VIII) chain**								
	MGKEAVPKKGKEIPLASLR	99	117			65	1.04		
P08123	**Collagen alpha-2(I) chain**								
	AAGAPGPHGPVGPAGKHGNR	959	978					81	0.71
	AGAAGQPGAKGER	729	741	60	0.07	52	0.55		
	AGEPGEPGQTGPAGAR	117	132			69	0.47		
	AGKEGPVGLPGIDGR	462	476					60	0.11
	AGPNGFAGPAGAAGQPGAKGER	720	741	52	0.08	80	0.64	81	
	AGPPGKAGEDGHPGKPGRPGER	135	156					95	0.17
	AGPSGPAGKDGR	1056	1067			51	1.24		
	AGVMGPPGSR	414	423			51	0.90		

	DGNPGNDGPPGR	927	938	49	0.34	57	0.81		
	FQGPAGEPGEPGQTGPAGAR	113	132			71	0.77		
	GAAGIPGGKGEKGEPGLR	646	663	63	0.10				
	GAAGLPGVAGAPGLPGPR	310	327	52	0.13	56	0.67		
	GAAGQPGAKGER	730	741			62	0.53		
	GAPGAVGAPGPAGATGDR	676	693	59	0.24	98	0.73		
	GASGPAGVR	424	432			57	1.10		
	GDGGPPGMTGFPGAAGR	778	794			71	0.85		
	GEAGAAGPAGPAGPR	694	708	66	1.27				
	GEIGAVGNAGPAGPAGPR	265	282	60	0.46	99	0.90		
	GETGPSGPVGPAGAVGPR	979	996	97	0.64	74	0.69	95	0.26
	GFAGPAGAAGQPGAKGER	724	741			104	0.76		
	GFPGTPGLPGFKGIR	166	180	56	0.09	83	0.73		
	GIPGPVGAAGATGAR	328	342	53	0.22	68	0.74		
	GLHGEFGLPGPAGPR	574	588	60	0.27	78	0.74		
	GLPGSPGNIGPAGKEGPVGLPGIDGR	451	476	57	0.18	67	0.76		
	GLPGVAGAVGEPGPLGIAGPPGAR	883	906			58	0.83		
	GPAGPSGPAGKDGR	1054	1067	57	0.79	69	1.01		
	GPPGAAGAPGPQGFQGPAGEPGEPGQTGPAGAR	100	132	69	0.15	56	0.69		
	GPPGAVGSPGVNGAPGEAGR	907	926	52	0.19	55	0.62		
	GPPGESGAAGPTGPIGSR	592	609	66	0.35	92	0.71		
	GPSGPQGIR	997	1005	62	0.56				
	GVGLGPGPMGLMGPR	85	99			66	0.95		
	GVVGPQGAR	157	165	58	0.43	48	0.91		
	GYPGNIGPVGAAGAPGPHGPVGPAGKHGNR	949	978			88	0.87		
	ISGPPGPPGPAGKEGLR	803	819	49	0.36	53	1.52	79	3.31
	KGPTGDPGKNGDKGHAGLAGAR	498	519					110	0.17
	LGIAGPPGAR	897	906					56	0.16
	LHGEFGLPGPAGPR	575	588					76	0.64
	LLGAPGILGLPGSR	866	879			51	0.72		
	NGEAGSAGPPGPPGLR	384	399			63	0.54	92	
	NGFAGPAGAAGQPGAKGER	723	741			69	0.55	119	0.10
	QGPPGPSGEEGKR	369	381	53	0.19	62	0.62		
	SGISGPPGPPGPAGKEGLR	801	819	85	0.13	99	0.56	82	
	SGPPGPDGNKGEPGVVGAVGTAGPSGPSGLPGER	612	645			72	0.43		

	SGPVGPAGAVGPR	984	996	50	0.48			83	0.40
	SLNNQIETLLTPEGSR	1141	1156			54	1.18		
	TGHPGTVGPAGIR	1068	1080			58	0.49	64	0.14
	TGPPGPSGISGPPGPPGPAGKEGLR	795	819	60	0.11	52	0.78		
	VGAPGPAGAR	225	234	55	0.27				
	VGPAGAVGPR	987	996					51	0.29
	VGPAGPIGSAGPPGFPGAPGPKGEIGAVGNAGPAG PAGPR	243	282			52	0.37		
	VGPPGNPGANGLTGAKGAAGLPGVAGAPGLPGPR	294	327			51	0.46		
P08572	**Collagen alpha-2(IV) chain**								
	GLDGYQGPDGPR	323	334			52	0.73		
	GVKKFDVPCGGR	34	45	50	0.74	66	0.63		
P05997	**Collagen alpha-2(V) chain**								
	GRPGPAGPPGSQGPR	129	143			67	0.51		
P12110	**Collagen alpha-2(VI) chain**								
	LYSIACDKPQQVR	772	784					52	CAM singleton
Q96CG8	**Collagen triple helix repeat-containing protein 1**								
	SEIPKGKQKAQLR	31	43			56	1.82	70	0.37
P00736	**Complement C1r subcomponent**								
	IIGGQKAKMGNFPWQVFTNIHGR	464	486			60	1.06		
P08603	**Complement factor H**								
	EYHFGQAVR	167	175					52	0.20
P42830	**C-X-C motif chemokine 5**								
	AGPAAAVLR	37	45					58	CAM singleton
P01034	**Cystatin-C**								
	LVGGPMDASVEEEGVR	35	50	61	0.48				
P07585	**Decorin**								
	ELHLDNNKLTR	273	283	54	1.70				
	GPFQQR	17	22	53	0.65	50	1.28	51	0.83
	HLDNNKLTR	275	283					61	0.63
	KKLSYIR	200	206					58	0.75
	SAIQLGNYK	351	359					75	0.78
	SISAVDNGSLANTPHLR	256	272					136	0.51
	SNPVQYWEIQPSTFR	331	345					89	0.80

Q8IXL6	**Dentin matrix protein 4**								
	IALDLLPR	11	18					47	1.25
Q9UBP4	**Dickkopf-related protein 3**								
	SETVITSVGDEEGR	129	142	60	0.93				
Q14118	**Dystroglycan**								
	SVPDIHGVEAPAR	270	282					55	0.60
Q9UNN8	**Endothelial protein C receptor**								
	SQDASDGLQR	18	27	63	0.63	64	1.48		
Q16610	**Extracellular matrix protein 1**								
	ASEGGFTATGQR	20	31	59	0.93	78	0.71	61	0.80
	EGGFTATGQR	22	31			64	1.08		
	PSPDNLNQICLPNR	172	185					104	0.66
	SEGGFTATGQR	21	31			56	0.91		
	SSYSHLTR	198	205					64	0.83
P35555	**Fibrillin-1**								
	ADANLEAGNVKETR	25	38	61	0.22	97	1.05		
	DANLEAGNVKETR	26	38	56	0.29	76	0.62		
	EAGNVKETR	30	38			64	0.77		
	NLEAGNVKETR	28	38			73	1.12		
	Fibromodulin								
	NLENLYLQGNR	314	324			73	ATM singleton		
P02751	**Fibronectin**								
	GATYNIIVEALKDQQR	2165	2180			79	0.79		
	HTSVQTTSSGSGPFTDVR	273	290	50	0.26	84	0.83	80	
	STGASKSKR	23	31			65	0.27		
	TAVPSTGASKSKR	19	31	56	2.88	87	0.06		
P23142	**Fibulin-1**								
	DVLLEACCADGHR	30	42	66	0.27	77	2.15	86	0.14
	GYHLNEEGTR	344	353			55	1.63	54	0.10
Q9UBX5	**Fibulin-5**								
	SCPPGYILLDDNR	272	284					71	1.15
Q12841	**Follistatin-related protein 1**								
	GAQTQTEEEMTR	274	285	76	1.37	58	0.95		
	SVSPSASPVVCYQSNR	103	118	76	2.03				

O60353	**Frizzled-6**								
	HSLFTCEPITVPR	19	31					74	0.84
P09382	**Galectin-1**								
	LVASNLNLKPGECLR	5	19			88	0.75		
Q08380	**Galectin-3-binding protein**								
	STHTLDLSR	129	137	66	0.57			67	0.55
P35052	**Glypican-1**								
	SHAELETALR	81	90					57	0.89
Q99988	**Growth/differentiation factor 15**								
	LSLAEASR	30	37					63	1.05
P09341	**Growth-regulated alpha protein**								
	ASVATELR	35	42	51	41.63				
P30443	**HLA class I histocompatibility antigen, A-1 alpha chain**								
	FDSDAASQKMEPR	60	72					76	CAM singleton
P01889	**HLA class I histocompatibility antigen, B-7 alpha chain**								
	YVDDTQFVR	51	59					59	CAM singleton
P10321	**HLA class I histocompatibility antigen, Cw-7 alpha chain**								
	FDTAVSR	32	38					58	CAM singleton
P01344	**Insulin-like growth factor II**								
	AYRPSETLCGGELVDTLQFVCGDR	25	48			79	0.94	99	0.22
P17936	**Insulin-like growth factor-binding protein 3**								
	GASSAGLGPVVR	28	39	68	0.13				
P22692	**Insulin-like growth factor-binding protein 4**								
	DEAIHCPPCSEEKLAR	22	37	82	1.20	82	1.30	110	1.30
	EDARPVPQGSCQSELHR	164	180			65	1.43		
	MKVNGAPR	156	163	56	1.89	62	1.65		
	STSGGKMKVNGAPR	150	163	53	1.28	59	1.31	62	1.39
	THEDLYIIPIPNCDR	192	206	76	1.88	77	1.18	102	1.21
P24593	**Insulin-like growth factor-binding protein 5**								
	AEAVKKDR	149	156			57	1.72		

	AVYLPNCDR	213	221					53	1.36
	ELKAEAVKKDR	146	156			49	0.69		
	FVGGAENTAHPR	165	176	72	0.29	85	1.60	89	0.43
	GGAENTAHPR	167	176			64	0.58		
	HMEASLQELK	195	204	60	1.23				
	HMEASLQELKASPR	195	208	93	0.63	66	3.05		
	IISAPEMR	177	184	53	0.21	66	1.64		
	ISELKAEAVKK	144	154	55	0.30	56	1.92		
	ISELKAEAVKKDR	144	156	76	0.18	66	1.84	71	0.86
	ISELKAEAVKKDRR	144	157			47	1.93		
	KAEAVKKDR	148	156	61	0.14	49	1.04		
	KFVGGAENTAHPR	164	176	113	0.07	112	1.44	117	0.31
	LKAEAVKKDR	147	156	72	0.53	55	2.43	57	2.85
	LTQSKFVGGAENTAHPR	160	176	75	0.35	85	1.97		
	QESEQGPCR	185	193	69	0.38	67	1.50		
	QSKFVGGAENTAHPR	162	176					77	2.78
	SELKAEAVKKDR	145	156	77	0.30	58	0.83		
	TQSKFVGGAENTAHPR	161	176	66	0.40				
	VGGAENTAHPR	166	176	63	0.60	62	1.20		
P24592	**Insulin-like growth factor-binding protein 6**								
	GAQTLYVPNCDHR	181	193	56	0.13				
Q16270	**Insulin-like growth factor-binding protein 7**								
	AGAAAGGPGVSGVCVCKSR	98	116	83	1.03	82	1.19		
	GKAGAAAGGPGVSGVCVCKSR	96	116	116	0.77	113	1.16		
	KGKAGAAAGGPGVSGVCVCKSR	95	116	53	0.82	93	1.04		
	SSSDTCGPCEPASCPPLPPLGCLLGETR	27	54			56	0.98		
	TELLPGDR	206	213					58	0.74
Q06033	**Inter-alpha-trypsin inhibitor heavy chain H3**								
	AVSQGKTAGLVKASGR	118	133			51	ATM singleton		
	TAGLVKASGR	124	133			51	ATM singleton		
Q86UX2	**Inter-alpha-trypsin inhibitor heavy chain H5**								
	PHFVVDFPLSR	682	692			52	ATM singleton		
P03956	**Interstitial collagenase**								

	ATLETQEQDVDLVQKYLEKYYNLKNDGR	22	49			51	CAM singleton		
	CGVPDVAQFVLTEGNPR	92	108	63	23.03				
	FPATLETQEQDVDLVQKYLEKYYNLKNDGR	20	49			61	28.34		
	LKVMKQPR	84	91			44	CAM singleton		
	VTGKPDAETLKVMKQPR	75	91	70	CAM singleton				
Q9BX67	**Junctional adhesion molecule C**								
	VNLKSSNR	32	39			50	1.65	51	1.32
Q08431	**Lactadherin**								
	LDICSKNPCHNGGLCEEISQEVR	24	46					85	0.25
	LYPTSCHTACTLR	207	219					76	0.31
P11047	**Laminin subunit gamma-1**								
	SAGYLDDVTLASAR	664	677					90	0.57
	SQECYFDPELYR	348	359					55	0.50
Q14766	**Latent-transforming growth factor beta-binding protein 1**								
	LQAEECGILNGCENGR	1732	1747			97	0.76		
Q14767	**Latent-transforming growth factor beta-binding protein 2**								
	EQDAPVAGLQPVER	74	87	62	0.25				
	IVFTPTICKQTCAR	353	366			61	0.83		
	SSAAGEGTLAR	249	259	56	0.28	66	0.70		
	STPLGQQQPAPR	124	135	72	0.31	52	0.60		
P22064	**Latent-transforming growth factor beta-binding protein, isoform 1S**								
	AKEEPVEALTFSR	449	461					62	CAM singleton
P51884	**Lumican**								
	SKIKHLR	304	310	51	0.18	47	1.38	54	0.16
Q9Y4K0	**Lysyl oxidase homolog 2**								
	NVAKIQLR	52	59					47	CAM singleton
P09603	**Macrophage colony-stimulating factor 1**								
	EEVSEYCSHMIGSGHLQSLQR	33	53			70		77	1.73
	MIGSGHLQSLQR	42	53					76	0.68

	SHSSGSVLPLGELEGR	428	443	62	1.72			143	1.59
P14174	**Macrophage migration inhibitory factor**								
	PMFIVNTNVPR	2	12	63	1.85	85	1.65		
	SIGKIGGAQNR	64	74			50	1.85	56	1.18
	SLHSIGKIGGAQNR	61	74					93	1.29
	SYSKLLCGLLAER	75	87			53	1.57		
P04156	**Major prion protein**								
	AVVGGLGGYMLGSAMSR	120	136	87	CAM singleton				
	IIHFGSDYEDR	138	148					71	CAM singleton
	VVGGLGGYMLGSAMSR	121	136	89	4.78			110	2.60
P50281	**Matrix metalloproteinase-14**								
	YGPNICDGNFDTVAMLR	314	330					79	0.96
P01033	**Metalloproteinase inhibitor 1**								
	CTCVPPHPQTAFCNSDLVIR	24	43	81	0.28	84	0.87	113	0.30
	FVYTPAMESVCGYFHR	83	98			89	0.82		
	SEEFLIAGKLQDGLLH	103	118			64	0.81		
	SFVAPWNSLSLAQR	123	136			61	0.88	92	0.39
	SLSLAQR	130	136			50	0.91	65	0.39
	YEIKMTKMYKGFQALGDAADIR	61	82			81	1.02		
	YKGFQALGDAADIR	69	82	98	0.23				
P16035	**Metalloproteinase inhibitor 2**								
	CSCSPVHPQQAFCNADVVIR	27	46	93	0.72	72	0.74	137	0.64
	SCSPVHPQQAFCNADVVIR	28	46					137	0.62
	SPVHPQQAFCNADVVIR	30	46					107	0.72
Q9UJJ9	**N-acetylglucosamine-1-phosphotransferase subunit gamma**								
	AKMKVVEEPNAFGVNNPFLPQASR	25	48			65	2.20		
P05408	**Neuroendocrine protein 7B2**								
	SVNPYLQGQR	182	191			58	0.75		
P80303	**Nucleobindin-2**								
	TKLDELKR	101	108			49	0.96	64	1.16
P01178	**Oxytocin-neurophysin 1**								
	CYIQNCPLGGKR	20	31					61	1.80
	Periostin								

	FIEGGDGHLFEDEEIKR	790	806			78	ATM singleton		
	IIDGVPVEITEKETR	736	750	52	0.40	58	0.20		
	KLQANKKVQGSR	816	827			97	0.18		
	NNHYDKILAHSR	22	33					91	0.12
	QANKKVQGSR	818	827			53	0.12		
Q92626	**Peroxidasin homolog**								
	SLEFSYQEDKPTKKTR	1337	1352			76	1.00		
P23634	**Plasma membrane calcium-transporting ATPase 4**								
	THPEFAIEEELPR	1168	1180	76	1.11			77	0.73
Q15113	**Procollagen C-endopeptidase enhancer 1**								
	ATSGTEHQFCGGR	150	162			51	0.53		
P01210	**Proenkephalin-A**								
	ECSQDCATCSYR	25	36			49	1.17		
	QLEDEAKELQKR	198	209	70	0.22	52	1.42		
	SPQLEDEAKELQKR	196	209			63	0.53		
Q02297	**Pro-neuregulin-1, membrane-bound isoform**								
	VQNQEKAEELYQKR	229	242					58	CAM singleton
P41222	**Prostaglandin-H2 D-isomerase**								
	APEAQVSVQPNFQQDKFLGR	23	42			78	0.07	91	0.84
P55145	**Protein ARMET**								
	LRPGDCEVCISYLGR	22	36					87	0.81
P07237	**Protein disulfide-isomerase**								
	DAPEEEDHVLVLR	18	30	83	1.23	86	1.33	90	0.62
P28300	**Protein-lysine 6-oxidase**								
	AAGQQQPPR	25	33			52	0.17		
	APPAAGQQQPPR	22	33			52	0.75		
	DPGAAVPGAANASAQQPR	71	88			65	0.84		
	PAAGQQQPPR	24	33			56	0.28		
	SLGSQYQPQR	59	68	67	0.23	61	0.62	63	0.26
	SLLSLGSQYQPQR	56	68	51	0.26				
	SMDEFSHYDLLDANTQR	297	313					86	0.32
	TAGSSGVTAGR	106	116	69	0.53	69	0.84		
P49788	**Retinoic acid receptor responder protein 1**								
	AGSGDPDDPGQPQDAGVPR	38	56	55	0.11				

	PAGSGDPDDPGQPQDAGVPR	37	56	50	ATM singleton				
Q99969	**Retinoic acid receptor responder protein 2**								
	EAEEHQETQCLR	126	137			78	1.32		
P13521	**Secretogranin-2**								
	ALEYIENLR	58	66	50	0.87				
	NQLLQKEPDLR	33	43	71	0.71	52	3.25		
	SGQLGIQEEDLR	285	296	59	0.89				
O75326	**Semaphorin-7A**								
	SKYHYQKVAVHR	404	415					66	0.22
Q92743	**Serine protease HTRA1**								
	SAPLAAGCPDR	30	40	50	1.48	62	0.67		
	SLTSSKAKELKDR	389	401			50	1.25		
P61278	**Somatostatin**								
	LSQAAEQDEMR	73	83	50	1.90				
Q9BUD6	**Spondin-2**								
	AFIPPAPVLPSR	250	261	48	2.53				
	LGGESICSAR	29	38					62	0.82
	QPLGGESICSAR	27	38					65	0.66
	SPSHPANSFYYPR	217	229					66	1.12
	SSPSHPANSFYYPR	216	229					58	1.00
P52823	**Stanniocalcin-1**								
	HEAEQNDSVSPR	19	30	63	2.32	78	2.97		
	NLRGEEDSPSHIKR	228	241			55	4.42		
	THEAEQNDSVSPR	18	30	74	1.65	77	2.95		
	TNEPQKLKVLLR	216	227	53	0.74	53	5.42		
	VAAQNSAEVVR	34	44	61	2.09	71	2.52		
O76061	**Stanniocalcin-2**								
	ECYLKHDLCAAAQENTR	138	154					123	1.47
P08254	**Stromelysin-1**								
	CGVPDVGHFR	92	101					53	CAM singleton
	DSGPVVKKIR	56	65	48	CAM singleton				
	LDSDTLEVMR	79	88	56	CAM singleton				

	YPLDGAAR	18	25			60	9.19		
O00391	**Sulfhydryl oxidase 1**								
	AAPGQEPPEHMAELQR	615	630	93	1.25	66	2.03		
	DTGAALLAESR	646	656			56	1.19		
	SALYSPSDPLTLLQADTVR	33	51	92	0.87	110	1.64	102	0.48
	SFFKTALDDR	369	378	50	0.47			83	0.54
	SFYTAYLQR	257	265			54	1.62		
	SKIYMADLESALHYILR	297	313			78	1.95		
	SSKQLVDIPEGQLEAR	674	689			50	1.77		
Q8TER0	**Sushi, nidogen and EGF-like domain-containing protein 1**								
	SSHQLQALAAGR	963	974					82	0.67
P35442	**Thrombospondin-2**								
	GHQDKDTTFDLFSISNINR	19	37	76	CAM singleton	102	0.30		
	LIGGPPKTR	307	315					58	1.45
P10646	**Tissue factor pathway inhibitor**								
	KGGLIKTKR	277	285					76	0.60
	SKGGLIKTKR	276	285					46	0.54
P48307	**Tissue factor pathway inhibitor 2**								
	DAAQEPTGNNAEICLLPLDYGPCR	23	46			63	0.68		
Q15582	**Transforming growth factor-beta-induced protein ig-h3**								
	AKSPYQLVLQHSR	26	38	67	1.36	73	0.65		
	DSALEIFKQASAFSR	648	662			65	1.11		
	EGVYTVFAPTNEAFR	534	548	91	1.27	76	0.55		
	GPAKSPYQLVLQHSR	24	38	77	1.23	82	0.65	108	0.78
Q4V9L6	**Transmembrane protein 119**								
	ATQNLKSPTR	179	188	52	3.67				
O43508	**Tumor necrosis factor ligand superfamily member 12**								
	VVSLGSR	41	47					49	1.55
Q9UBN6	**Tumor necrosis factor receptor superfamily member 10D**								
	SLKEEECPAGSHR	77	89	58	CAM singleton				

Q9GZX9	**Twisted gastrulation protein homolog 1**								
	CNKALCASDVSKCLIQELCQCR	26	47					64	2.68
Q13308	**Tyrosine-protein kinase-like 7**								
	AIVFIKQPSSQDALQGR	31	47	94	1.93	85	1.69		
Q969H8	**UPF0556 protein C19orf10**								
	VSEPTTVAFDVR	32	43	75	1.36			77	0.67
P00749	**Urokinase-type plasminogen activator**								
	SDALQLGLGKHNYCR	109	123	69	6.78	65	5.90	95	8.12
P13611	**Versican core protein**								
	LHKVKVGKSPPVR	21	33			65	0.79	78	0.23
Q86Y38	**Xylosyltransferase 1**								
	GGAAVGGGEQPPPAPAPR	47	64			58	0.52		

Supporting Information Table S7. All quantified neo-N-terminal peptides derived from extracellular proteins, identified by experiments using AcD3 tagging of N-terminal peptides with either SCX or N-terminal COFRADIC enrichment of N-terminal peptides. Ratios expressed as relative abundance in CAM media compared with ATM. Where a peptide was uniquely identified in either the CAM or ATM sample of an experiment this is denoted as a singleton in the relevant fold change column. Start and end position of each peptide shown, relative to the unprocessed protein. Mascot score for each peptide shown alongside the quantification for each experiment.