Arteriosclerosis, Thrombosis, and Vascular Biology

Journal of the American Heart Association

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Arterioscler Thromb Vasc Biol 2010;30;1325-1332; originally published online Apr 29, 2010;
DOI: 10.1161/ATVBAHA.110.204651
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 1079-5642. Online ISSN: 1524-4636

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Objective—Recent studies on cardiovascular progenitors have led to a new appreciation that paracrine factors may support the regeneration of damaged tissues.

Methods and Results—We used a shotgun proteomics strategy to compare the secretome of peripheral blood–derived smooth muscle progenitors (SPCs) with human aortic smooth muscle cells. The late-outgrowth SPCs produced fewer proteolytic enzymes and inflammatory cytokines and showed reduced invasive capacity. Similar to smooth muscle cells, SPCs secreted extracellular matrix. However, SPCs produced different matrix proteins, as evidenced by the truncation of proangiogenic domains in collagen α-1 (I) and increased production of periostin. Moreover, SPCs retained serum proteins, including proteoglycans, regulating collagen assembly; and pigment epithelium–derived factor, a potent inhibitor of angiogenesis. As a functional consequence, their conditioned medium was less angiogenic, as demonstrated by endothelial tube formation assays in vitro and implantation of Matrigel plugs into nude, severe combined immunodeficient mice (NOD/SCID).

Conclusion—The present study represents an important conceptual development, suggesting that SPCs may contribute to extracellular matrix production. **(*Arterioscler Thromb Vasc Biol*. 2010;30:1325-1332.)**

Key Words: angiogenesis ■ extracellular matrix ■ proteolytic enzymes ■ vascular biology ■ vascular muscle ■ proteomics

Several studies[1,2] have shown that vascular progenitor cells are present in circulating blood. This new concept in vascular biology resulted in a rapid translation into a clinical context. Trials have already been conducted to evaluate the therapeutic potential of bone marrow–derived and circulating progenitor cells in patients.[3–5] Yet, the contribution of cell therapy to cardiovascular repair is still debated. Much of the controversy arises from the fact that there is little evidence to suggest that these cells are present in large numbers and permanently incorporate into the vessel wall.[6–8] Most cells are immediately lost after injection, with additional loss occurring in the months that follow. Therefore, cell therapy might stimulate vessel formation and functional improvement in a paracrine manner.[9]

Our proteomic study of the secretome of colony-forming units and endothelial progenitor cell cultures (EPCs)[10] confirmed that their conditioned medium is proangiogenic but revealed that the markers used to define their endothelial potential may arise from an uptake of platelet microparticles by adherent mononuclear cells and that platelet microparticles contribute to the angiogenic activity of the conditioned medium.[11] In addition, platelet factors may induce an angiogenic monocyte/macrophage phenotype.[10] These studies demonstrated how the use of proteomics can provide new insights, which were not obtained by conventional techniques. Little is known about secreted factors produced by other putative progenitor cell populations. The aim of the present study is to compare the secretome of late-outgrowth smooth muscle progenitors (SPCs) with early angiogenic cells (EACs), previously referred to as EPCs, and human aortic smooth muscle cells (SMCs).

Methods

An expanded supplemental Methods section is available online (http://atvb.ahajournals.org).

Cell Culture

The study was approved by the institutional review board of the Phoenix VA Health Care System, Phoenix, Ariz, and the ethics

Received on: January 2, 2009; final version accepted on: April 15, 2010.

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Arterioscler Thromb Vasc Biol **is available at http://atvb.ahajournals.org** **DOI: 10.1161/ATVBAHA.110.204651**

review board of J. W. Goethe University, University of Frankfurt, Frankfurt, Germany and King's College London, London, England. Cell culture of peripheral blood mononuclear cells was performed as previously described.[2,9] Before sampling, cells were washed carefully 3 times and placed in serum-free medium. After 24 hours, the conditioned media were harvested, centrifuged for 2 hours at 20 000*g* to remove particulates, and frozen at −80°C. Four replicates were obtained for late-outgrowth SPCs and EACs; 3 replicates were analyzed for human aortic SMCs.

Liquid Chromatography-Tandem Mass Spectrometry Analysis

Proteins in the conditioned media were subject to an in-solution digest with trypsin. Tryptic peptides were separated by reverse-phase nanoflow liquid chromatography (Easy-nanoLC) and analyzed online by tandem mass spectrometry using a linear ion trap with high mass accuracy (LTQ-Orbitrap). The resultant mass spectra were matched to database entries (UniProtKB/Swiss-Prot, release version 10.5) using the version of the SEQUEST algorithm contained in Bioworks 3.3 and imported into Scaffold, version 1.7. Assignments were accepted when the Xcorr score was greater than 1.9 for singly charged ions, greater than 2.5 for doubly charged ions, and greater than 3.0 for triply charged ions, along with a peptide probability of less than $1e^{-3}$. Results were further filtered for 2 or more independent peptides per protein identification. Protocols are available at http://www.vascular-proteomics.com.

Methods for immunoblotting, RT-PCR, immunofluorescence staining, matrix metalloproteinase (MMP) 1 ELISA, 27-plex cytokine measurements, cell invasion, tube formation, and Matrigel plug assays are available online at http://atvb.ahajournals.org.

Results

Comparison of SPCs With EACs

Late-outgrowth SPCs were generated by removing vascular endothelial growth factor and adding platelet-derived growth factor when first primordial outgrowth colonies formed in cultured cells. Differences in secreted proteins were investigated using liquid chromatography-tandem mass spectrometry. Label-free differential expression analysis returned protein features distinguishing EACs from SPCs (supplemental Table I and supplemental II; available online at http://atvb.ahajournals.org). Reconstructed ion chromatograms for selected proteins are shown in supplemental Figure I (available online at http://atvb.ahajournals.org). The proteomic data confirmed that EACs are of monocytic origin (CD14) and that their conditioned medium is rich in platelet proteins (CXCL7).[11] Consistent with previous microarray analysis,[9] EACs secreted high levels of cathepsins, including cathepsin L. The latter has been implicated for neovascularization.[12] In contrast, CD14, platelet proteins, and cathepsins were not detected in SPCs staining positive for smooth muscle α-actin (Figure 1A). Their conditioned medium contained a variety of collagen chains (supplemental Figure II). Thus, the 2 cell populations showed a distinct protein profile in their conditioned medium. To validate the proteomic findings, the differential expression of CD14 and selected extracellular matrix proteins was verified at the mRNA level (Figure 1B).

Comparison of SPCs With Aortic SMCs

To further characterize SPCs, we compared their secretome with human aortic SMCs. The classification of all identified proteins according to the Gene Ontology Annotation returned "extracellular matrix" and "proteinaceous extracellular matrix" as major categories in SMCs and SPCs, but not in

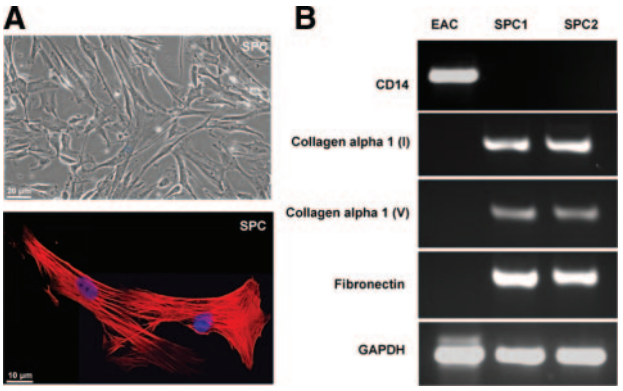

Figure 1. Late-outgrowth SPCs vs EACs. A, Morphological features of SPCs and immunofluorescent staining for smooth muscle α-actin (red). Nuclei were counterstained with Hoechst 33258 (blue). B, RT-PCR for mRNA expression of CD14 and extracellular matrix proteins.

EACs (supplemental Figure III). The consensus report for proteins present in both SMCs and SPCs contained 100 proteins (supplemental Table III). Proteins predominantly found in either SMCs or SPCs are listed in supplemental Table IV and supplemental Table V. Proteolytic enzymes and extracellular matrix proteins are highlighted in the Table.

SPCs Produce Extracellular Matrix

A significant degree of overlap was observed among the matrix proteins identified in the conditioned medium of SPCs and SMCs. Similar to SMCs, SPCs express fibronectin, collagen α-1 (I), and collagen α-1 (V) (Figure 2A). However, unlike SMCs, there was no spectral evidence for the *N*-terminal domains of collagen α-1 (I) in SPCs that contain a von Willebrand factor type C module and a heparin-binding domain implicated in endothelial tube formation[13] (supplemental Figure IV). Matrix proteins predominantly expressed in SPCs included collagen α-1 (XIV), which plays an adhesive role by integrating collagen bundles; and periostin, which is required for maturation and extracellular matrix stabilization.[14]

SPCs Retain Serum Proteins

Although all cell lines were cultured in serum-free media before sampling and the carryover for high abundant serum proteins was identical in both cell types (bovine albumin and fetuin A represented on average 5.0% and 0.85% of the total spectra in SPCs, respectively), and 5.3% and 0.86% of the total spectra in SPCs, respectively; the conditioned medium of SPCs contained additional matrix proteins, which were not of human, but of bovine, origin. For 3 proteoglycans (biglycan, decorin, and lumican), there was clear spectral evidence for the bovine protein in SPCs and the human homologue in SMCs (supplemental Table VI). Consistent with the observed reduction of human-specific peptides, mRNA levels of biglycan, decorin, and lumican were downregulated in SPCs (Figure 2A). Similarly, other matrix-binding proteins (ie, pigment epithelium–derived factor [PEDF], a potent inhibitor of angiogenesis; and insulin-like growth factor–binding protein 2) were detected as bovine proteins in the conditioned medium of SPCs in the absence of corresponding mRNA

Table. Extracellular Components in the Conditioned Medium of SPC and SMC Cultures

Protein Name*	Entry Name	Molecular Weight, kDa	SMC (n=3)†	SPC (n=4)†	*P* Value‡
Proteases and protease inhibitors					
Matrix metalloproteinase 1	MMP1_HUMAN	54	158±28	12±8	0.03§
72-kDa type IV collagenase	MMP2_HUMAN	74	10±2	8±2	0.60
Metalloproteinase inhibitor 1	TIMP1_HUMAN	23	22±2	1±1	0.004§
Metalloproteinase inhibitor 2	TIMP2_HUMAN	24	5±1	6±1	0.90
Procollagen C–endopeptidase enhancer 1	PCOC1_HUMAN	48	7±3	3±0	0.30
Pappalysin-1 (IGF-dependent IGFBP-4 protease)	PAPP1_HUMAN	181	2±1	ND	0.20
Collagen chains					
Collagen α-1 (I)	CO1A1_HUMAN	139	32±9	114±24	0.04§
Collagen α-1 (III)	CO3A1_HUMAN	139	20±6	16±2	0.61
Collagen α-1 (V)	CO5A1_HUMAN	184	2±0	11±2	0.03§
Collagen α-1 (VI)	CO6A1_HUMAN	109	23±3	15±4	0.16
Collagen α-1 (XIV)	COEA1_HUMAN	194	ND	4±1	0.04§
Collagen α-2 (I)	CO1A2_HUMAN	129	59±17	67±9	0.70
Collagen α-2 (IV)	CO4A2_HUMAN	168	2±1	1±1	0.13
Collagen α-2 (V)	CO5A2_HUMAN	145	6±2	13±3	0.17
Collagen α-2 (VI)	CO6A2_HUMAN	109	6±2	8±2	0.52
Collagen α-3 (VI)	CO6A3_HUMAN	344	13±3	ND	0.06
Laminin subunits					
Laminin α-4	LAMA4_HUMAN	203	20±3	ND	0.02§
Laminin α-5	LAMA5_HUMAN	400	1±0	2±0	0.09
Laminin β-1	LAMB1_HUMAN	198	17±5	3±0	0.11
Laminin γ-1	LAMC1_HUMAN	178	22±8	8±2	0.20
Proteoglycans and glycoproteins					
Fibronectin	FINC_HUMAN	263	27±8	68±12	0.04§
Versican	CSPG2_HUMAN	373	20±3	ND	0.03§
Periostin	POSTN_HUMAN	93	ND	8±4	0.18
Perlecan	PGBM_HUMAN	469	77±15	17±3	0.06
Decorin	PGS2_HUMAN	40	9±2	2±0	0.09
Lumican	LUM_HUMAN	38	3±2	ND	0.19
Biglycan	PGS1_HUMAN	42	6±1	ND	0.03§
Fibrillin-1	FBN1_HUMAN	312	23±13	7±14	0.18
EGF-containing fibulinlike ECM protein 1 (fibulin 3)	FBLN3_HUMAN	55	3±1	ND	0.15
Follistatin-related protein 1	FSTL1_HUMAN	35	14±5	8±2	0.33
SPARC (osteonectin)	SPRC_HUMAN	35	14±4	11±2	0.52
Nidogen-1	NID1_HUMAN	136	2±1	1±0	0.30
Nidogen-2	NID2_HUMAN	151	1±0	1±1	0.52
EMILIN-1	EMIL1_HUMAN	107	5±3	1±0	0.23
Thrombospondin 1	TSP1_HUMAN	130	1±1	1±1	0.95
Thrombospondin 2	TSP2_HUMAN	130	16±9	ND	0.20
Galectin 1	LEG1_HUMAN	15	7±2	4±1	0.22
IGF-binding proteins					
4	IBP4_HUMAN	28	4±1	ND	0.06
6	IBP6_HUMAN	25	4±1	1±0	0.08
7 (PGI2-stimulating factor)	IBP7_HUMAN	29	17±2	4±1	0.009§

(*Continued*)

Table. Continued

Protein Name*	Entry Name	Molecular Weight, kDa	SMC (n=3)†	SPC (n=4)†	*P* Value‡
Other ECM-associated proteins					
Growth-regulated protein α (CXCL1)	GROA_HUMAN	11	36±8	4±3	0.04§
Pentraxin-related protein PTX3	PTX3_HUMAN	42	4±2	ND	0.15
Extracellular matrix protein 1	ECM1_HUMAN	61	4±1	5±1	0.36
EGF-like repeat and discoidin I-like domain-containing protein 3	EDIL3_HUMAN	54	ND	3±1	0.02§
Galectin-3-binding protein	LG3BP_HUMAN	65	2±2	ND	0.42
TGF-β–induced protein ig-h3	BGH3_HUMAN	75	12±4	ND	0.12
Latent TGF β–binding protein 2	LTBP2_HUMAN	195	3±1	ND	0.03§
Latent TGF-binding protein, isoform 1S	LTB1S_HUMAN	153	5±5	1±1	0.48
Pregnancy zone protein	PZP_HUMAN	164	2±3	4±4	0.53
Sulfhydryl oxidase 1	QSCN6_HUMAN	83	4±2	ND	0.22
Lysyl oxidase homolog 2	LOXL2_HUMAN	87	2±1	4±1	0.39

CXCL indicates chemokine (C-X-C motif) ligand; ECM, extracellular matrix; EGF, epidermal growth factor; IGFBP, insulin growth factor–binding protein; MMP, matrix metalloproteinase; ND, not detected; PGI, prostacyclin; PTX, pentraxin; SMC, smooth muscle cell; SPARC, secreted protein acidic and rich in cysteine; SPC, smooth muscle progenitor; TGF, transforming growth factor; TIMP, tissue inhibitor of metalloproteinases.

*The table highlights proteins that were chosen for their potential importance in the ECM. The complete list of identified proteins and their normalized spectral counts (percentage of total spectra) are available in supplemental Tables III through V (available online at http://atvb.ahajournals.org).

†Data are given as mean±SE number of assigned tryptic peptides, determined by liquid chromatography–tandem mass spectrometry.

‡Derived from *t* tests.

§$P<0.05$.

expression (Figure 2A [PEDF] and data not shown [insulin-like growth factor–binding protein 2]), suggesting cell type–specific retention from bovine serum. Differences for periostin, thrombospondin 2, biglycan, PEDF, and insulin-like growth factor–binding protein 2 were verified by immunoblotting (Figure 2B).

Low Proteolytic and Inflammatory Activity in SPCs

In agreement with the spectral counts in the proteomic data set (Table), ELISA measurements established that the concentrations of MMP-1 in the conditioned medium of serum-

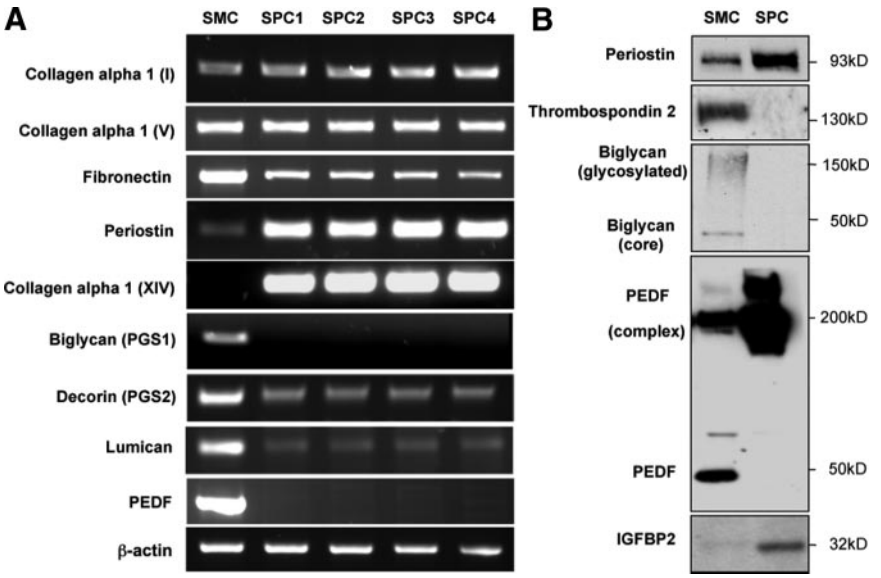

Figure 2. Expression of extracellular matrix proteins. A, RT-PCR for mRNA levels of selected extracellular matrix proteins and pigment epithelium–derived factor (PEDF) in SMCs and SPCs. B, Serum-free culture media conditioned by SMCs and SPCs were probed with antibodies to periostin, thrombospondin 2, biglycan, PEDF, and insulin-like growth factor–binding protein (IGFBP-2). The antibody against biglycan is specific for the human protein, as confirmed by the absence of staining with purified bovine biglycan (data not shown); the antibodies against PEDF and IGFBP-2 recognize both the human and the bovine protein. The additional PEDF band at greater than 200 kDa is likely the result of binding to other proteins. Irreversible reduction and alkylation with dithiothreitol and iodoacetamide abolished the high-molecular-weight staining and increased the intensity of the 50-kDa band. The presence of PEDF in both bands was confirmed by liquid chromatography-tandem mass spectrometry (data not shown).

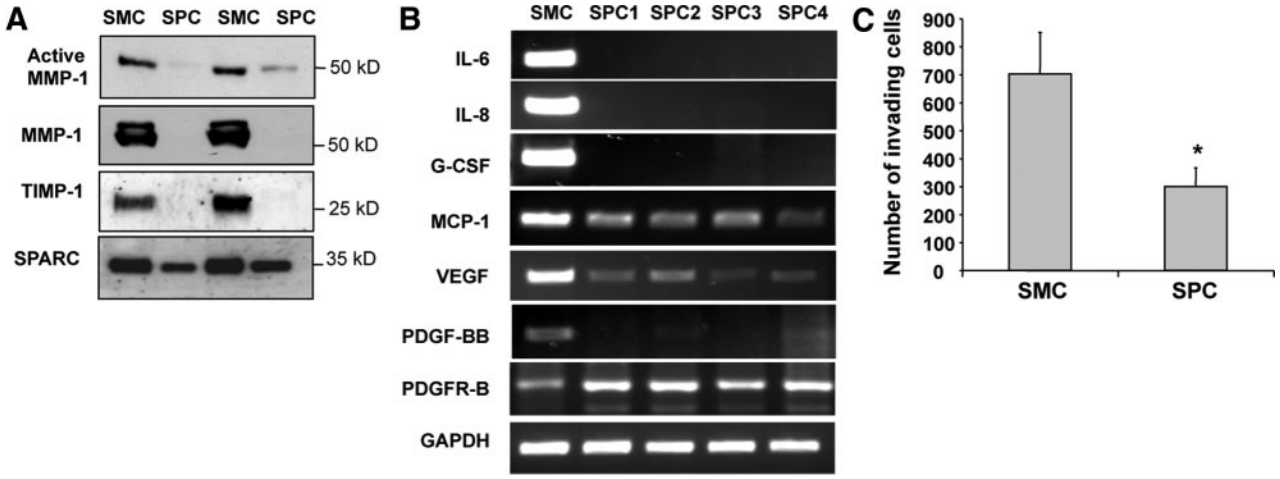

Figure 3. Proteolytic and inflammatory activity. A, Cell culture supernatants of SMCs and SPCs were probed with antibodies to active MMP-1, total MMP-1, and TIMP-1. Differences for total MMP-1 are more pronounced than for active MMP-1. Because there are no "housekeeping proteins" in conditioned medium, secreted protein acidic and rich in cysteine (SPARC) was chosen as the loading control based on the proteomic data presented in supplemental Table III (available online at http://atvb.ahajournals.org; protein No. 20, 0.20% vs 0.14% of total spectra in SMCs and SPCs, respectively). B, Cytokine expression evaluated by RT-PCR. Corresponding protein levels are listed in supplemental Table VII. SPCs express platelet-derived growth factor receptor beta (PDGFR-B). C, Invasion assay comparing SMCs with SPCs. Results were derived from 3 independent experiments, each performed in triplicate. *Significant difference by paired *t* test, $P<0.05$.

starved SMCs exceeded 100 ng/mL, whereas MMP-1 levels in the supernatant of SPCs were less than 1 ng/mL (n=3, data not shown). Comparable results were obtained by immunoblotting (Figure 3A). Differences became less pronounced if antibodies for active MMP-1 were used (top panel) because tissue inhibitor of metalloproteinases-1 (TIMP-1), a potent MMP inhibitor, was enriched in the conditioned medium of SMCs. Yet, *N*-cadherin, an established MMP target on the SMC surface,[15] was shedded in their conditioned medium (supplemental Table IV). Similarly, the cytokine secretion of SPCs was remarkably low given their origin from the myeloid lineage. This was confirmed at the mRNA (Figure 3B) and protein levels (supplemental Table VII). More important, SPCs produced less vascular endothelial growth factor and showed reduced invasive capacity (Figure 3C), suggesting that SPCs are unlikely to promote angiogenesis.

Functional Validation

To explore whether the observed changes in SPCs were functionally important, we assessed endothelial tube formation in vitro. As shown in Figure 4A and B, the formation of new tubelike structures in Matrigel was supported by conditioned medium from SMCs, but not from SPCs. Supplementing cultures of human umbilical vein endothelial cells with conditioned medium of SMCs or SPCs did not alter endothelial proliferation and survival (Figure 4C). However, endothelial cell numbers were higher if dishes were precoated with conditioned medium of SPCs than SMCs (Figure 4D), suggesting that the matrix of SPCs has distinct functional properties. Thus, it was interesting to observe that endothelial growth factor–like repeat and discoidin I–like domain-containing protein 3, which promotes adhesion of endothelial cells through interaction with the $\alpha_v\beta_3$ integrin receptor and

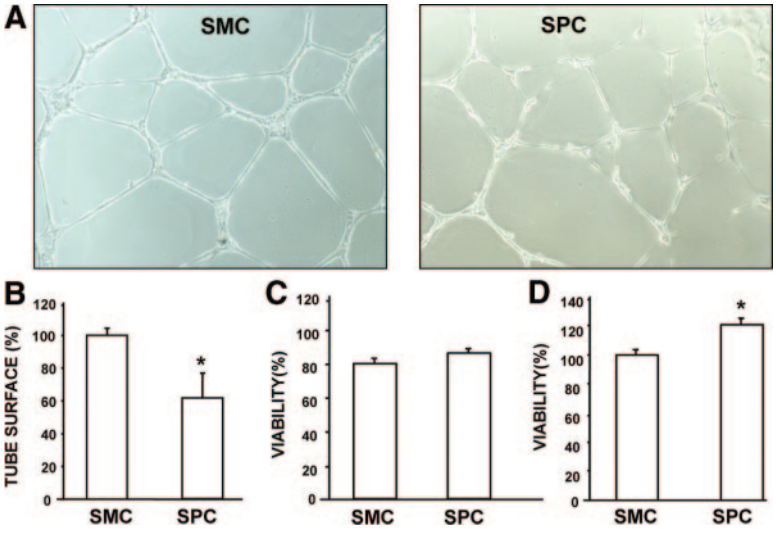

Figure 4. Angiogenic activity in vitro. A, Endothelial tube formation in Matrigel was quantified in the presence of conditioned medium of SMCs and SPCs. B, Reduced tube surface in the presence of conditioned medium of SPCs. Data are given as mean±SE of 3 independent experiments, each performed in duplicate. C, Conditioned medium of SMCs or SPCs was added to human umbilical vein endothelial cells (HUVECs) at a dilution of 1:1. The supplementation had no effect on cell numbers (n=3). D, In contrast, coating dishes with conditioned medium of SPCs before seeding of HUVECs increased endothelial cell numbers by 20% vs conditioned medium of SMCs (n=4). Experiments were performed in triplicate. *Significant difference by a *t* test, $P<0.05$.

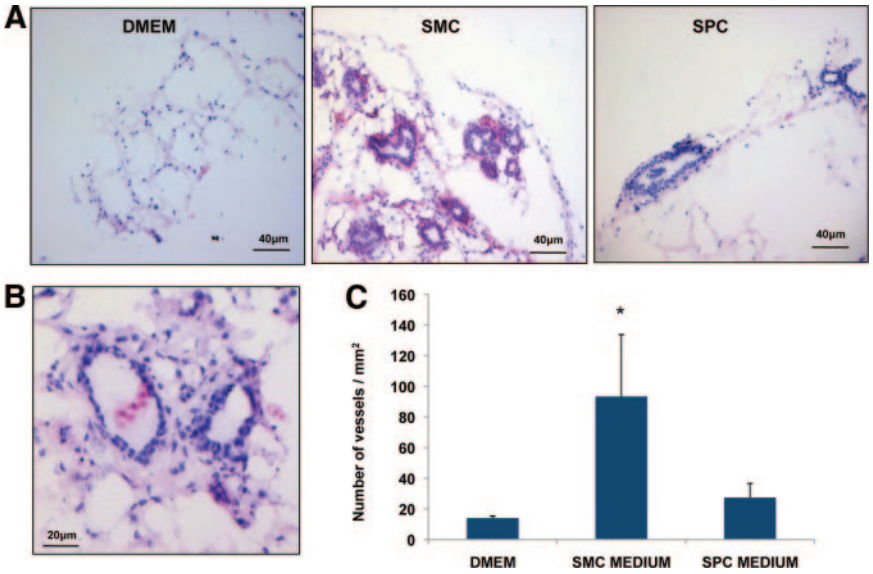

Figure 5. Angiogenesis in vivo. A, DMEM or conditioned medium from SMCs or SPCs was mixed with Matrigel and injected into mice with severe combined immunodeficiency. Sections of the plugs were stained with hematoxylin-eosin. B and C, Matrigel plugs with conditioned medium from SMCs, but not SPCs, showed a significant increase in the number of neovessels. Data are representative of at least 3 independent experiments. *Significant difference by a *t* test, $P<0.05$.

inhibits formation of vascular-like structures,[16] was only identified in the conditioned medium of SPCs (Table). Finally, the angiogenic effect was investigated by implanting Matrigel plugs injected into nude, severe immunodeficient mice (NOD.CB17-Prkdc^{scid}). Compared with the conditioned medium of SMCs, plugs treated with the conditioned medium of SPCs showed reduced vascularization over the implantation period (Figure 5).

Discussion

Although vascular progenitor cells may contribute to tissue repair, the mechanisms by which they act remain unsettled. Herein, we demonstrated that late-outgrowth SPCs show a distinct secretion profile compared with EACs. Similar to their SMC counterparts, SPCs express a range of extracellular matrix and matricellular proteins, some unique to SPCs only, but released less proteases and inflammatory cytokines. In this respect, SPCs displayed properties that were also distinct from aortic SMCs.

SPCs Secrete Fewer Proteolytic Enzymes

One of the most prominent differences between SMCs and SPCs was observed for the interstitial collagenase MMP-1. Several lines of evidence suggest that SMCs constitutively express MMPs; however, when stimulated by cytokines, SMCs also produce activated forms of MMPs, which is essential for their invasive capacity.[17,18] Because cytokines augment the production of MMPs without appreciably affecting the synthesis of TIMPs, they can tip the regional balance of MMP activity in favor of vascular matrix degradation, making atherosclerotic plaques vulnerable to rupture.[19] Notably, baseline secretion of MMP-1 in SMCs appears to be influenced by age: human newborn but not adult SMCs produced high amounts of MMP-1 in vitro, which correlated with the presence of a_vb_3 integrin on their surface.[20] In contrast, SPCs produced less MMP-1, a finding consistent with a previous report[21] that SPCs express high levels of β_1, but less of $\alpha_v\beta_3$ integrin. The β_3 integrin receptor mRNA has been shown to be upregulated early after injury of the rat carotid artery, with a time course correlating to SMC proliferation and migration to the intima, whereas a β_3 integrin–blocking antibody almost completely blocked SMC migration from the media to the intima.[22] Thus, the lack of β_3 integrin on SPCs provides a likely explanation for their reduced MMP secretion and impaired invasive capacity, as observed in the present study.

SPCs Produce Extracellular Matrix

Consistent with their integrin profile, SPCs show increased adherence to collagen type I[21]; this matrix protein was also found in abundance in their conditioned medium. EACs produced predominantly proteases and inflammatory molecules, which would facilitate the breakdown of existing matrix and the recruitment of mononuclear cells to the site of injury. Late-outgrowth SPCs secreted barely any inflammatory cytokines or matrix-degrading enzymes; however, they expressed extracellular matrix components. For example, levels of periostin, one of the most abundant mRNAs associated with vascular injury[23] and essential for cardiac repair,[24,25] were higher in SPCs than in SMCs. These findings provide a mechanistic underpinning for recent observations that injections of SPCs have beneficial effects on atherosclerosis by promoting changes in plaque composition toward a stable phenotype[26]: when human EPCs or SPCs were injected every other week in apolipoprotein $E^{-/-}$ recombination activating gene-2 $(RAG2)^{-/-}$ mice, injection of SPCs, but not EPCs, increased collagen and SMC content and reduced the number of macrophages in atherosclerotic plaques. Furthermore, an interaction between EPCs and SPCs was recently shown to enhance the formation of a mature and functional vascular network after cell-based therapy.[27] Consistent with these in vivo data, our proteomic findings provided direct evidence that late-outgrowth SPCs express extracellular matrix and are likely to play a distinct role from EACs, referred to as EPCs in the publications previously mentioned.

SPCs Retain Serum Proteins

Although all cells were cultured in serum-free media before sampling to ensure that the collected conditioned media

contain no other extraneous proteins, except for the secreted or shed proteins, SPCs selectively retained specific bovine proteins from the serum supplement. This conclusion was supported by 3 independent lines of evidence: (1) The proteins were identified as bovine rather than human by tandem mass spectrometry. (2) Gene expression was absent or markedly downregulated at the transcriptional level. (3) There was positive or negative immunostaining, depending on whether the antibody recognizes both the human and the bovine protein or the human protein only. Examples included PEDF, a potent inhibitor of angiogenesis[28] that binds to newly formed collagen and counters the effects of vascular endothelial growth factor; and biglycan, which is involved in collagen assembly and is essential for the functional integrity of the vascular wall.[29] The fact that proteins from the bovine serum supplement can bind to extracellular matrix clearly illustrates the advantage of a proteomics approach, which can distinguish between proteins from different species.

Limitations of the Study

Although mass spectrometry is a valuable tool to array secreted proteins, minor components can remain undetected. Moreover, it is possible that SPCs are specialist myeloid cells,[30] bone marrow mesenchymal stem cells, or pericyte-like cells ($CD14^-$, SM α-$actin^+$, and platelet-derived growth factor receptor B^+). Similarly, SMCs do not undergo terminal differentiation, and heterogeneity is observed among different SMC isolates from human aortas, in particular for cytokine secretion (data not shown); their differentiation state is plastic and rapidly influenced by external stimuli. As with any in vitro study, findings in cultured cells may not allow a straightforward translation onto their phenotype in vivo. However, without expansion in culture, it is impossible to sample their secretome and obtain sufficient material for proteomic analysis.

Conclusion

In conclusion, proteomics is an evolving field in cardiovascular research and proteomic techniques offer an unbiased approach to phenotype putative progenitor cell populations.[31,32] As demonstrated in this study, a comprehensive description of their secretome can advance our understanding of their biological potential.

Acknowledgements

We thank Xiaoke Yin, PhD; Qiuru Xing, MSc; Anthony Sullivan, PhD; and Gary Woffendin, PhD for their technical assistance.

Sources of Funding

This study was supported by the European Vascular Genomics Network (LSHM-CT-2003-503254) as part of the 6th European Framework Programme; a grant from the British Heart Foundation; a grant from the Oak Foundation; a grant from the Juvenile Diabetes Research Foundation (Dr Simper); and resources and facilities at the Phoenix VA Health Care System (Dr Simper). Dr Mayr is a Senior Research Fellow from the British Heart Foundation.

Disclosures

None.

References

1. Asahara T, Murohara T, Sullivan A, Silver M, van der Zee R, Li T, Witzenbichler B, Schatteman G, Isner JM. Isolation of putative progenitor endothelial cells for angiogenesis. *Science*. 1997;275:964–967.
2. Simper D, Stalboerger PG, Panetta CJ, Wang S, Caplice NM. Smooth muscle progenitor cells in human blood. *Circulation*. 2002;106:1199–1204.
3. Losordo DW, Dimmeler S. Therapeutic angiogenesis and vasculogenesis for ischemic disease, part II: cell-based therapies. *Circulation*. 2004;109:2692–2697.
4. Losordo DW, Dimmeler S. Therapeutic angiogenesis and vasculogenesis for ischemic disease, part I: angiogenic cytokines. *Circulation*. 2004;109:2487–2491.
5. Rafii S, Lyden D. Therapeutic stem and progenitor cell transplantation for organ vascularization and regeneration. *Nat Med*. 2003;9:702–712.
6. Torsney E, Mandal K, Halliday A, Jahangiri M, Xu Q. Characterisation of progenitor cells in human atherosclerotic vessels. *Atherosclerosis*. 2007;191:259–264.
7. Simper D, Wang S, Deb A, Holmes D, McGregor C, Frantz R, Kushwaha SS, Caplice NM. Endothelial progenitor cells are decreased in blood of cardiac allograft patients with vasculopathy and endothelial cells of non-cardiac origin are enriched in transplant atherosclerosis. *Circulation*. 2003;108:143–149.
8. Caplice NM, Bunch TJ, Stalboerger PG, Wang S, Simper D, Miller DV, Russell SJ, Litzow MR, Edwards WD. Smooth muscle cells in human coronary atherosclerosis can originate from cells administered at marrow transplantation. *Proc Natl Acad Sci U S A*. 2003;100:4754–4759.
9. Urbich C, Aicher A, Heeschen C, Dernbach E, Hofmann WK, Zeiher AM, Dimmeler S. Soluble factors released by endothelial progenitor cells promote migration of endothelial cells and cardiac resident progenitor cells. *J Mol Cell Cardiol*. 2005;39:733–742.
10. Pula G, Mayr U, Evans C, Prokopi M, Vara DS, Yin X, Astroulakis Z, Xiao Q, Hill J, Xu Q, Mayr M. Proteomics identifies thymidine phosphorylase as a key regulator of the angiogenic potential of colony-forming units and endothelial progenitor cell cultures. *Circ Res*. 2009;104:32–40.
11. Prokopi M, Pula G, Mayr U, Devue C, Gallagher J, Xiao Q, Boulanger CM, Westwood N, Urbich C, Willeit J, Steiner M, Breuss J, Xu Q, Kiechl S, Mayr M. Proteomic analysis reveals presence of platelet microparticles in endothelial progenitor cell cultures. *Blood*. 2009;114:723–732.
12. Urbich C, Heeschen C, Aicher A, Sasaki K, Bruhl T, Farhadi MR, Vajkoczy P, Hofmann WK, Peters C, Pennacchio LA, Abolmaali ND, Chavakis E, Reinheckel T, Zeiher AM, Dimmeler S. Cathepsin L is required for endothelial progenitor cell-induced neovascularization. *Nat Med*. 2005;11:206–213.
13. Sweeney SM, Guy CA, Fields GB, San Antonio JD. Defining the domains of type I collagen involved in heparin-binding and endothelial tube formation. *Proc Natl Acad Sci U S A*. 1998;95:7275–7280.
14. Snider P, Hinton RB, Moreno-Rodriguez RA, Wang J, Rogers R, Lindsley A, Li F, Ingram DA, Menick D, Field L, Firulli AB, Molkentin JD, Markwald R, Conway SJ. Periostin is required for maturation and extracellular matrix stabilization of noncardiomyocyte lineages of the heart. *Circ Res*. 2008;102:752–760.
15. Uglow EB, Slater S, Sala-Newby GB, Aguilera-Garcia CM, Angelini GD, Newby AC, George SJ. Dismantling of cadherin-mediated cell-cell contacts modulates smooth muscle cell proliferation. *Circ Res*. 2003;92:1314–1321.
16. Hidai C, Zupancic T, Penta K, Mikhail A, Kawana M, Quertermous EE, Aoka Y, Fukagawa M, Matsui Y, Platika D, Auerbach R, Hogan BL, Snodgrass R, Quertermous T. Cloning and characterization of developmental endothelial locus-1: an embryonic endothelial cell protein that binds the alphavbeta3 integrin receptor. *Genes Dev*. 1998;12:21–33.
17. Galis ZS, Muszynski M, Sukhova GK, Simon-Morrissey E, Unemori EN, Lark MW, Amento E, Libby P. Cytokine-stimulated human vascular smooth muscle cells synthesize a complement of enzymes required for extracellular matrix digestion. *Circ Res*. 1994;75:181–189.
18. Bond M, Chase AJ, Baker AH, Newby AC. Inhibition of transcription factor NF-kappaB reduces matrix metalloproteinase-1, -3 and -9 production by vascular smooth muscle cells. *Cardiovasc Res*. 2001;50:556–565.
19. Sukhova GK, Schonbeck U, Rabkin E, Schoen FJ, Poole AR, Billinghurst RC, Libby P. Evidence for increased collagenolysis by interstitial collagenases-1 and -3 in vulnerable human atheromatous plaques. *Circulation*. 1999;99:2503–2509.
20. Bendeck MP, Irvin C, Reidy M, Smith L, Mulholland D, Horton M, Giachelli CM. Smooth muscle cell matrix metalloproteinase production is

stimulated via alpha(v)beta(3) integrin. *Arterioscler Thromb Vasc Biol*. 2000;20:1467–1472.
21. Deb A, Skelding KA, Wang S, Reeder M, Simper D, Caplice NM. Integrin profile and in vivo homing of human smooth muscle progenitor cells. *Circulation*. 2004;110:2673–2677.
22. Stouffer GA, Hu Z, Sajid M, Li H, Jin G, Nakada MT, Hanson SR, Runge MS. Beta3 integrins are upregulated after vascular injury and modulate thrombospondin- and thrombin-induced proliferation of cultured smooth muscle cells. *Circulation*. 1998;97:907–915.
23. Lindner V, Wang Q, Conley BA, Friesel RE, Vary CP. Vascular injury induces expression of periostin: implications for vascular cell differentiation and migration. *Arterioscler Thromb Vasc Biol*. 2005;25:77–83.
24. Kuhn B, del Monte F, Hajjar RJ, Chang YS, Lebeche D, Arab S, Keating MT. Periostin induces proliferation of differentiated cardiomyocytes and promotes cardiac repair. *Nat Med*. 2007;13:962–969.
25. Shimazaki M, Nakamura K, Kii I, Kashima T, Amizuka N, Li M, Saito M, Fukuda K, Nishiyama T, Kitajima S, Saga Y, Fukayama M, Sata M, Kudo A. Periostin is essential for cardiac healing after acute myocardial infarction. *J Exp Med*. 2008;205:295–303.
26. Zoll J, Fontaine V, Gourdy P, Barateau V, Vilar J, Leroyer A, Lopes-Kam I, Mallat Z, Arnal JF, Henry P, Tobelem G, Tedgui A. Role of human smooth muscle cell progenitors in atherosclerotic plaque development and composition. *Cardiovasc Res*. 2008;77:471–480.
27. Foubert P, Matrone G, Souttou B, Lere-Dean C, Barateau V, Plouet J, Le Ricousse-Roussanne S, Levy BI, Silvestre JS, Tobelem G. Coadministration of endothelial and smooth muscle progenitor cells enhances the efficiency of proangiogenic cell-based therapy. *Circ Res*. 2008;103:751–760.
28. Dawson DW, Volpert OV, Gillis P, Crawford SE, Xu H, Benedict W, Bouck NP. Pigment epithelium-derived factor: a potent inhibitor of angiogenesis. *Science*. 1999;285:245–248.
29. Heegaard AM, Corsi A, Danielsen CC, Nielsen KL, Jorgensen HL, Riminucci M, Young MF, Bianco P. Biglycan deficiency causes spontaneous aortic dissection and rupture in mice. *Circulation*. 2007;115:2731–2738.
30. Metharom P, Liu C, Wang S, Stalboerger P, Chen G, Doyle B, Ikeda Y, Caplice NM. Myeloid lineage of high proliferative potential human smooth muscle outgrowth cells circulating in blood and vasculogenic smooth muscle-like cells in vivo. *Atherosclerosis*. 2008;198:29–38.
31. Didangelos A, Simper D, Monaco C, Mayr M. Proteomics of acute coronary syndromes. *Curr Atheroscler Rep*. 2009;11:188–195.
32. Mayr M, Zampetaki A, Sidibe A, Mayr U, Yin X, De Souza AI, Chung YL, Madhu B, Quax PH, Hu Y, Griffiths JR, Xu Q. Proteomic and metabolomic analysis of smooth muscle cells derived from the arterial media and adventitial progenitors of apolipoprotein E-deficient mice. *Circ Res*. 2008;102:1046–1056.

ONLINE MATERIAL

COMPARATIVE PROTEOMICS PROFILING REVEALS ROLE OF SMOOTH MUSCLE PROGENITORS IN EXTRACELLULAR MATRIX PRODUCTION

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Material and Methods

Progenitor cell culture. Progenitor cell culture was performed as previously described [1, 2]. Mononuclear cells were isolated by density gradient centrifugation from peripheral blood of healthy human volunteers and plated on culture dishes coated with human fibronectin. For SPCs, the Cambrex EGM-2 medium was enriched by PDGF-BB and stripped of VEGF at the time when first primordial outgrowth colonies formed in cultured cells. Ultimately, confirmed SPCs were propagated in a SMC-like medium Cambrex SmGM-2 containing 5% FBS, 2 ng/mL human basic fibroblast growth factor, 0.5 ng/mL human epidermal growth factor, 50 µg/mL gentamycin, and 5 µg/mL bovine insulin enriched by 10 ng/ml PDGF-BB. For comparison, human aortic SMCs were obtained from young donors (Cambrex) and cultivated under identical conditions. These cells stain positive for smooth muscle alpha-actin and negative for von Willebrand factor antigen. Experiments were conducted on SMCs between passage 10 and 15. EACs were obtained from peripheral blood mononuclear cells (8 x 10^6 cells/ml medium) as previously described [3, 4] and maintained in endothelial basal medium (EBM; Cambrex, Verviers, Belgium) supplemented with hydrocortisone, bovine brain extract, gentamicin, amphotericin B, epidermal growth factor, and 20% foetal calf serum (FCS). After 3 washes to minimize cross-contamination with proteins of the bovine serum supplement, 2x10e^6 cells were incubated with 10 mL serum-free medium in 10 cm petridishes. The conditioned media were sampled after 24 h and centrifuged for 2 h at 20,000 g to remove particulates. 4 biological replicates were obtained for SPCs and EACs and 3 for aortic SMCs.

In-solution digest. Frozen volumes of conditioned medium were removed from –80° C and thawed at 4° C. 500 µl were placed in a Microcon Ultracel YM–3 and

centrifuged for 45 min at 12,000 rpm. The procedure was repeated three times. A total volume of 1.5 ml conditioned medium was concentrated about 50-fold. Protein concentrations were determined using the Bradford assay (Bio-rad). Subsequently, proteins were denatured in the spin columns by addition of 6M guanidine hydrochloride (buffered with Tris base to pH 8.3), reduced with 10 mM DTT and alkalyated with 25 mM iodoacetamide for 20 min at RT. Buffer exchange was performed using 50 mM ammonium bicarbonate before samples were subject to an overnight tryptic digest at 37 ˚C (modified trypsin, Promega). Following enzymatic degradation, digested peptides were recovered from the spin columns by centrifugation.

LC-MS/MS analysis. Tryptic peptides were separated by nanoLC (Easy-nanoLC, Proxeon) on a 2 cm peptide trap and a 10 cm C18 column (BioBasic-18, Thermo Fisher Scientific) with a mobile phase (A) formed from HPLC grade water (JT Baker) containing 0.1% formic acid and (B) HPLC grade acetonitrile containing 0.1% formic acid, according to the gradient 0-30% B in 70 min, 30-50% B in 20 min, 50-80% B in 10 min. A nanospray source (Proxeon Biosystems, Odense) equipped with a metal emitter to ensure flow stability and a stable spray over a long time period was interfaced to a LTQ-Orbitrap mass spectrometer (Thermo Fisher Scientific). The mass spectrometry acquisition method involved one high-resolution full MS scan, over a mass range encompassing 465-1600 Da, immediately followed by data-dependent MS/MS scans of the 5 most intense ions detected in the full scan, subject to dynamic exclusion criteria. The resultant MS/MS data were matched to database entries (UniProtKB/Swiss-Prot, release version 10.5) using the version of the SEQUEST algorithm contained in Bioworks 3.3 (Thermo Fisher Scientific). All peptide sequence assignments were required to result from fully tryptic cleavages of

the corresponding proteins. Assignments were accepted when Xcorr score was > 1.9 for singly charged ions, > 2.5 for doubly charged ions, and > 3.0 for triply charged ions, along with peptide probability <1 e^{-3}. Results were then further filtered for ≥2 independent peptides per protein identification. Proteins that contained similar peptides and could not be differentiated based on MS/MS analysis alone were grouped to satisfy the principles of parsimony using the Occam's Razor approach (Table VI, available online at http://atvb.ahajournals.org).

Statistical Iterative Exploratory Visualization Environment (SIEVE). For SIEVE analysis (Thermo Fisher Scientific), SPCs were selected controls, with one sample used as the reference file for performing the time alignment of the LC runs. EACs were designated as sample files. The parameters for frame creation were retention time, m/z range, threshold, frame time width, and search peak width. The retention time and m/z ranges were used to reflect the time and mass range of the peptides being analyzed. The threshold parameter was set to 100,000, indicating the lowest signal intensity at which a frame would be generated. Frame time and m/z width are dependent on the quality of the chromatographic separation and the resolution of the mass spectrometer used. In this experiment, LC peaks were ~30 to 40 sec wide and the full scan resolution was set to 30,000, resulting in values of 2.5 min for frame time width, and 1.0 amu was used for frame m/z width to avoid the creation of isotope frames. For database searching using SEQUEST® the parameters were set to XCorr *vs* charge state 1.5 (1+), 2.5 (2+), 3.0 (3+) and 3.5 (4+).

Immunofluorescent staining. Immunofluorescent staining was performed with antibodies against alpha-actin (Sigma-Aldrich, St. Louis, Missouri, USA) as previously described[5].

Reverse Transcription-Polymerase Chain Reaction. Levels of mRNA transcripts were determined in cells cultivated in the presence of serum. Total RNA was extracted using the Qiagen kit according to the manufacturer's instructions. In brief, 2 μg of RNA were converted to cDNA using Promega Reverse Transcription System (Promega, Madison WI). cDNA products were amplified by PCR using human gene specific primers. The primers used were: CD14 Forward "CCA TGG AGC GCG CGT CCT GC", CD14 Reverse "GTC TTG GAT CTT AGG CAA AGC"; CO1A1 Forward "CCA AAG GAT CTC CTG GTG AA", CO1A1 Reverse "CTC CAG CCT CTC CAT CTT TG"; CO5A1 Forward "CT CCC GTC TTC CTC TAC GA", CO5A1 Reverse "AAA CAC GAT GAT GCC ATT GA"; FN1 Forward "CAA ATG GAG AGC CAT GTG TCT TAC", FN1 Reverse "ATC CCA CTG ATC TCC AAT GC"; POSTN Forward "CAA ATG TCT GTG CCC TTC AA", POSTN Reverse "GAT CCC TTT CCC TCG ATC TC"; COEA1 Forward "GAT TTC ATG GAA GGC TCC AA", COEA1 Reverse "CTT GAG CTG GCT TGC TTT CT"; PG-S1 Forward "CGC TGA CAC CTC GGG CGT CC", PG-S1 Reverse "AGC TCG GAG ATG TCG TTG TT"; PG-S2 Forward "AGT TCC TGA TGA CCG CGA CT", PG-S2 Reverse "CGC AGC TCC TGA AGA GTT TT"; LUM1 Forward "CCG TCC TGA CAG AGT TCA CA", LUM1 Reverse "TCA TAA TCA TAG TAC TGG CC"; PEDF Forward "TTC TTC AAA GTC CCC GTG AA" , PEDF Reverse "GTC TGG GCT GCT GAT CAA GT"; β-actin Forward "CAC AAC TGG GAC GAC ATG GAG", β-actin Reverse "TTC ATG AGG TAG TCA GTC TGG"; IGFBP-2 Forward "GCG AGG GCA CTT GTG AGA", IGFBP-2 Reverse "GCT GCT CAG TGA CCT TCT CC"; IL6 Forward "TAC CCC CAG GAG AAG ATT CC", IL6 Reverse "TTT CAG CCA TCT TTG GAA GG"; IL8 Forward " CAG TTT TGC CAA GGA GTG CT", IL8 Reverse "ACT TCT CCA CAA CCC TCT GC"; G-CSF Forward "CAC

TCT GGA CAG TGC AGG AA", G-CSF Reverse "AGC CCC TGG TAG AGG AAA AG"; MCP-1 Forward "CCC CAG TCA CCT GCT GTT AT", MCP-1 Reverse "GAG TTT GGG TTT GCT TGT CC"; PDGF-BB Forward "CTC ATA GAC CGC ACC AAC G", PDGF-BB Reverse "CAG CTG CCA CTG TCT CAC AC"; VEGF Forward "TCT TCA AGC CAT CCT GTG TG", VEGF Reverse "TTC TTG CGC TTT CGT TTT T"; PDGFR-B Forward "CTC ATA GAC CGC ACC AAC G", PDGFR-B Reverse "CAG CTG CCA CTG TCT CAC AC"; GAPDH Forward "TCA CCA GGG CTG CTT TTA AC", GAPDH Reverse "TTG ATT TTG GAG GGA TCT CG". PCR conditions were as follows: 94°C for 3 min and then 32 cycles for LUM1, COEA1, IL6, IL8, PDGFR-B, PDGF-BB, VEGF, MCP-1, CD14, GCSF, GAPDH, 30 cycles for CO1A1, CO5A1, FN1, 28 cycles for PG-S1, PG-S2, POSTN, and 26 cycles for β-actin at 94°C for 30 sec, 58°C for 1 min and 72°C for 1 min, followed by 72°C for 10 min. PCR products were separated by agarose gel electrophoresis and visualized by ethidium bromide staining.

MMP-1 ELISA. Serum-free conditioned medium of SMCs and SPCs was collected and assayed for MMP-1 production by a two-antibody sandwich ELISA SYStem (BIOTRAK ELISA System, Amersham. Int). Briefly, culture medium was diluted 1:10 in assay buffer. MMP-1 expression was determined according to the manufacturer's protocol. MMP-1 concentration was calculated using the Multiscan reader and software (Thermo Fisher Scientific).

Immunoblotting. Proteins in cell culture supernatants were separated on 4-20% gradient gels (Novex, Invitrogen) and transferred to nitrocellulose membranes. Membranes were blocked (overnight, 4 °C) in 5% PBS milk. Subsequently, they were probed with antibodies against MMP-1 (Chemicon, ABK830) and SPARC (1:200, Abcam, ab14071). An antibody specific to active MMP-1, which does not cross-react

with the inactive precursor, was obtained from Chemicon (MAB3323). The following other antibodies were purchased: TIMP-1 (Bethyl Laboratories Inc., A300-403A), periostin (Santa Cruz, sc-67233), thrombospondin 2 (Santa Cruz, sc-12313), biglcyan (Abcam, ab54855), PEDF (Abcam, ab14993) and IGFBP-2 (R&D , AF797, 0.1 μg/ml). HRP-conjugated secondary antibodies (Dako, 1:2000) were diluted in 5% PBS milk. After washing 3 times for 5 minutes each in 0.1% Tween 20 5% PBS milk, immunoglobulins were detected on X-ray films using enhanced chemiluminescence (ECL, GE Healthcare). In order to ensure the specificity of the anti-human biglycan antibody and to exclude cross-reactivity with bovine biglycan, we immunoblotted 12 µg of purified bovine biglycan (B8041, SigmaAldrich).

Cytokine assays. Human 27-plex cytokine assays were obtained from Biorad (Bioplex) and performed according to the manufacturer's instruction. Readings were obtained using the broad range standard curve with low CAL2 settings.

Cell invasion assay. To measure invasion capacity of SMCs and SPCs in response to PDGF, the BioCoatTM Matrigel^{TM} invasion chamber system (Becton Dickinson Labware 354165) was used according to the manufacturer's instruction. In brief, cells were were fluorescently labeled (CMFDA, Molecular Probes) while cultured in SmGM-2 medium and serum starved for 24 h. Labeled cells were resuspended in SMBM-2 medium with 1% BSA and seeded in the upper chamber of this modified Boyden chamber filled with Matrigel. PDGF-BB 10 ng/ml (R&D Systems) served as chemoattractant. After 24 h of incubation at 37°C, cells invaded through Matrigel layer were imaged on microscope and cell counts per high power fields quantified with help of NIH ImageJ software. Experiments were performed in triplicates in three independent assays.

***In vitro* tube formation assay.** Cell suspensions containing $4x10^4$ human

umbilical venous endothelial cells (HUVECs) were placed on top of the 50 µl/well Matrigel (10 mg/ml, Matrigel Basement Membrane Matrix, Phenol-Red Free [BD Biosciences], 50 µL/well) in 8-well chamber slides. HUVECs were cultured and identified as previously described[19]. Rearrangement of cells and the formation of capillary-like structures were observed in the presence of 50 ng/ml VEGF at 4 and 24 h. Pictures were taken on a Nikon Eclipse TS100 inverted microscope (objective 10x/0.25). The length of the capillaries was measured by the AxioVision 3.0 Software (Carl Zeiss Vision) and expressed as pixels^2 from 5 different reference points in duplicate wells. The values of the length of the tubes are given as mean ± SE.

Cell viability assay. For cell viability assays, HUVECs (2 x 10^3) were cultured in 96-well plates. After 24 h, a solution (Aqueous One Solution Cell Proliferation Assay, Promega) was added 2 h before the end of the incubation period and the optical density at 490 nm was recorded by photometry.

Matrigel plug assays. 150 µl Matrigel was mixed with 100 µl conditioned medium, and then injected subcutaneously into the back or flank of nude, severe combined immunodeficient mice (NOD.CB17-Prkdc^{scid}). Three injections were performed for each group. The mice were killed on day 14, and the plugs were harvested, washed with PBS followed by embedding with OCT, sectioning and hematoxylin-staining. The sections were visualized on a Zeiss Axioplan 2ie microscope (objective 20x/0.5) interfaced to AxioVision software (version 3.0.6). 60 images were taken across sections from 3 different matrigel plugs to quantify the number of neovessels.

Statistical analysis. Statistical analysis was performed using the analysis of variance and unpaired Student's *t*-test. Pairwise comparisons in the invasion assay

were analyzed using the paired Student's *t* -test. Results were given as means±SE. A *P* value <0.05 was considered significant.

References

1. Simper D, Stalboerger PG, Panetta CJ, Wang S, Caplice NM. Smooth muscle progenitor cells in human blood. *Circulation.* 2002;106:1199-1204.
2. Urbich C, Aicher A, Heeschen C, Dernbach E, Hofmann WK, Zeiher AM, Dimmeler S. Soluble factors released by endothelial progenitor cells promote migration of endothelial cells and cardiac resident progenitor cells. *J Mol Cell Cardiol.* 2005;39:733-742.
3. Dimmeler S, Aicher A, Vasa M, Mildner-Rihm C, Adler K, Tiemann M, Rutten H, Fichtlscherer S, Martin H, Zeiher AM. HMG-CoA reductase inhibitors (statins) increase endothelial progenitor cells via the PI 3-kinase/Akt pathway. *J Clin Invest.* 2001;108:391-397.
4. Vasa M, Fichtlscherer S, Aicher A, Adler K, Urbich C, Martin H, Zeiher AM, Dimmeler S. Number and migratory activity of circulating endothelial progenitor cells inversely correlate with risk factors for coronary artery disease. *Circ Res.* 2001;89:E1-7.
5. Mayr U, Mayr M, Li C, Wernig F, Dietrich H, Hu Y, Xu Q. Loss of p53 accelerates neointimal lesions of vein bypass grafts in mice. *Circ Res.* 2002;90:197-204.

Online Figures

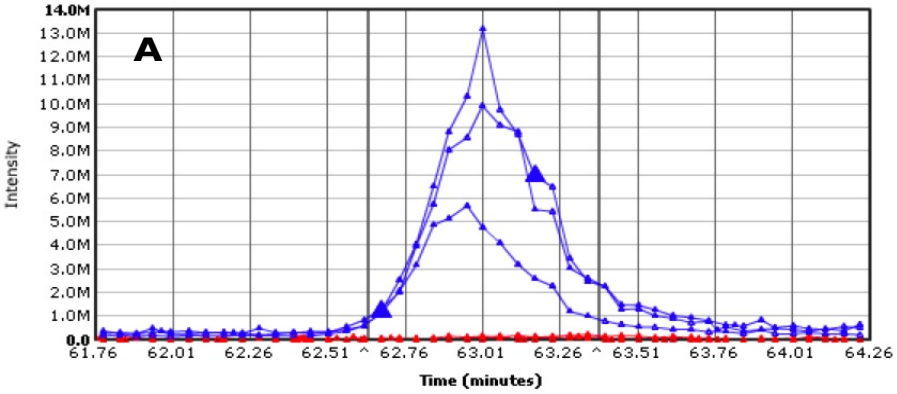
Figure I. SIEVE analysis with reconstructed ion chromatograms. The blue and red lines represent three replicates of EACs and SPCs, respectively. Each data point corresponds to the intensities of the precursor ion observed in the full MS scan across the time range. Triangle shapes represent MS/MS events.

Figure II. Protein signatures. 4 biological replicates of EACs (A-D) and 3 replicates of SPCs (A-C) were analyzed in at least 2 technical replicates. In total, 18 LC-MS/MS runs were performed. The sample window of the Scaffold software summarises the proteins identified. Only cathepsins and collagens are shown (rows show proteins, columns show samples). Stringent filter criteria were applied to reject false positive identifications (a minimum of 2 unique peptides with a peptide probability >95% and a protein probability >99.9%). Color-coded numbers represent the spectral counts (assigned tryptic peptides per protein) and the probability that each protein identification is correct (see legend). The similar spectral counts demonstrate the robustness of our proteomic approach.

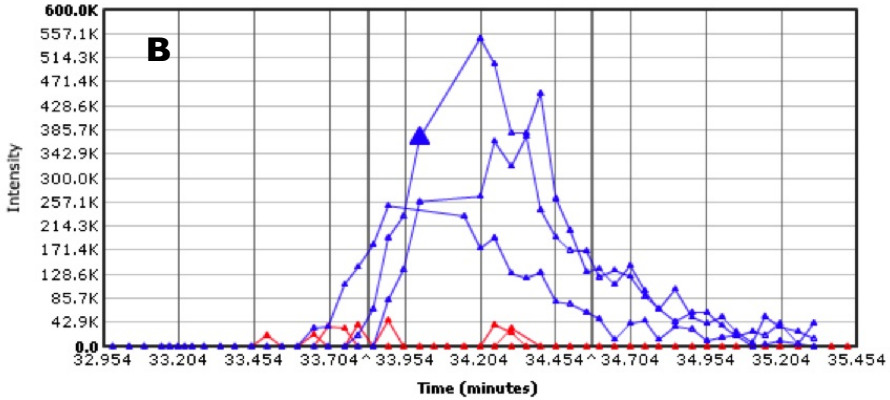
Figure III. Gene Ontology Annotation. Assignments of identified proteins in the conditioned medium of EACs, SPCs, and SMCs to Gene Ontology (GO) terms were obtained from the Gene Ontology Annotation (GOA) database ftp site (ftp://ftp.ebi.ac.uk/pub/databases/GO/goa). Proteins were mapped onto the GO graph recursively that is proteins annotated with a particular term were also assigned to all ancestors of that term. Only terms with a frequency of >20% in at least one of the samples (EAC, SPC, SMC) are included in the final dendrogram. The overlap among secreted proteins of SMCs and SPCs is depicted as insert in Figure III.

Figure IV. A comparison of the sequence coverage obtained for collagen alpha 1 (I) revealed that no spectral evidence was found for the N-terminal von Willebrand factor type C domain (VWC, $AA_{40\text{-}95}$) and the first triple-helical peptide ($AA_{109\text{-}22}$) in SPCs **(A, C)** although peptides covering this region were consistently detected in SMCs **(A, B)**.

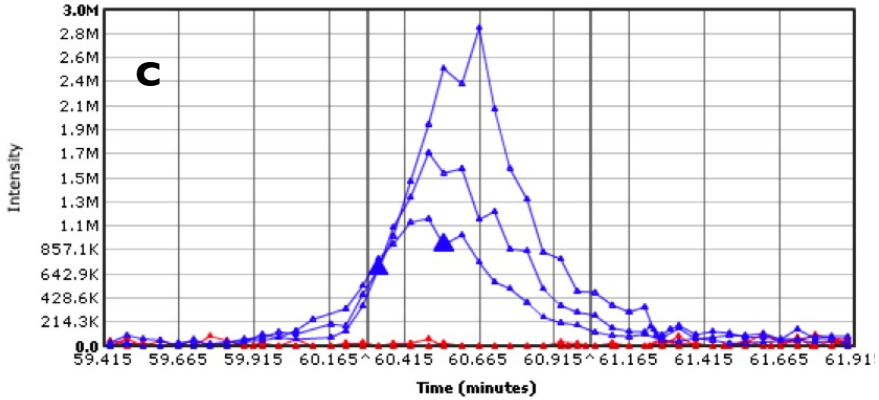
Figure I



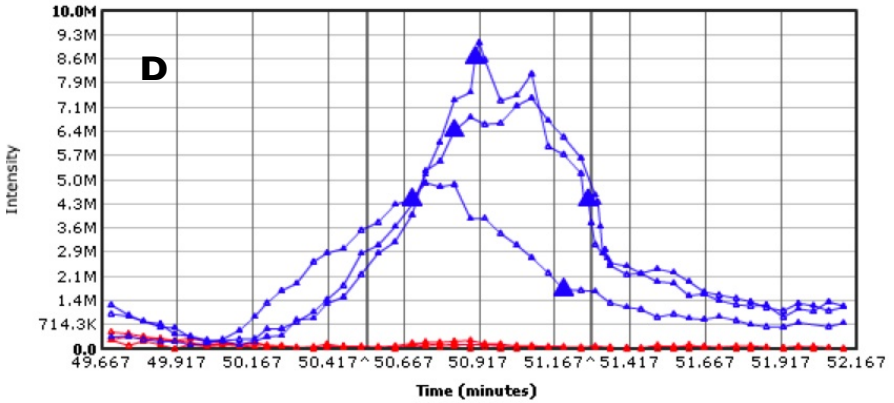
P07339|CATD_HUMAN Cathepsin D
K.AIGAVPLIQGEYMIPCEK.V



P28799|GRN_HUMAN Granulins
K.CDMEVSCPDGYTCCR.L

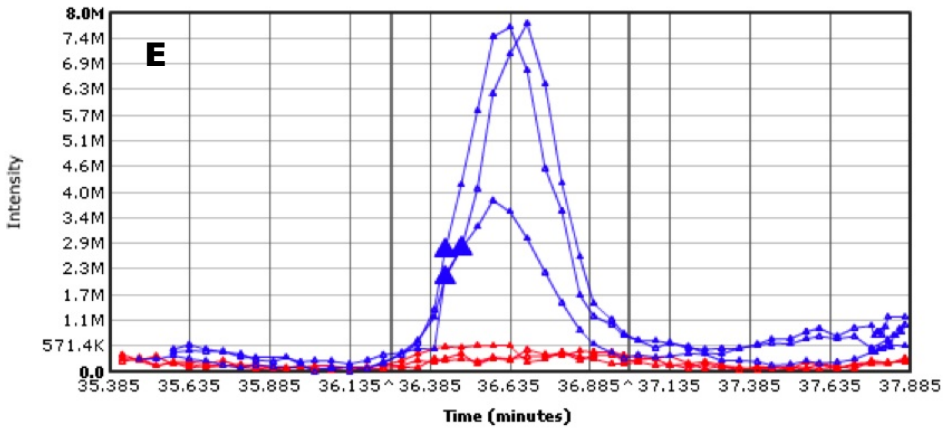


Q9UBR2|CATZ_HUMAN Cathepsin Z
R.YNLAIEEHCTFGDPIV.-

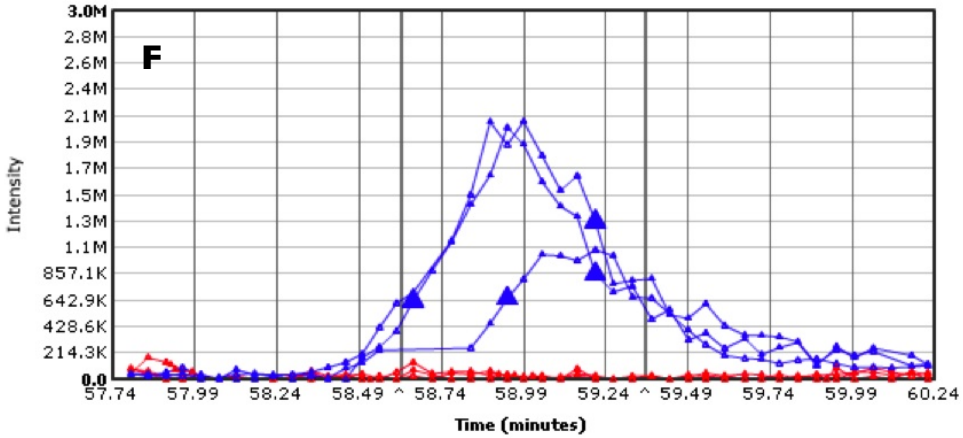


P61626|LYSC_HUMAN Lysozyme C
R.STDYGIFQINSR.Y

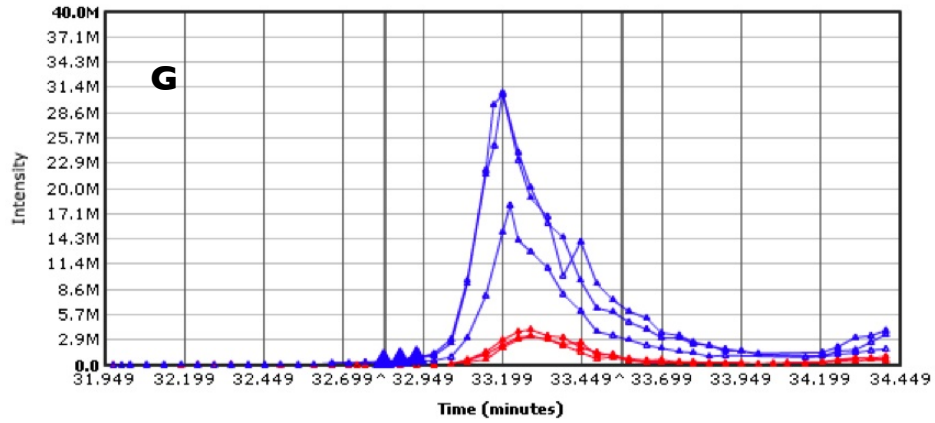
Figure I



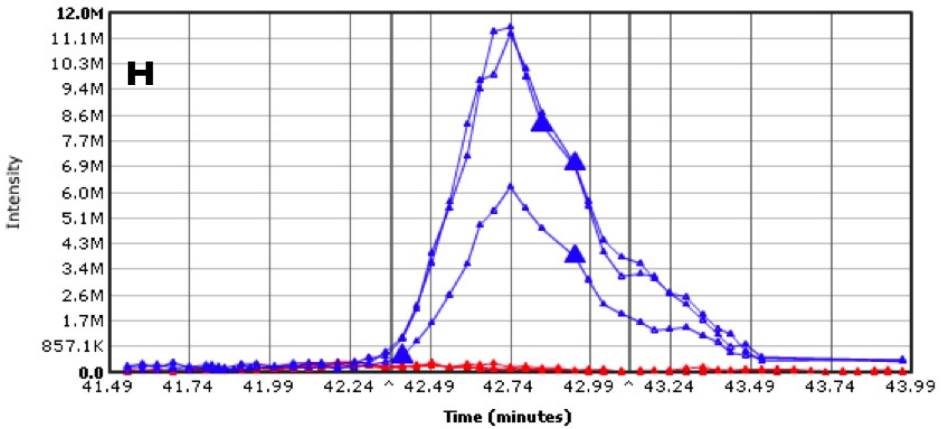
P07602|SAP_HUMAN Proactivator polypeptide
R.LGPGMADICK.N



P00746|CFAD_HUMAN Complement factor D
R.RPDSLQHVLLPVLDR.A

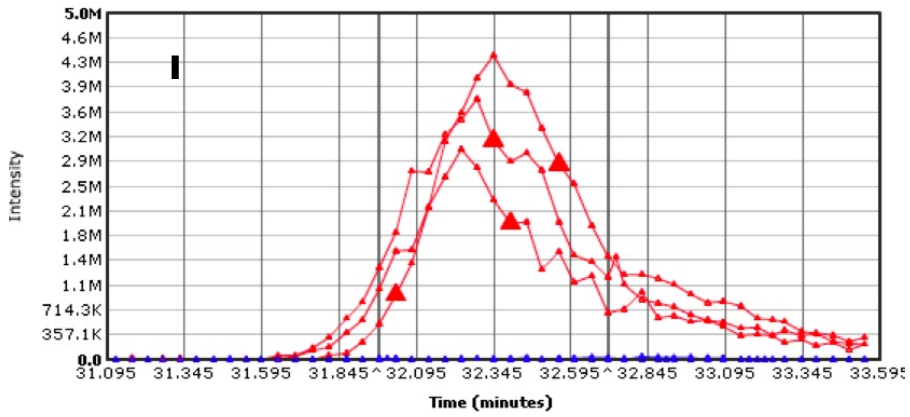


Q99538|LGMN_HUMAN Legumain
K.LMNTNDLEESR.Q

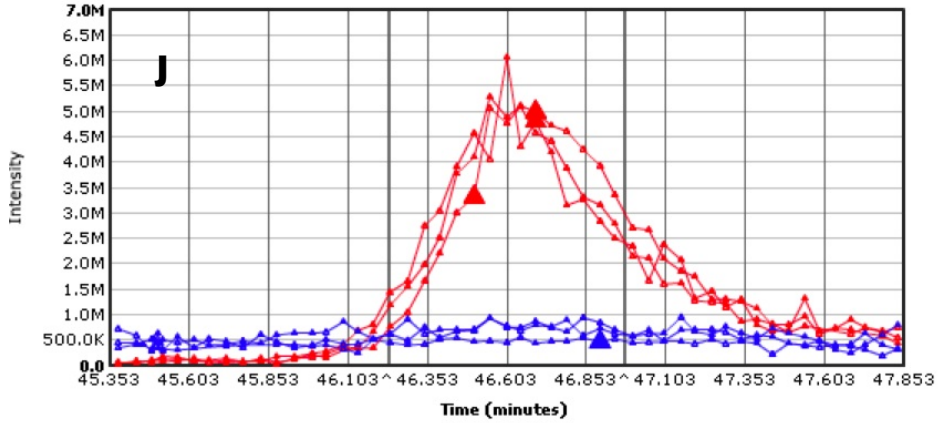


P02775|SCYB7_HUMAN Platelet basic protein (CXCL7)
K.NIQSLEVIGK.G

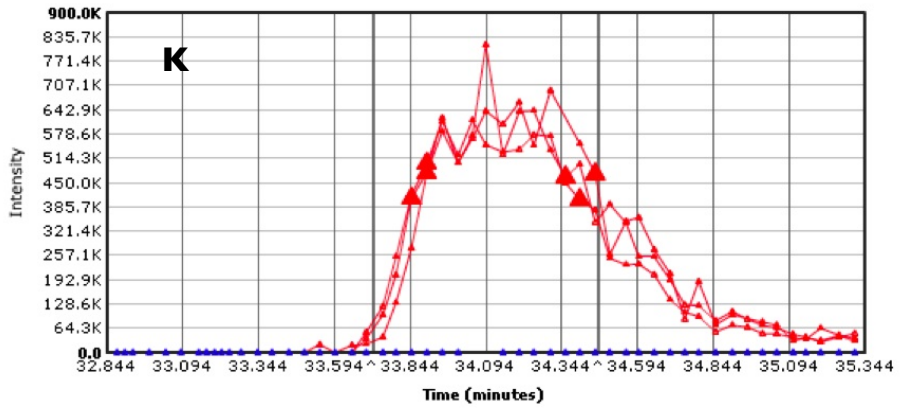
Figure I



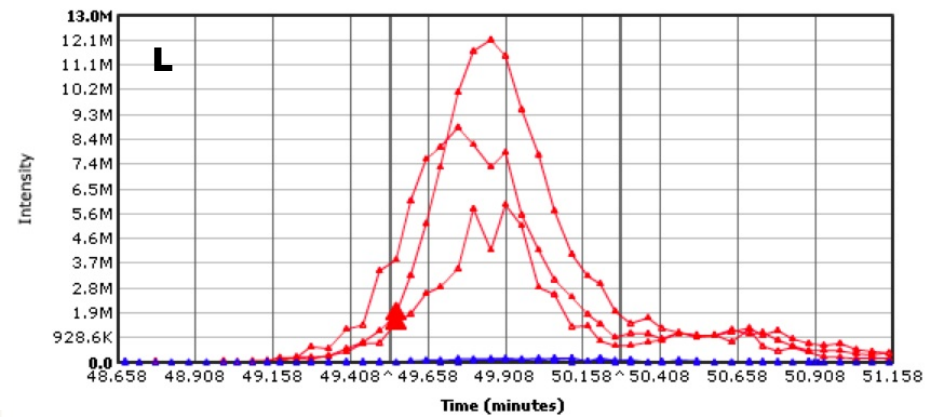
P02452|CO1A1_HUMAN Collagen alpha-1 (I)
R.VGPPGPSGNAGPPGPPGPAGK.E



P12109|CO6A1_HUMAN Collagen alpha 1 (VI)
R.VPSYQALLR.G

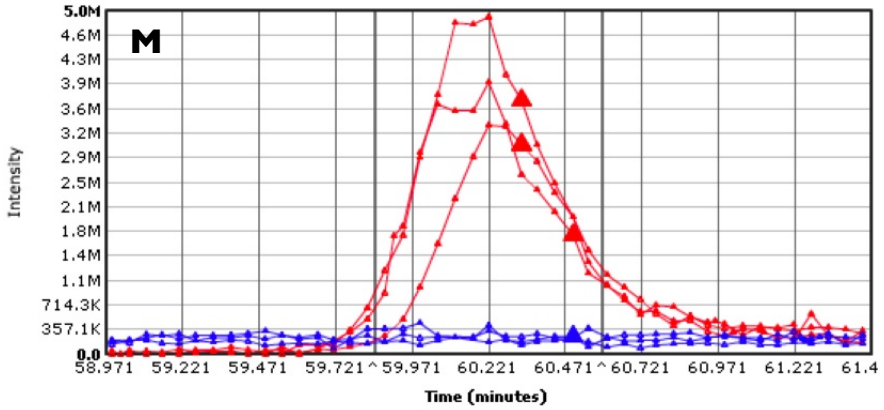


P08123|CO1A2_HUMAN Collagen alpha 2(I)
K.DYEVDATLK.S

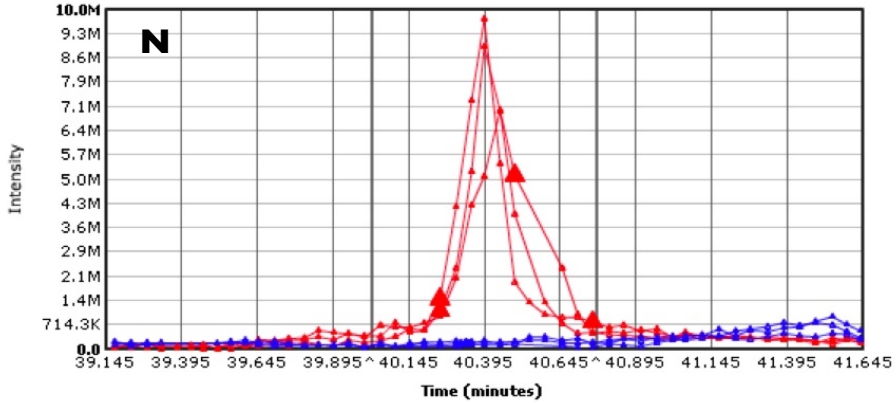


P02751|FINC_HUMAN Fibronectin
R.TKTETITGFQVDAVPANGQTPIQR.T

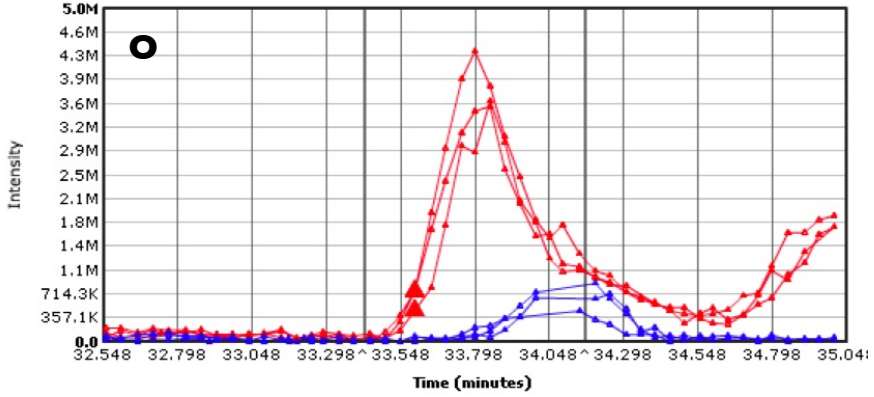
Figure I



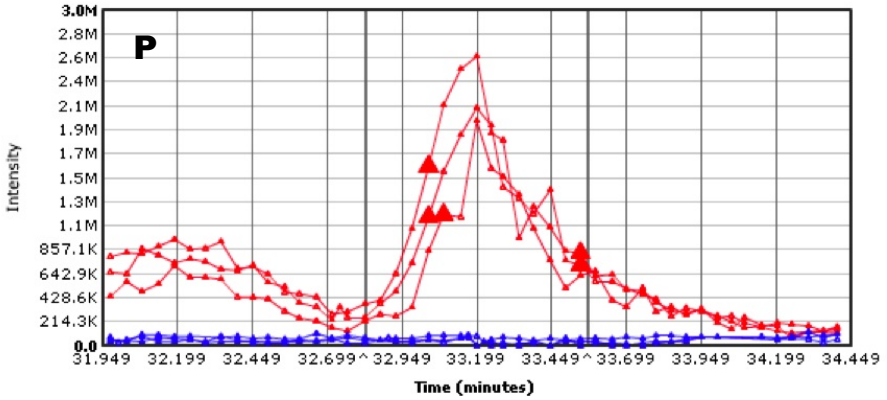
Q12841|FSTL1_HUMAN Follistatin-related protein 1
K.LSFQEFLK.C



P09486|P13213|SPRC_HUMAN SPARC
K.LSFQEFLK.C



P21809|PGS1_BOVIN Biglycan
R.VVQCSDLGLK.A



P13384|IBP2_BOVIN Insulin-like growth factor-binding protein 2
R.GECWCVNPNTGK.L

Figure II

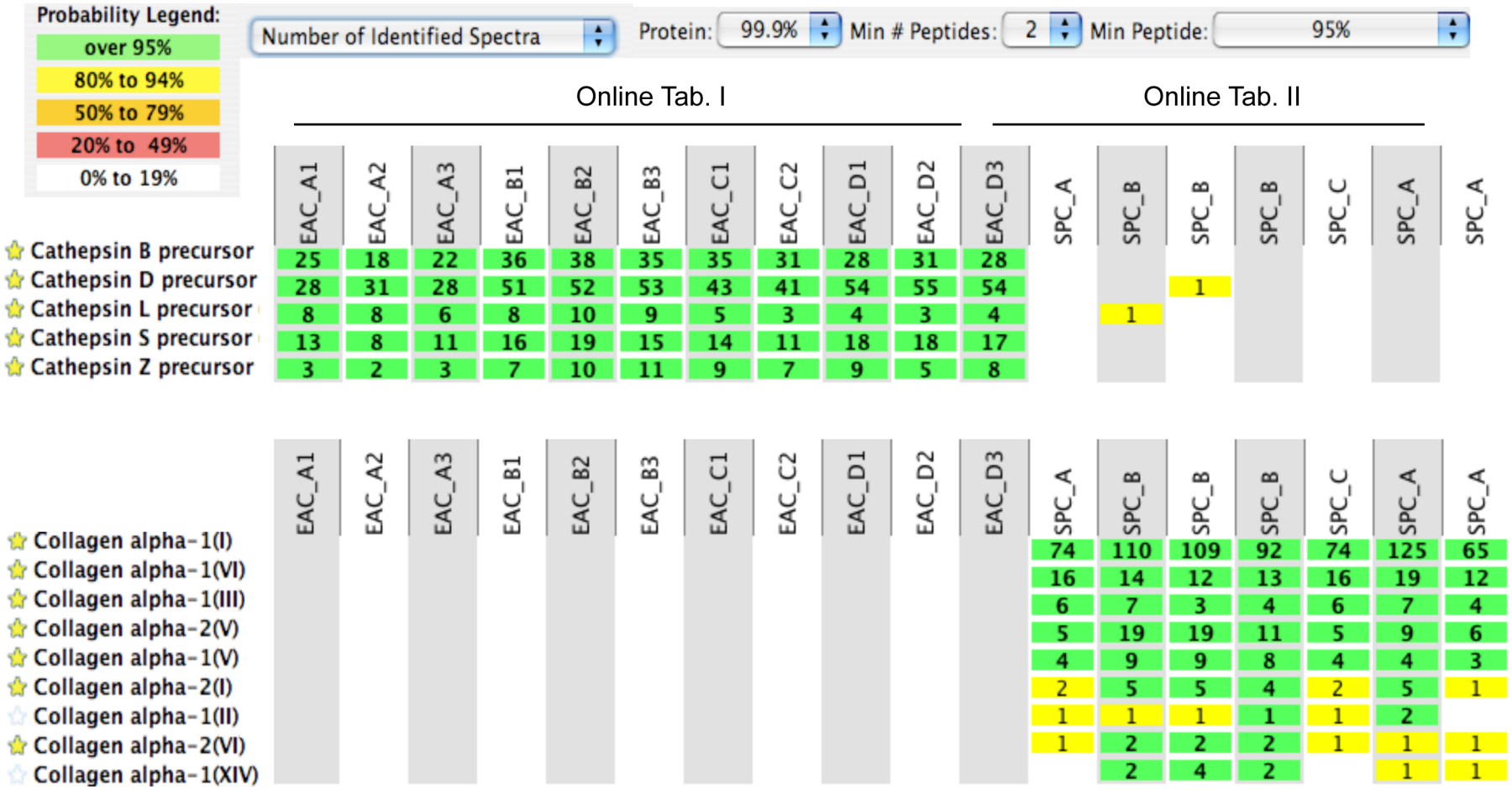


Figure III

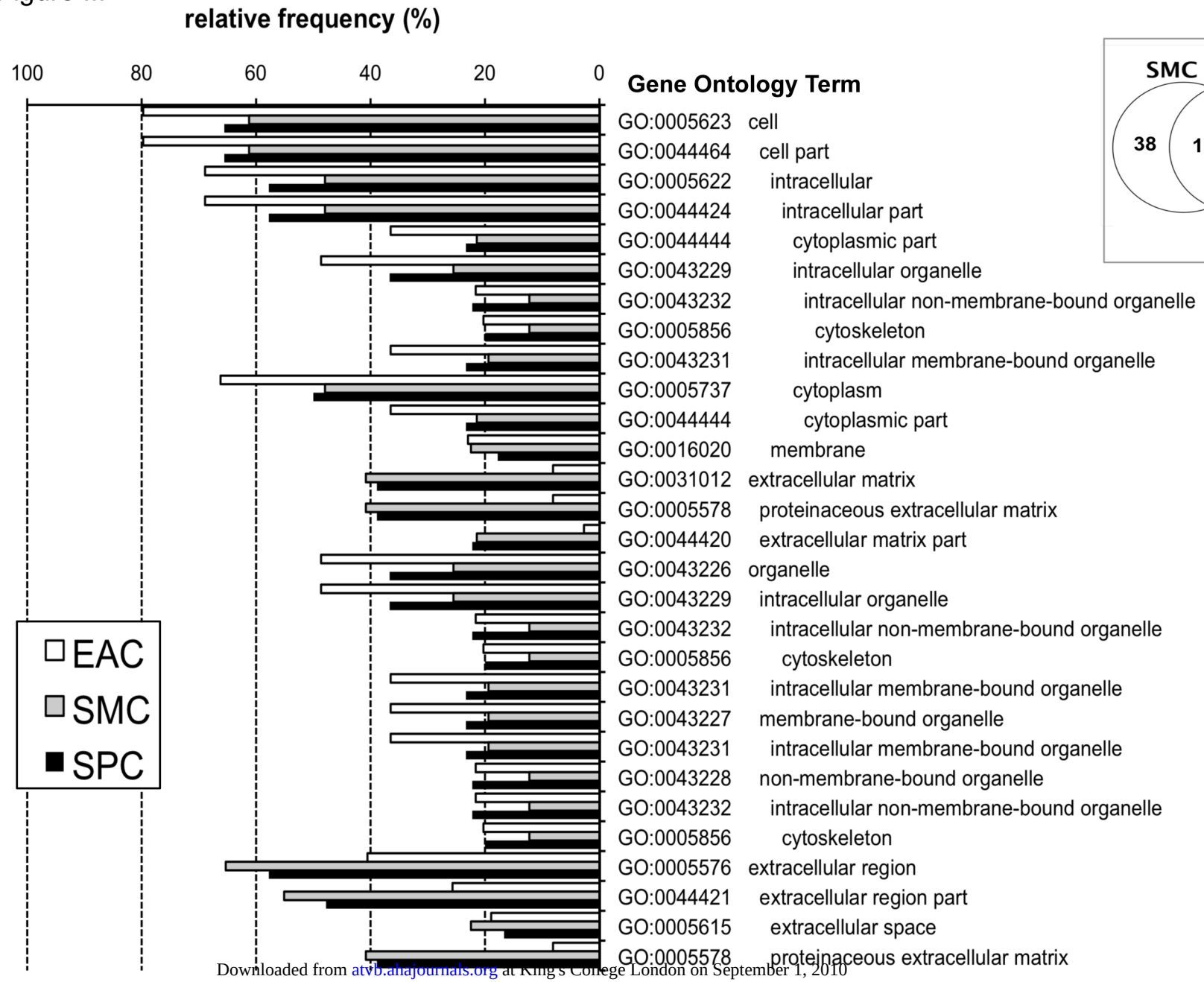
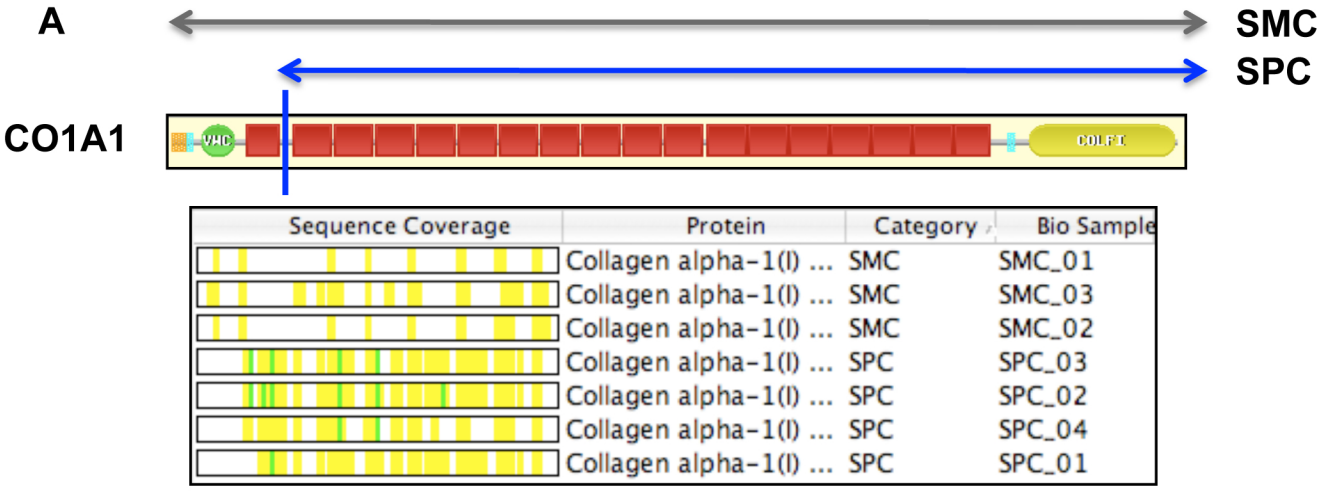
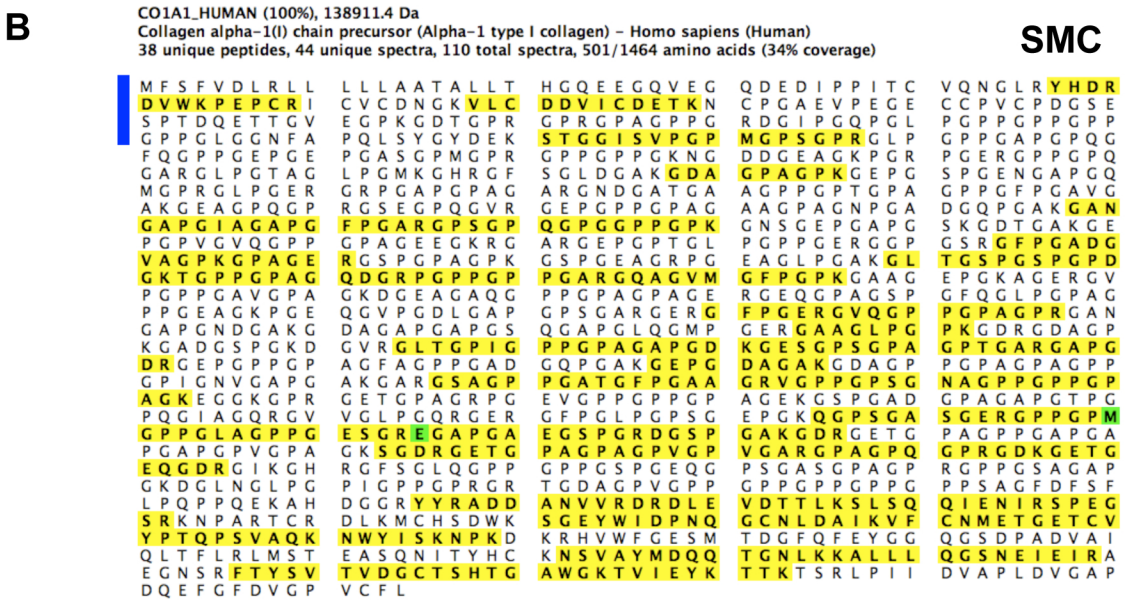


Figure IV





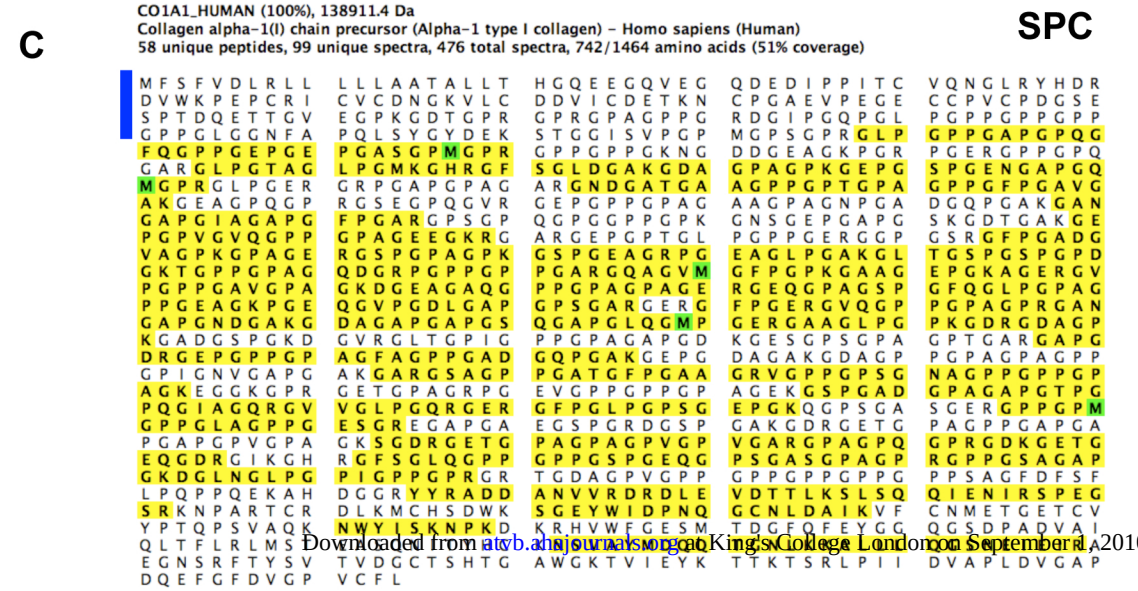


TABLE I: PEPTIDES SIGNIFICANTLY INCREASED IN THE CONDITIONED MEDIUM OF EACs

SIEVE Frames, elution time of peptide, p-value, ratio compared to SPCs, protein accession number, peptide sequence, Xcorr score and charge state of the peptide

Peptide sequences identified using filters described in text

Description	FrameID	M/z	Time	pValue	Protein	Peptide	XCorr	Charge	MS2
Actin	625	599.856	43.595	5.24E-03	P62736|ACTA_HUMAN	R.AVFPSIVGRPR.H	2.8	2	17
	1563	654.642	52.8728	1.36E-01	P62736|ACTA_HUMAN	K.YPIEHGIITNWDDMEK.I	3.9	3	13
	5251	980.962	53.0364	6.26E-02	P62736|ACTA_HUMAN	K.YPIEHGIITNWDDMEK.I	4.0	2	2
	5278	981.463	53.0364	6.29E-02	P62736|ACTA_HUMAN	K.YPIEHGIITNWDDMEK.I	4.2	2	8
	887	895.951	55.4009	9.17E-06	P62736|ACTA_HUMAN	K.SYELPDGQVITIGNER.F	3.8	2	22
	1019	896.451	55.4009	7.15E-06	P62736|ACTA_HUMAN	K.SYELPDGQVITIGNER.F	4.6	2	10
	3206	774.909	39.6834	2.89E-05	P62736|ACTA_HUMAN	R.MQKEITALAPSTMK.I	4.5	2	13
	1185	517.275	39.6834	2.56E-06	P62736|ACTA_HUMAN	R.MQKEITALAPSTMK.I	3.8	3	3
	1025	516.941	39.6834	9.70E-07	P62736|ACTA_HUMAN	R.MQKEITALAPSTMK.I	4.0	3	17
Alpha-2-macroglobulin	9350	708.918	50.7364	1.14E-02	P01023|A2MG_HUMAN	K.MVSGFIPLKPTVK.M	3.0	2	6
	1547	558.805	38.5461	4.32E-07	P01023|A2MG_HUMAN	R.QTVSWAVTPK.S	2.5	2	35
Alpha-1-antiproteinase	5747	1190.62	68.8174	9.91E-06	P34955|A1AT_BOVIN	K.SVLGDVGITEVFSDRADLSGITK.E	4.6	2	6
	16576	584.807	48.0523	3.30E-05	P34955|A1AT_BOVIN	K.LSISETYDLK.S	2.6	2	5
	12309	700.391	39.2803	8.75E-05	P34955|A1AT_BOVIN	R.ADLSGITKEQPLK.V	2.8	2	4
	4884	584.809	46.3307	1.73E-04	P34955|A1AT_BOVIN	K.LSISETYDLK.S	2.6	2	8
	1801	584.807	45.0398	1.98E-04	P34955|A1AT_BOVIN	K.LSISETYDLK.S	2.9	2	9
	43	584.808	43.7841	4.16E-04	P34955|A1AT_BOVIN	K.LSISETYDLK.S	3.0	2	9
	1313	1168.61	43.7841	6.27E-04	P34955|A1AT_BOVIN	K.LSISETYDLK.S	1.7	1	8
Alpha-2-HS-glycoprotein	3301	846.963	45.5789	1.54E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.5	2	4
	4415	816.392	41.8844	1.74E-05	P12763|FETUA_BOVIN	K.CNLLAEKQYGFCK.G	4.5	2	2
	9847	565.311	48.3999	1.94E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.1	3	6
	3152	564.976	47.0218	2.15E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.2	3	11
	3711	815.89	41.9283	2.50E-05	P12763|FETUA_BOVIN	K.CNLLAEKQYGFCK.G	4.2	2	4
	3552	847.463	45.6299	2.63E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.1	2	1
	10321	564.976	50.5884	4.22E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.1	3	3
	144	564.977	45.6299	4.43E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.2	3	8
	12860	565.31	49.8701	5.23E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.0	3	1
	1590	707.86	33.9341	5.66E-05	P12763|FETUA_BOVIN	K.QYGFCKGSVIQK.A	2.9	2	7
	17602	564.976	55.9704	6.80E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.1	3	3
	145	565.31	45.6299	7.32E-05	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.5	3	4
	1891	635.327	55.2013	1.61E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.7	2	13
	15361	565.311	51.7124	1.66E-04	P12763|FETUA_BOVIN	K.HTLNQIDSVKVWPR.R	4.0	3	3
	19	635.328	52.5768	3.35E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.8	2	14
	273	635.328	53.9342	4.66E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.7	2	14
	3441	635.328	57.003	4.89E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.8	2	2
	5309	635.328	58.3077	4.89E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.7	2	1
	16348	635.328	70.7302	8.07E-04	P12763|FETUA_BOVIN	K.QDGQFSVLFTK.C	2.7	2	7
Alpha-enolase	9135	1177.58	82.1713	4.87E-02	P06733|ENOA_HUMAN	R.SGETEDTFIADLVVGLCTGQIK.T	5.7	2	15
	9833	996.138	74.6445	1.35E-08	P06733|ENOA_HUMAN	K.SFIKDYPVVSIEDPFDQDDWGAWQK.F	5.4	3	10
	9002	954.999	77.0218	9.38E-09	P06733|ENOA_HUMAN	K.LAMQEFMILPVGAANFR.E	5.1	2	15
	9172	954.497	76.9639	5.96E-05	P06733|ENOA_HUMAN	K.LAMQEFMILPVGAANFR.E	4.0	2	6
	2691	703.861	52.1193	3.96E-13	P06733|ENOA_HUMAN	R.GNPTVEVDLFTSK.G	3.3	2	19
	9297	1017.53	56.5325	6.96E-04	P06733|ENOA_HUMAN	K.FTASAGIQVVGDDLTVTNPK.R	5.1	2	1
AMBP protein	2091	721.382	68.9852	5.10E-05	P00978|AMBP_BOVIN	R.SYIQLWAFDAVK.G	4.0	2	2
	1659	720.881	68.9852	1.65E-04	P00978|AMBP_BOVIN	R.SYIQLWAFDAVK.G	3.5	2	7
	8581	857.924	44.89	1.76E-04	P00978|AMBP_BOVIN	R.TVEACNLPIVQGPCR.S	4.3	2	3
	6899	857.424	44.8362	3.28E-04	P00978|AMBP_BOVIN	R.TVEACNLPIVQGPCR.S	3.9	2	4
Apolipoprotein A-I	2039	630.803	38.119	2.81E-07	P15497|APOA1_BOVIN	K.WHEEVEIYR.Q	2.6	2	12
	716	789.416	65.2229	4.94E-07	P15497|APOA1_BOVIN	K.LLDNWDTLASTLSK.V	4.7	2	3
	390	591.644	36.0407	1.34E-06	P15497|APOA1_BOVIN	R.LEALKEGGGSLAEYHAK.A	4.9	3	6
	2352	697.869	39.5468	1.71E-06	P15497|APOA1_BOVIN	K.VQPYLDEFQKK.W	2.7	2	6
	522	788.914	65.2824	1.84E-06	P15497|APOA1_BOVIN	K.LLDNWDTLASTLSK.V	4.3	2	12
	433	591.978	36.0407	1.86E-06	P15497|APOA1_BOVIN	R.LEALKEGGGSLAEYHAK.A	4.6	3	4
	1250	608.843	59.2562	4.16E-06	P15497|APOA1_BOVIN	K.VSILAAIDEASK.K	3.5	2	11
	2006	699.848	55.2013	4.99E-06	P15497|APOA1_BOVIN	R.DYVAQFEASALGK.Q	3.7	2	9
	2238	672.891	55.8192	5.25E-05	P15497|APOA1_BOVIN	K.VSILAAIDEASKK.L	2.7	2	10
	15125	623.348	53.7336	6.65E-05	P15497|APOA1_BOVIN	K.VQELQDKLSPLAQELR.D	4.0	3	4
	5848	715.871	37.7114	7.85E-05	P15497|APOA1_BOVIN	K.VAPLGEEFREGAR.Q	2.7	2	10
	3492	673.392	55.7618	1.07E-04	P15497|APOA1_BOVIN	K.VSILAAIDEASKK.L	2.8	2	1
	10262	605.295	55.6086	2.84E-04	P15497|APOA1_BOVIN	K.DSGRDYVAQFEASALGK.Q	4.0	3	4
	6541	730.375	64.7525	2.98E-04	P15497|APOA1_BOVIN	K.VREQLGPVTQEFWDNLEK.E	5.6	3	4
Apolipoprotein A-II	9502	684.364	45.1425	1.38E-05	P81644|APOA2_BOVIN	K.TQEELTPFFKK.A	2.7	2	3
	4004	620.317	52.5768	5.42E-05	P81644|APOA2_BOVIN	K.TQEELTPFFK.K	2.8	2	8
Apolipoprotein E	4363	899.443	49.9842	1.79E-04	P02649|APOE_HUMAN	R.FWDYLR.W	1.5	1	15
	1919	1366.2	72.1054	5.97E-04	P02649|APOE_HUMAN	R.WVQTLSEQVQEELLSSQVTQELR.A	5.1	2	18
	692	749.404	38.9676	2.69E-09	P02649|APOE_HUMAN	R.AATVGSLAGQPLQER.A	3.6	2	21
	11909	619.76	26.5527	1.27E-04	P02649|APOE_HUMAN	R.LGADM*EDVCGR.L	3.3	2	13
	782	824.904	50.7883	1.26E-07	P02649|APOE_HUMAN	R.GEVQAMLGQSTEELR.V	5.0	2	3
	582	889.45	67.1877	6.78E-11	P02649|APOE_HUMAN	R.LKSWFEPLVEDMQR.Q	4.3	2	20
	569	889.952	67.1877	2.89E-11	P02649|APOE_HUMAN	R.LKSWFEPLVEDMQR.Q	4.6	2	3
	604	824.403	50.7883	5.07E-08	P02649|APOE_HUMAN	R.GEVQAMLGQSTEELR.V	4.3	2	25
	812	911.137	71.9994	3.87E-07	P02649|APOE_HUMAN	R.WVQTLSEQVQEELLSSQVTQELR.A	5.0	3	20
	223	484.779	32.2513	5.88E-10	P02649|APOE_HUMAN	R.LGPLVEQGR.V	3.0	2	22
	627	768.861	66.4789	2.94E-13	P02649|APOE_HUMAN	K.SWFEPLVEDMQR.Q	3.7	2	20
	419	517.274	31.0897	1.62E-06	P02649|APOE_HUMAN	R.LQAEAFQAR.L	2.7	2	20
	1908	865.926	43.4445	1.56E-03	P02649|APOE_HUMAN	K.SELEEQLTPVAEETR.A	4.6	2	12
	1920	952.491	53.8816	2.79E-04	P02649|APOE_HUMAN	R.GEVQAMLGQSTEELRVR.L	3.4	2	10
	192	611.763	33.4001	1.40E-10	P02649|APOE_HUMAN	R.LGADMEDVCGR.L	3.4	2	23
	1893	844.469	48.2439	3.10E-04	P02649|APOE_HUMAN	R.WELALGR.F	1.8	1	11
	235	810.902	30.7578	2.04E-07	P02649|APOE_HUMAN	K.VQAAVGTSAAPVPSDNH.-	4.5	2	22
	205	593.303	66.8025	8.30E-13	P02649|APOE_HUMAN	R.LKSWFEPLVEDMQR.Q	4.5	3	14
	2269	866.427	43.4445	5.30E-03	P02649|APOE_HUMAN	K.SELEEQLTPVAEETR.A	5.4	2	2
	723	654.831	44.5911	1.05E-04	P02649|APOE_HUMAN	R.ALMDETMKELK.A	2.8	2	9
	8912	474.766	28.724	2.55E-04	P02649|APOE_HUMAN	R.LAVYQAGAR.E	2.7	2	22
	225	593.637	66.8025	4.50E-05	P02649|APOE_HUMAN	R.LKSWFEPLVEDMQR.Q	4.8	3	8
	282	811.403	30.7578	2.75E-05	P02649|APOE_HUMAN	K.VQAAVGTSAAPVPSDNH.-	5.1	2	2
	2034	1047.53	46.1227	3.38E-06	P02649|APOE_HUMAN	K.AYKSELEEQLTPVAEETR.A	6.1	2	15
	2131	1047.03	46.221	4.58E-08	P02649|APOE_HUMAN	K.AYKSELEEQLTPVAEETR.A	5.7	2	2
	1765	951.99	53.9342	1.77E-08	P02649|APOE_HUMAN	R.GEVQAMLGQSTEELRVR.L	3.5	2	6
Beta-2-microglobulin	3975	1278.12	73.7428	3.65E-04	P61769|B2MG_HUMAN	K.SNFLNCYVSGFHPSDIEVDLLK.N	4.7	2	12
	576	852.416	73.5978	2.62E-07	P61769|B2MG_HUMAN	K.SNFLNCYVSGFHPSDIEVDLLK.N	4.0	3	19
Cathepsin B	18982	764.91	38.8667	2.13E-11	P07858|CATB_HUMAN	R.LCGTFLGGPKPPQR.V	3.4	2	1
	14924	764.409	38.9676	1.65E-10	P07858|CATB_HUMAN	R.LCGTFLGGPKPPQR.V	3.6	2	3
	6307	725.309	63.0784	2.53E-03	P07858|CATB_HUMAN	R.DQGSCGSCWAFGAVEAISDR.I	4.2	3	12
	4126	858.052	61.6222	2.28E-05	P07858|CATB_HUMAN	K.EIRDQGSCGSCWAFGAVEAISDR.I	5.2	3	15
	852	912.441	47.7593	3.94E-06	P07858|CATB_HUMAN	R.GQDHCGIESEVVAGIPR.T	5.2	2	29
	2224	1086.96	63.244	4.64E-05	P07858|CATB_HUMAN	R.DQGSCGSCWAFGAVEAISDR.I	4.7	2	4
	2158	1087.46	63.244	4.54E-05	P07858|CATB_HUMAN	R.DQGSCGSCWAFGAVEAISDR.I	5.9	2	17
	8661	736.385	47.8083	1.04E-06	P07858|CATB_HUMAN	K.ILRGQDHCGIESEVVAGIPR.T	5.2	3	9
	6534	658.307	32.3036	2.27E-05	P07858|CATB_HUMAN	K.ICEPGYSPTYK.Q	2.9	2	2
	4902	657.805	32.4148	9.02E-06	P07858|CATB_HUMAN	K.ICEPGYSPTYK.Q	2.9	2	16
	4048	1003.5	76.3063	2.91E-06	P07858|CATB_HUMAN	K.NGPVEGAFSVYSDFLLYK.S	4.7	2	5
	3609	1004	76.3063	2.13E-07	P07858|CATB_HUMAN	K.NGPVEGAFSVYSDFLLYK.S	5.4	2	22
	2770	920.971	62.6786	6.16E-08	P07858|CATB_HUMAN	R.VMFTEDLKLPASFDAR.E	4.4	2	10
	2948	920.471	62.6786	2.89E-09	P07858|CATB_HUMAN	R.VMFTEDLKLPASFDAR.E	3.8	2	3
	4896	649.639	37.1143	7.90E-07	P07858|CATB_HUMAN	K.SGVYQHVTGEMM*GGHAIR.I	4.7	3	1
	821	613.982	62.5645	7.80E-11	P07858|CATB_HUMAN	R.VMFTEDLKLPASFDAR.E	4.0	3	8
	3269	644.307	42.0393	1.31E-12	P07858|CATB_HUMAN	K.SGVYQHVTGEMMGGHAIR.I	4.8	3	8
	701	614.316	62.5645	2.11E-12	P07858|CATB_HUMAN	R.VMFTEDLKLPASFDAR.E	4.1	3	14
	472	541.761	43.6391	4.26E-10	P07858|CATB_HUMAN	R.TDQYWEKI.-	3.0	2	14
	5647	1082.52	43.595	5.44E-04	P07858|CATB_HUMAN	R.TDQYWEKI.-	1.8	1	5
	3501	643.973	42.0393	8.07E-05	P07858|CATB_HUMAN	K.SGVYQHVTGEMMGGHAIR.I	4.7	3	5
Cathepsin D	3938	703.374	58.243	4.58E-02	P07339|CATD_HUMAN	K.LLDIACWIHHK.Y	3.4	2	12
	4792	933.518	44.6944	7.08E-03	P07339|CATD_HUMAN	R.VGFAEAARL.-	1.8	1	11
	7158	707.365	42.8637	3.92E-02	P07339|CATD_HUMAN	K.GYKLSPEDYTLK.V	2.5	2	2
	8751	779.038	60.5356	1.27E-02	P07339|CATD_HUMAN	K.EGCEAIVDTGTSLMVGPVDEVR.E	4.1	3	7

	8698	894.41	41.4703	4.81E-04	P07339|CATD_HUMAN	R.DPDAQPGGELMLGGTDSK.Y	4.6	2	8
	5362	703.875	58.2581	3.99E-04	P07339|CATD_HUMAN	K.LLDIACWIHHK.Y	3.3	2	1
	7404	945.467	67.4783	3.62E-07	P07339|CATD_HUMAN	K.EGCEAIVDTGTSLMVGPVDEVRELQK.A	3.9	3	4
	1069	636.353	51.762	4.18E-05	P07339|CATD_HUMAN	R.QVFGEATKQPGITFIAAK.F	4.2	3	6
	6559	945.132	67.4239	1.01E-07	P07339|CATD_HUMAN	K.EGCEAIVDTGTSLMVGPVDEVRELQK.A	3.9	3	8
	1410	768.385	53.5933	1.90E-08	P07339|CATD_HUMAN	R.TMSEVGGSVEDLIAK.G	4.4	2	22
	4689	731.838	35.8266	5.16E-09	P07339|CATD_HUMAN	R.YYTVFDRDNNR.V	2.6	2	19
	4201	953.526	51.7124	4.30E-08	P07339|CATD_HUMAN	R.QVFGEATKQPGITFIAAK.F	4.0	2	3
	3989	653.684	75.6841	1.06E-07	P07339|CATD_HUMAN	R.ISVNNVLPVFDNLMQQK.L	4.2	3	6
	250	467.262	44.6944	3.18E-09	P07339|CATD_HUMAN	R.VGFAEAARL.-	2.9	2	19
	591	620.313	58.8013	9.35E-11	P07339|CATD_HUMAN	K.FDGILGMAYPR.I	3.3	2	36
	901	995.011	62.6236	7.70E-11	P07339|CATD_HUMAN	K.AIGAVPLIQGEYMIPCEK.V	3.3	2	4
	815	995.513	62.6236	8.43E-11	P07339|CATD_HUMAN	K.AIGAVPLIQGEYMIPCEK.V	4.1	2	18
	3621	954.028	51.7124	5.39E-04	P07339|CATD_HUMAN	R.QVFGEATKQPGITFIAAK.F	4.0	2	9
	9844	1003.02	56.5889	1.48E-03	P07339|CATD_HUMAN	R.TMSEVGGSVEDLIAKGPVSK.Y	4.9	2	7
	1244	980.524	75.6841	1.81E-04	P07339|CATD_HUMAN	R.ISVNNVLPVFDNLMQQK.L	4.4	2	23
	3529	654.018	75.6841	1.91E-04	P07339|CATD_HUMAN	R.ISVNNVLPVFDNLMQQK.L	4.2	3	13
	1312	980.022	75.6841	3.00E-04	P07339|CATD_HUMAN	R.ISVNNVLPVFDNLMQQK.L	3.6	2	8
	1508	949.517	58.1484	1.15E-04	P07339|CATD_HUMAN	K.YSQAVPAVTEGPIPEVLK.N	3.8	2	6
	2637	1168.05	60.5845	1.44E-04	P07339|CATD_HUMAN	K.EGCEAIVDTGTSLMVGPVDEVR.E	5.7	2	17
	1487	950.018	58.1484	3.35E-05	P07339|CATD_HUMAN	K.YSQAVPAVTEGPIPEVLK.N	4.9	2	20
Cathepsin L	3058	748.384	55.2014	2.39E-04	P07711|CATL_HUMAN	K.VFQEPLFYEAPR.S	3.5	2	19
	5580	800.348	55.6086	6.30E-07	P07711|CATL_HUMAN	K.NSWGEEWGMGGYVK.M	3.6	2	18
	2516	724.335	39.3385	2.66E-07	P07711|CATL_HUMAN	R.NHCGIASAASYPTV.-	3.0	2	7
	8439	800.85	55.6634	1.20E-08	P07711|CATL_HUMAN	K.NSWGEEWGMGGYVK.M	4.3	2	2
	1748	555.918	42.8637	7.72E-06	P25774|CATS_HUMAN	K.NSWGHNFGEEGYIR.M	3.9	3	7
Cathepsin S	5608	608.279	31.4222	1.40E-03	P25774|CATS_HUMAN	K.GIDSDASYPYK.A	3.1	2	20
	7432	946.446	54.7026	4.63E-05	P25774|CATS_HUMAN	R.NKGNHCGIASFPSYPEI.-	3.7	2	10
	8592	1019.46	75.9691	2.57E-04	P25774|CATS_HUMAN	K.GCNGGFMTTAFQYIIDNK.G	4.9	2	6
	3582	882.446	50.024	1.74E-04	P25774|CATS_HUMAN	K.LVSLSAQNLVDCSTEK.Y	4.6	2	12
	4824	882.949	49.917	3.59E-04	P25774|CATS_HUMAN	K.LVSLSAQNLVDCSTEK.Y	5.2	2	4
	5635	791.909	42.9187	4.66E-10	P25774|CATS_HUMAN	K.YTELPYGREDVLK.E	3.3	2	9
	6043	833.373	42.9187	3.30E-07	P25774|CATS_HUMAN	K.NSWGHNFGEEGYIR.M	4.1	2	9
	6697	833.877	42.8102	2.81E-06	P25774|CATS_HUMAN	K.NSWGHNFGEEGYIR.M	4.3	2	2
	1649	556.252	42.8102	1.73E-08	P25774|CATS_HUMAN	K.NSWGHNFGEEGYIR.M	4.1	3	5
	1460	555.918	42.8102	2.86E-10	P25774|CATS_HUMAN	K.NSWGHNFGEEGYIR.M	3.9	3	16
Cathepsin Z	6999	663.285	41.9874	5.46E-08	Q9UBR2|CATZ_HUMAN	R.NQHIPQYCGSCWAHASTSAMADR.I	4.6	4	2
	7406	609.27	42.6359	1.72E-06	Q9UBR2|CATZ_HUMAN	R.NSWGEPWGER.G	2.5	2	10
	3377	658.004	43.2292	3.43E-09	Q9UBR2|CATZ_HUMAN	R.STYPRPHEYLSPADLPK.S	4.7	3	2
	3630	657.669	43.3408	5.12E-10	Q9UBR2|CATZ_HUMAN	R.STYPRPHEYLSPADLPK.S	4.2	3	9
	4059	939.943	60.4842	2.20E-07	Q9UBR2|CATZ_HUMAN	R.YNLAIEEHCTFGDPIV.-	3.5	2	8
	3477	939.442	60.4311	1.49E-03	Q9UBR2|CATZ_HUMAN	R.YNLAIEEHCTFGDPIV.-	2.9	2	6
Cofilin-1	4253	1022.21	73.1812	2.00E-02	P23528|COF1_HUMAN	K.NIILEEGKEILVGDVGQTVDDPYATFVK.M	6.5	3	4
	3825	1021.87	73.1812	3.27E-02	P23528|COF1_HUMAN	K.NIILEEGKEILVGDVGQTVDDPYATFVK.M	5.4	3	17
	3424	670.893	54.5945	4.46E-03	P23528|COF1_HUMAN	K.LGGSAVISLEGKPL.-	3.2	2	23
	2690	669.316	38.9676	1.76E-02	P23528|COF1_HUMAN	R.YALYDATYETK.E	2.9	2	20
	3855	669.817	39.0148	1.35E-02	P23528|COF1_HUMAN	R.YALYDATYETK.E	3.2	2	1
Complement factor D	6886	851.069	55.6086	5.80E-07	P00746|CFAD_HUMAN	R.DSCKGDSGGPLVCGGVLEGVVTSGSR.V	5.2	3	9
	3360	586.672	58.8546	5.95E-11	P00746|CFAD_HUMAN	R.RPDSLQHVLLPVLDR.A	4.0	3	13
	4450	587.006	58.9084	8.98E-04	P00746|CFAD_HUMAN	R.RPDSLQHVLLPVLDR.A	4.2	3	10
Dipeptidyl-peptidase 1	9557	611.329	34.6058	1.52E-06	P53634|CATC_HUMAN	K.KVGTASENVYVNTAHLK.N	4.5	3	5
	7637	610.995	34.6598	9.37E-05	P53634|CATC_HUMAN	K.KVGTASENVYVNTAHLK.N	4.4	3	3
Epididymal secretory protein E1	7996	959.456	51.0952	2.47E-05	P61916|NPC2_HUMAN	K.DCGSVDGVIKEVNVSPCPTQPCQLSK.G	5.0	3	2
	5343	922.438	35.406	1.78E-05	P61916|NPC2_HUMAN	K.EVNVSPCPTQPCQLSK.G	3.4	2	3
	5979	922.939	35.5079	2.39E-06	P61916|NPC2_HUMAN	K.EVNVSPCPTQPCQLSK.G	3.8	2	6
	6854	959.121	50.9904	2.02E-02	P61916|NPC2_HUMAN	K.DCGSVDGVIKEVNVSPCPTQPCQLSK.G	5.2	3	6
Gelsolin (Actin-depolymerizing factor)	9749	915.486	56.9489	8.10E-05	P06396|GELS_HUMAN	K.QTQVSVLPEGGETPLFK.Q	3.2	2	3
	12157	660.349	46.4228	7.34E-04	P06396|GELS_HUMAN	K.AGALNSNDAFVLK.T	2.7	2	4
Glutathione S-transferase P	5689	709.726	62.4489	1.13E-06	P09211|GSTP1_HUMAN	K.ALPGQLKPFETLLSQNQGGK.T	4.2	3	7
	7448	942.981	56.7316	1.86E-09	P09211|GSTP1_HUMAN	K.FQDGDLTLYQSNTILR.H	5.5	2	9
	8936	568.792	38.0543	2.29E-09	P09211|GSTP1_HUMAN	K.ASCLYGQLPK.F	2.8	2	12
	6747	942.479	56.6867	3.02E-09	P09211|GSTP1_HUMAN	K.FQDGDLTLYQSNTILR.H	4.5	2	3
	4462	669.368	57.0558	3.56E-06	P09211|GSTP1_HUMAN	-.PPYTVVYFPVR.G	3.0	2	10
	6728	669.868	57.0986	2.70E-03	P09211|GSTP1_HUMAN	-.PPYTVVYFPVR.G	3.2	2	4
Glyceraldehyde-3-phosphate dehydrogenase	5444	765.9	47.9037	4.24E-02	P04406|G3P_HUMAN	R.VPTANVSVVDLTCR.L	3.5	2	8
	9669	917.463	42.6926	2.26E-07	P04406|G3P_HUMAN	K.IISNASCTTNCLAPLAK.V	3.6	2	6
	8675	917.965	42.6926	6.35E-08	P04406|G3P_HUMAN	K.IISNASCTTNCLAPLAK.V	4.2	2	3
Granulins	6568	1015.92	56.48	6.67E-04	P28799|GRN_HUMAN	R.LQSGAWGCCPFTQAVCCEDHIHCCPAGFTCDTQK.G	5.2	4	4
	7745	1016.16	56.3768	2.85E-04	P28799|GRN_HUMAN	R.LQSGAWGCCPFTQAVCCEDHIHCCPAGFTCDTQK.G	5.3	4	1
	21079	955.336	34.6058	6.95E-04	P28799|GRN_HUMAN	K.CDMEVSCPDGYTCCR.L	4.6	2	2
Hemoglobin subunit alpha-1	1973	510.582	33.4001	2.36E-04	P01967|HBA1_BOSMU	K.VGGHAAEYGAEALER.M	4.3	3	9
	6019	765.371	33.4566	6.56E-04	P01967|HBA1_BOSMU	K.VGGHAAEYGAEALER.M	4.0	2	6
	1332	637.867	59.0687	1.25E-06	P04346|HBBA_BOSJA	R.LLVVYPWTQR.F	2.6	2	12
Hemoglobin fetal subunit beta	4156	1008.49	68.6414	2.04E-04	P02081|HBBF_BOVIN	R.FFESFGDLSSADAILGNPK.V	6.3	2	5
	5945	1007.99	68.7006	2.73E-04	P02081|HBBF_BOVIN	R.FFESFGDLSSADAILGNPK.V	4.9	2	2
	1474	637.867	59.0687	1.59E-11	P02081|HBBF_BOVIN	R.LLVVYPWTQR.F	2.6	2	19
Inter-alpha-trypsin inhibitor heavy chain H2	3476	710.366	43.595	7.41E-06	P19823|ITIH2_HUMAN	K.VQFELHYQEVK.W	3.6	2	11
	4221	669.364	48.8467	2.46E-08	P19823|ITIH2_HUMAN	K.FYNQVSTPLLR.N	2.7	2	27
	3488	792.433	44.7437	7.07E-10	P19823|ITIH2_HUMAN	K.IQPSGGTNINEALLR.A	3.0	2	1
	2576	791.932	44.7437	7.71E-10	P19823|ITIH2_HUMAN	K.IQPSGGTNINEALLR.A	3.0	2	8
Kininogen-1	16373	667.844	40.2963	5.64E-05	P01044|KNG1_BOVIN	K.LISDFPETTSPK.C	2.5	2	3
	7863	484.782	51.5138	1.38E-04	P01044|KNG1_BOVIN	K.YSIVFIAR.E	2.6	2	6
Legumain	8046	661.306	33.291	1.24E-02	Q99538|LGMN_HUMAN	K.LMNTNDLEESR.Q	3.1	2	10
	9270	969.486	71.5011	8.12E-05	Q99538|LGMN_HUMAN	K.DYTGEDVTPQNFLAVLR.G	3.8	2	4
	2661	484.738	35.9351	1.43E-10	Q99538|LGMN_HUMAN	K.VMQFQGMK.R	2.7	2	20
Lysozyme C	433	682.347	68.5281	2.88E-08	P61626|LYSC_HUMAN	R.GISLANWMCLAK.W	3.7	2	16
	851	700.843	50.9356	2.72E-12	P61626|LYSC_HUMAN	R.STDYGIFQINSR.Y	3.8	2	28
	2925	976.8	60.2839	1.65E-03	P61626|LYSC_HUMAN	K.TPGAVNACHLSCSALLQDNIADAVACAK.R	4.7	3	7
	3118	977.135	60.2839	1.28E-03	P61626|LYSC_HUMAN	K.TPGAVNACHLSCSALLQDNIADAVACAK.R	4.4	3	2
	20847	788.706	49.5259	6.28E-04	P61626|LYSC_HUMAN	R.ATNYNAGDRSTDYGIFQINSR.Y	4.2	3	1
Monocyte differentiation antigen CD14	19361	820.155	62.6786	4.43E-05	P08571|CD14_HUMAN	R.NTGMETPTGVCAALAAAGVQPHSLDLSHNSLR.A	4.5	4	2
	5727	987.004	64.9241	1.75E-07	P08571|CD14_HUMAN	R.AFPALTSLDLSDNPGLGER.G	4.7	2	4
	8747	667.672	45.4918	1.48E-03	P08571|CD14_HUMAN	K.VLSIAQAHSPAFSCEQVR.A	3.8	3	6
	6180	987.507	64.9313	4.85E-04	P08571|CD14_HUMAN	R.AFPALTSLDLSDNPGLGER.G	5.5	2	12
Nucleobindin-1	4861	636.862	62.2279	4.01E-02	Q02818|NUCB1_HUMAN	R.DLELLIQTATR.D	2.7	2	16
	7018	580.819	51.3713	1.69E-07	Q02818|NUCB1_HUMAN	R.LPEVEVPQHL.-	3.2	2	2
Phosphoglycerate kinase 1	9800	877.897	39.6416	1.87E-03	P00558|PGK1_HUMAN	R.GCITIIGGGDTATCCAK.W	4.7	2	2
	8044	590.671	65.2825	7.59E-06	P00558|PGK1_HUMAN	K.ALESPERPFLAILGGAK.V	3.8	3	12
Phospholipid transfer protein	7626	908.989	71.3425	1.60E-07	P55058|PLTP_HUMAN	R.FLEQELETITIPDLR.G	2.8	2	6
	7694	909.492	71.392	6.11E-08	P55058|PLTP_HUMAN	R.FLEQELETITIPDLR.G	3.2	2	10
Plastin-2 (Lymphocyte cytosolic protein 1)	9046	793.428	56.8958	8.34E-10	P13796|PLSL_HUMAN	R.VYALPEDLVEVNPK.M	2.6	2	2
	7604	568.308	39.0706	6.56E-08	P13796|PLSL_HUMAN	R.QFVTATDVVR.G	2.5	2	9
Platelet basic protein (CXCL7)	2154	528.76	35.5079	5.61E-05	P02775|SCYB7_HUMAN	K.ICLDPDAPR.I	2.8	2	19
	1300	575.615	50.8391	8.07E-07	P02775|SCYB7_HUMAN	K.GKEESLDSDLYAELR.C	4.2	3	18
	1472	575.95	50.9183	3.88E-08	P02775|SCYB7_HUMAN	K.GKEESLDSDLYAELR.C	4.0	3	6
	2836	862.92	50.8391	8.22E-08	P02775|SCYB7_HUMAN	K.GKEESLDSDLYAELR.C	5.1	2	19
	3044	863.422	50.8391	1.10E-08	P02775|SCYB7_HUMAN	K.GKEESLDSDLYAELR.C	5.2	2	3
	1510	633.321	39.2803	2.72E-06	P02775|SCYB7_HUMAN	K.GTHCNQVEVIATLKDGR.K	3.9	3	7
	373	550.819	43.0299	1.70E-10	P02775|SCYB7_HUMAN	K.NIQSLEVIGK.G	2.5	2	22
	4814	1100.63	43.2293	1.52E-04	P02775|SCYB7_HUMAN	K.NIQSLEVIGK.G	1.8	1	11
	1613	633.656	39.2803	1.86E-06	P02775|SCYB7_HUMAN	K.GTHCNQVEVIATLKDGR.K	4.1	3	4
Platelet factor 4 variant (CXCL4L1)	8756	789.428	49.4245	1.07E-02	P10720|PF4V_HUMAN	K.AGPHCPTAQLIATLK.N	3.4	2	6
	8596	789.929	49.4245	2.68E-03	P10720|PF4V_HUMAN	K.AGPHCPTAQLIATLK.N	3.3	2	1
Proactivator polypeptide	1496	824.37	64.8104	6.99E-05	P07602|SAP_HUMAN	K.SDVYCEVCEFLVK.E	3.5	2	21
	9279	922.787	71.618	3.41E-05	P07602|SAP_HUMAN	K.EICALVGFCDEVKEMPMQTLVPAK.V	4.1	3	9
	1814	789.37	50.9356	7.18E-04	P07602|SAP_HUMAN	K.GEMSRPGEVCSALNLCESLQK.H	4.9	3	18
	4226	652.39	42.9187	1.87E-03	P07602|SAP_HUMAN	R.LPALTVHVTQPK.D	3.8	2	8
	1923	782.48	62.0434	3.32E-04	P07602|SAP_HUMAN	K.NVIPALELVEPIKK.H	3.4	2	9
	8472	1024.43	54.1953	1.04E-05	P07602|SAP_HUMAN	K.CIWGPSYWCQNTETAAQCNAVEHCK.R	3.8	3	4
	1576	781.979	62.0434	2.80E-06	P07602|SAP_HUMAN	K.NVIPALELVEPIKK.H	3.4	2	19
	1327	656.305	47.1739	1.79E-08	P07602|SAP_HUMAN	K.GCSFLPDPYQK.Q	2.7	2	26
	4001	807.85	51.9155	3.90E-02	P07602|SAP_HUMAN	K.CIWGPSYWCQNTETAAQCNAVEHCKR.H	5.1	4	4
	2165	789.036	50.9356	1.64E-06	P07602|SAP_HUMAN	K.GEMSRPGEVCSALNLCESLQK.H	4.4	3	1
	2525	574.779	32.6844	1.14E-08	P07602|SAP_HUMAN	R.GSAVWCQNVK.T	2.9	2	25
	9849	923.121	71.618	1.15E-02	P07602|SAP_HUMAN	K.EICALVGFCDEVKEMPMQTLVPAK.V	4.2	3	2

	771	531.259	36.8419	5.86E-08	P07602|SAP_HUMAN	R.LGPGMADICK.N	2.7	2	18
	7589	717.933	67.6978	4.01E-03	P07602|SAP_HUMAN	K.NVIPALELVEPIK.K	2.8	2	13
	9535	1183.55	50.8391	9.63E-02	P07602|SAP_HUMAN	K.GEMSRPGEVCSALNLCESLQK.H	4.7	2	2
	566	537.954	34.7666	4.84E-09	P07602|SAP_HUMAN	K.HCLQTVWNKPTVK.S	4.2	3	5
	512	537.62	34.7666	9.79E-10	P07602|SAP_HUMAN	K.HCLQTVWNKPTVK.S	4.1	3	15
	9292	1220.04	61.9208	3.50E-04	P07602|SAP_HUMAN	K.DNGDVCQDCIQMVTDIQTAVR.T	5.5	2	8
	9165	1024.76	54.1953	1.36E-04	P07602|SAP_HUMAN	K.CIWGPSYWCQNTETAAQCNAVEHCK.R	3.9	3	2
Profilin-1	7252	958.037	63.0784	5.22E-03	P07737|PROF1_HUMAN	K.TFVNITPAEVGVLVGKDR.S	4.3	2	7
	7555	958.539	62.9703	4.50E-05	P07737|PROF1_HUMAN	K.TFVNITPAEVGVLVGKDR.S	4.9	2	4
	8627	748.027	62.3341	1.84E-06	P07737|PROF1_HUMAN	K.CSVIRDSLLQDGEFSMDLR.T	5.7	3	10
	4074	735.884	51.8603	4.59E-08	P07737|PROF1_HUMAN	R.SSFYVNGLTLGGQK.C	4.1	2	3
	3011	813.878	61.0791	5.00E-08	P07737|PROF1_HUMAN	R.DSLLQDGEFSMDLR.T	4.8	2	2
	2760	813.377	61.0791	1.17E-07	P07737|PROF1_HUMAN	R.DSLLQDGEFSMDLR.T	4.1	2	16
	5858	736.386	52.022	4.51E-11	P07737|PROF1_HUMAN	R.SSFYVNGLTLGGQK.C	4.7	2	14
	1667	690.361	39.7798	3.87E-11	P07737|PROF1_HUMAN	K.STGGAPTFNVTVTK.T	3.0	2	13
Protein S100-A11 (Calgizzarin)	3905	925.456	81.2666	1.79E-03	P31949|S10AB_HUMAN	K.TEFLSFMNTELAAFTK.N	4.4	2	9
	3687	925.958	81.2666	5.75E-06	P31949|S10AB_HUMAN	K.TEFLSFMNTELAAFTK.N	5.3	2	9
	4487	654.355	66.0515	1.17E-06	P31949|S10AB_HUMAN	R.CIESLIAVFQK.Y	3.1	2	12
Ribonuclease pancreatic (Rnase 1)	2164	697.846	56.1292	4.46E-09	P07998|RNAS1_HUMAN	R.CKPVNTFVHEPLVDVQNVCFQEK.V	5.0	4	9
	1693	877.749	56.6446	3.57E-09	P07998|RNAS1_HUMAN	R.HIIVACEGSPYVPVHFDASVEDST.-	3.8	3	2
	1341	877.415	56.6446	2.18E-09	P07998|RNAS1_HUMAN	R.HIIVACEGSPYVPVHFDASVEDST.-	3.9	3	20
	4941	1315.62	56.6867	6.18E-03	P07998|RNAS1_HUMAN	R.HIIVACEGSPYVPVHFDASVEDST.-	4.1	2	3
	5578	1316.12	56.5325	1.47E-03	P07998|RNAS1_HUMAN	R.HIIVACEGSPYVPVHFDASVEDST.-	4.3	2	1
	2209	930.127	56.0723	8.65E-05	P07998|RNAS1_HUMAN	R.CKPVNTFVHEPLVDVQNVCFQEK.V	5.3	3	9
	1228	812.982	32.2513	1.37E-08	P07998|RNAS1_HUMAN	R.QHMDSDSSPSSSSTYCNQMMR.R	5.6	3	22
Serum albumin	8128	927.493	40.424	8.74E-05	P02769|ALBU_BOVIN	K.YLYEIAR.R	1.8	1	34
	170	927.494	37.7114	1.06E-04	P02769|ALBU_BOVIN	K.YLYEIAR.R	1.8	1	46
	1209	547.651	47.1739	5.48E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.8	3	13
	6047	547.652	56.1746	7.43E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.5	3	10
	5969	547.317	55.2013	1.01E-04	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.1	3	30
	9508	547.652	64.431	2.21E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.6	3	8
	9035	547.318	64.4918	1.54E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.3	3	26
	4722	547.651	52.8728	1.96E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.3	3	8
	4016	547.318	52.7776	6.98E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.4	3	25
	8099	547.652	61.8724	6.34E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.7	3	7
	6229	547.317	61.9861	2.70E-05	P02768|ALBU_HUMAN	K.KVPQVSTPTLVEVSR.N	4.3	3	19
	8794	927.495	44.7797	1.03E-04	P02769|ALBU_BOVIN	K.YLYEIAR.R	1.8	1	12
	7083	547.652	59.4359	1.02E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.1	3	14
	5219	547.318	58.1997	8.72E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.4	3	27
	3534	547.651	49.6706	5.38E-07	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.6	3	14
	3216	547.317	49.5727	6.94E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.4	3	31
	751	547.317	46.7297	3.82E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.7	3	34
	1224	756.425	47.3772	4.28E-05	P02769|ALBU_BOVIN	K.VPQVSTPTLVEVSR.N	3.1	2	26
	8	547.318	44.3888	3.55E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.5	3	25
	15	547.65	44.89	2.71E-06	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	4.8	3	1
	4652	820.975	47.1739	4.94E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	3.7	2	8
	4230	820.473	47.1158	4.33E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	3.6	2	30
	8843	820.974	49.6706	5.17E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	3.6	2	6
	6674	820.473	49.6706	8.54E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	3.6	2	15
	35	820.472	44.7797	1.58E-05	P02769|ALBU_BOVIN	K.KVPQVSTPTLVEVSR.N	3.7	2	34
Tartrate-resistant acid phosphatase type 5	5851	607.293	62.5645	7.49E-07	P13686|PPA5_HUMAN	R.WNFPSPFYR.L	2.6	2	20
	3353	664.823	39.3385	1.74E-06	P13686|PPA5_HUMAN	K.EMTVTYIEASGK.S	3.1	2	11
	2409	667.006	58.3077	2.70E-10	P13686|PPA5_HUMAN	R.FVAVGDWGGVPNAPFHTAR.E	3.8	3	16
Thrombospondin-1	4251	924.962	62.8599	3.43E-04	P07996|TSP1_HUMAN	K.MENAELDVPIQSVFTR.D	4.1	2	8
	3199	604.82	48.3998	1.21E-04	P07996|TSP1_HUMAN	K.SITLFVQEDR.A	3.2	2	1
	8193	880.771	73.272	5.24E-06	P07996|TSP1_HUMAN	K.TKDLQAICGISCDELSSMVLELR.G	5.0	3	1
	8457	880.437	73.2395	6.96E-06	P07996|TSP1_HUMAN	K.TKDLQAICGISCDELSSMVLELR.G	4.8	3	10
	8881	495.31	67.3062	2.59E-08	P07996|TSP1_HUMAN	K.GFLLLASLR.Q	2.8	2	16
	2659	809.411	51.762	2.13E-08	P07996|TSP1_HUMAN	K.GGVNDNFQGVLQNVR.F	4.3	2	4
	3677	860.785	70.2035	5.70E-10	P07996|TSP1_HUMAN	R.IEDANLIPPVPDDKFQDLVDAVR.A	4.0	3	16
	1983	604.318	48.3998	1.03E-06	P07996|TSP1_HUMAN	K.SITLFVQEDR.A	3.1	2	15
	1483	623.854	52.7776	2.25E-09	P07996|TSP1_HUMAN	R.TIVTTLQDSIR.K	2.7	2	23
	2246	808.911	51.7124	5.76E-09	P07996|TSP1_HUMAN	K.GGVNDNFQGVLQNVR.F	3.9	2	7
	1077	697.87	62.6237	1.00E-09	P07996|TSP1_HUMAN	R.FVFGTTPEDILR.N	3.0	2	25
	3299	686.833	35.5612	1.94E-09	P07996|TSP1_HUMAN	K.GTSQNDPNWVVR.H	2.9	2	21
	4378	925.465	62.9161	3.38E-03	P07996|TSP1_HUMAN	K.MENAELDVPIQSVFTR.D	4.8	2	5
	8475	775.896	35.882	6.47E-03	P07996|TSP1_HUMAN	R.NALWHTGNTPGQVR.T	3.3	2	10
Tissue alpha-L-fucosidase	8328	602.661	52.5768	4.12E-08	P04066|FUCO_HUMAN	K.DVGPHRDLVGELGTALR.K	4.7	3	7
	2803	572.322	60.2839	4.71E-04	P04066|FUCO_HUMAN	R.DLVGELGTALR.K	3.1	2	11
V-set and immunoglobulin domain-containing protein	3407	552.806	57.6675	2.38E-05	Q9Y279|VSIG4_HUMAN	R.GSDPVTIFLR.D	2.5	2	11
	9822	1191.1	66.644	8.01E-05	Q9Y279|VSIG4_HUMAN	K.GDVNLPCTYDPLQGYTQVLVK.W	4.2	2	7
Vitamin D-binding protein	3253	1028.44	46.3776	2.06E-04	Q3MHN5|VTDB_BOVIN	K.GQELCADYSENTFTEYK.K	5.9	2	12
	4070	1027.94	45.9318	4.63E-05	Q3MHN5|VTDB_BOVIN	K.GQELCADYSENTFTEYK.K	5.1	2	2
	5140	903.744	58.1134	2.36E-02	Q3MHN5|VTDB_BOVIN	K.HQPQEFPTYVEPTNDEICEAFR.K	5.5	3	1
	4076	903.41	58.1134	2.23E-02	Q3MHN5|VTDB_BOVIN	K.HQPQEFPTYVEPTNDEICEAFR.K	5.0	3	15

TABLE II: PEPTIDES SIGNIFICANTLY INCREASED IN THE CONDITIONED MEDIUM OF SPCs

SIEVE Frames, elution time of peptide, p-value, ratio compared to EACs, protein accession number, peptide sequence, Xcorr score and charge state of the peptide

Peptide sequences identified using filters described in text

Description	FrameID	M/z	Time	pValue	Protein	Peptide	XCorr	Charge	MS2
72kDa type IV collagenase (Matrix metalloproteinase-2)	8059	530.257	51.8085	2.45E-08	Q9GLE5|MMP2_BOVIN	R.IHDGEADIMINFGR.W	3.7	3	2
	8034	716.688	58.4171	4.67E-06	Q9GLE5|MMP2_BOVIN	K.TDKELAVQYLNTFYGCPK.E	4.6	3	2
	11693	717.021	58.4171	1.43E-05	Q9GLE5|MMP2_BOVIN	K.TDKELAVQYLNTFYGCPK.E	4.1	3	1
	11489	695.869	55.3087	6.05E-05	Q9GLE5|MMP2_BOVIN	K.QDIVFDGISQIR.G	3.2	2	2
	14973	702.358	56.3768	8.30E-05	Q9GLE5|MMP2_BOVIN	K.TYIFAGDKFWR.Y	2.8	2	3
	20410	794.381	51.8085	1.84E-04	Q9GLE5|MMP2_BOVIN	R.IHDGEADIMINFGR.W	3.6	2	1
	12199	835.871	52.7776	3.86E-04	Q9GLE5|MMP2_BOVIN	R.CGNPDVANYNFFPR.K	3.9	2	1
Biglycan	1834	656.877	68.0193	4.53E-07	P21809|PGS1_BOVIN	K.IQAIELEDLLR.Y	3.6	2	3
	3810	747.873	55.9704	7.11E-07	P21809|PGS1 BOVIN	K.VGVNDFCPVGFGVK.R	3.8	2	6
	13091	909.54	40.594	6.71E-04	P21809|PGS1 BOVIN	R.VPAGLPDLK.L	2.0	1	4
Collagen alpha-1(I) chain	13299	528.64	48.9542	7.11E-05	P02453|CO1A1_BOVIN	K.KALLLQGSNEIEIR.A	3.7	3	1
	931	545.291	25.7136	2.85E-05	P02452|CO1A1 HUMAN	R.GVQGPPGPAGPR.G	3.2	2	15
	396	573.291	40.5039	9.19E-06	P02452|CO1A1 HUMAN	R.GQAGVMGFPGPK.G	3.3	2	11
	654	594.322	40.7404	1.31E-13	P02452|CO1A1 HUMAN	K.SLSQQIENIR.S	3.0	2	14
	3612	613.804	25.0114	9.10E-07	P02452|CO1A1 HUMAN	K.GLTGSPGSPGPDGK.T	2.9	2	17
	3468	648.831	45.1856	1.22E-13	P02452|CO1A1 HUMAN	R.GFPGLPGPSGEPGK.Q	2.7	2	12
	1664	652.837	35.1292	1.36E-09	P02452|CO1A1 HUMAN	R.DRDLEVDTTLK.S	3.2	2	16
	19757	654.663	33.9838	2.27E-06	P02452|CO1A1 HUMAN	K.SGDRGETGPAGPAGPVGPVGAR.G	3.8	3	1
	560	654.663	32.5762	1.40E-05	P02452|CO1A1 HUMAN	K.SGDRGETGPAGPAGPVGPVGAR.G	3.9	3	1
	18210	654.997	33.8295	6.30E-06	P02452|CO1A1 HUMAN	K.SGDRGETGPAGPAGPVGPVGAR.G	4.0	3	3
	547	654.997	32.5762	1.08E-05	P02452|CO1A1 HUMAN	K.SGDRGETGPAGPAGPVGPVGAR.G	4.4	3	3
	1833	714.353	34.7666	5.20E-10	P02452|CO1A1 HUMAN	R.GSAGPPGATGFPGAAGR.V	4.3	2	17
	2762	769.396	43.1747	8.72E-08	P02452|CO1A1_HUMAN	K.GANGAPGIAGAPGFPGAR.G	3.1	2	6
	6800	779.919	39.6834	7.28E-05	P02452|CO1A1 HUMAN	R.GLTGPIGPPGPAGAPGDK.G	3.0	2	3
	6106	797.755	48.9008	1.93E-03	P02452|CO1A1 HUMAN	R.GPPGSAGAPGKDGLNGLPGPIGPPGPR.G	4.0	3	3
	8736	804.41	28.6062	1.99E-05	P02452|CO1A1 HUMAN	K.GSPGEAGRPGEAGLPGAK.G	3.5	2	6
	4783	810.414	34.2489	2.06E-03	P02452|CO1A1 HUMAN	K.NWYISK.N	2.0	1	8
	5767	820.41	35.3569	1.32E-03	P02452|CO1A1_HUMAN	R.GFPGADGVAGPKGPAGER.G	3.6	2	6
	7275	820.913	35.406	2.03E-03	P02452|CO1A1 HUMAN	R.GFPGADGVAGPKGPAGER.G	3.5	2	6
	6345	834.412	46.2729	1.57E-02	P02452|CO1A1 HUMAN	R.GNDGATGAAGPPGPTGPAGPPGFPGAVGAK.G	4.6	3	5
	9568	834.747	46.1699	6.91E-06	P02452|CO1A1 HUMAN	R.GNDGATGAAGPPGPTGPAGPPGFPGAVGAK.G	5.5	3	1
	3316	845.889	26.2956	1.55E-04	P02452|CO1A1_HUMAN	K.DGEAGAQGPPGPAGPAGER.G	4.5	2	12
	3937	846.391	26.2956	5.80E-04	P02452|CO1A1_HUMAN	K.DGEAGAQGPPGPAGPAGER.G	4.6	2	4
	2090	848.918	32.0841	6.03E-11	P02452|CO1A1 HUMAN	K.NSVAYMDQQTGNLKK.A	4.4	2	7
	2449	849.419	31.9741	1.18E-09	P02452|CO1A1 HUMAN	K.NSVAYMDQQTGNLKK.A	4.4	2	5
	3163	880.757	39.1234	5.70E-04	P02452|CO1A1 HUMAN	R.GAPGDRGEPGPPGPAGFAGPPGADGQPGAK.G	5.8	3	11
	4259	881.092	39.1234	4.69E-07	P02452|CO1A1 HUMAN	R.GAPGDRGEPGPPGPAGFAGPPGADGQPGAK.G	6.3	3	1
	1731	882.953	32.6252	3.63E-05	P02452|CO1A1_HUMAN	R.VGPPGPSGNAGPPGPPGPAGK.E	4.2	2	3
	1914	883.454	32.6252	5.97E-05	P02452|CO1A1 HUMAN	R.VGPPGPSGNAGPPGPPGPAGK.E	4.6	2	12
	7597	886.761	44.237	2.65E-04	P02452|CO1A1 HUMAN	R.GFSGLQGPPGPPGSPGEQGPSGASGPAGPR.G	5.1	3	6
	9591	887.096	44.1956	5.34E-06	P02452|CO1A1 HUMAN	R.GFSGLQGPPGPPGSPGEQGPSGASGPAGPR.G	5.8	3	1
	7237	892.94	42.3971	4.89E-04	P02452|CO1A1 HUMAN	R.GPPGPMGPPGLAGPPGESGR.E	4.8	2	8
	8745	893.441	42.3971	2.98E-04	P02452|CO1A1_HUMAN	R.GPPGPMGPPGLAGPPGESGR.E	5.4	2	4
	8245	981.491	32.5762	1.16E-04	P02452|CO1A1 HUMAN	K.SGDRGETGPAGPAGPVGPVGAR.G	4.5	2	3
	8834	1037.01	34.5101	1.74E-16	P02452|CO1A1 HUMAN	K.GSPGADGPAGAPGTPGPQGIAGQR.G	3.8	2	2
	7936	1037.51	34.4559	5.34E-04	P02452|CO1A1 HUMAN	K.GSPGADGPAGAPGTPGPQGIAGQR.G	4.4	2	2
	1158	1040.48	54.5538	3.76E-11	P02452|CO1A1 HUMAN	K.SGEYWIDPNQGCNLDAIK.V	4.3	2	1
	986	1040.98	54.6485	3.57E-03	P02452|CO1A1_HUMAN	K.SGEYWIDPNQGCNLDAIK.V	5.4	2	14
	3564	1049.16	38.7107	4.91E-06	P02452|CO1A1 HUMAN	R.GANGAPGNDGAKGDAGAPGAPGSQGAPGLQGMPGER.G	4.4	3	2
	3506	1049.49	38.7107	4.42E-05	P02452|CO1A1 HUMAN	R.GANGAPGNDGAKGDAGAPGAPGSQGAPGLQGMPGER.G	4.4	3	2
	3701	1068	39.6834	2.69E-04	P02452|CO1A1 HUMAN	K.GDAGAPGAPGSQGAPGLQGMPGER.G	3.6	2	2
	3169	1068.5	39.6834	4.82E-05	P02452|CO1A1 HUMAN	K.GDAGAPGAPGSQGAPGLQGMPGER.G	4.3	2	8
	6896	1251.12	46.1227	3.94E-19	P02452|CO1A1_HUMAN	R.GNDGATGAAGPPGPTGPAGPPGFPGAVGAK.G	5.1	2	5
	4739	1340.32	52.3648	2.06E-08	P02452|CO1A1 HUMAN	R.GEQGPAGSPGFQGLPGPAGPPGEAGKPGEQGVPGDLGAPGPSGAR.G	4.5	3	1
	5894	1340.66	52.3183	2.81E-04	P02452|CO1A1 HUMAN	R.GEQGPAGSPGFQGLPGPAGPPGEAGKPGEQGVPGDLGAPGPSGAR.G	4.4	3	1
	15267	997.004	30.3854	4.14E-04	P02453|CO1A1_BOVIN	K.TGPPGPAGQDGRPGPPGPPGAR.G	3.2	2	1
	635	728.411	53.8382	9.20E-08	P02453|CO1A1 BOVIN	K.ALLLQGSNEIEIR.A	3.8	2	7
	14208	728.411	55.3087	9.05E-06	P02453|CO1A1 BOVIN	K.ALLLQGSNEIEIR.A	2.8	2	1
	17827	728.912	55.3087	1.66E-05	P02453|CO1A1 BOVIN	K.ALLLQGSNEIEIR.A	3.6	2	1
	10910	784.87	35.0208	4.55E-04	P02453|CO1A1 BOVIN	K.NSVAYMDQQTGNLKK.A	3.5	2	4
Collagen alpha-1(III) chain	4474	819.907	52.7776	9.47E-04	P02461|CO3A1_HUMAN	K.GEMGPAGIPGAPGLMGAR.G	3.4	2	5
	3940	770.33	36.559	5.46E-03	P02461|CO3A1 HUMAN	K.SGEYWVDPNQGCK.L	3.9	2	6
	1650	632.826	50.1326	1.09E-12	P02461|CO3A1 HUMAN	K.INTDEIMTSLK.S	3.3	2	10
	2527	633.327	50.1326	2.87E-11	P02461|CO3A1 HUMAN	K.INTDEIMTSLK.S	3.0	2	1
	6494	556.257	31.3677	6.96E-09	P02461|CO3A1 HUMAN	K.LMGSNEGEFK.A	2.6	2	6
	4775	717.334	43.6391	1.95E-10	P02461|CO3A1 HUMAN	K.FTYTVLEDGCTK.H	3.1	2	4
	3830	829.92	52.4175	1.21E-05	P02461|CO3A1 HUMAN	K.SVNGQIESLISPDGSR.K	3.5	2	2
	5462	820.409	52.7776	2.80E-07	P02461|CO3A1 HUMAN	K.GEMGPAGIPGAPGLMGAR.G	3.8	2	1
	4781	830.422	52.3183	3.71E-04	P02461|CO3A1 HUMAN	K.SVNGQIESLISPDGSR.K	4.5	2	1
	15728	800.745	34.356	1.94E-11	P04258|CO3A1_BOVIN	R.GPVGPSGPPGKDGASGHPGPIGPPGPR.G	4.3	3	2
	2269	540.783	36.2417	5.92E-06	P04258|CO3A1 BOVIN	R.GLAGPPGMPGAR.G	2.7	2	5
	1846	621.303	31.0345	6.35E-05	P04258|CO3A1_BOVIN	R.GSPGPGAAGFPGGR.G	2.8	2	6
Collagen alpha-1(V) chain	2667	835.09	81.1669	8.80E-08	P20908|CO5A1_HUMAN	R.ILDEEVFEGDIQQLLFVSDHR.A	4.0	3	8
	7849	1064.55	75.2775	1.77E-05	P20908|CO5A1 HUMAN	K.QLYPASAFPEDFSILTTVK.A	3.7	2	5
Collagen alpha-1(VI) chain	4928	999.917	38.4344	2.26E-03	P12109|CO6A1_HUMAN	K.NNVEQVCCSFECQPAR.G	4.7	2	3
	3069	1059.19	57.8891	8.89E-03	P12109|CO6A1 HUMAN	K.YLIVVTDGHPLEGYKEPCGGLEDAVNEAK.H	6.0	3	4
	5012	790.924	51.4583	1.68E-02	P12109|CO6A1 HUMAN	K.VFSVAITPDHLEPR.L	3.2	2	7
	5025	999.416	38.3837	2.09E-03	P12109|CO6A1 HUMAN	K.NNVEQVCCSFECQPAR.G	4.1	2	4
	3393	1058.85	57.8891	1.60E-02	P12109|CO6A1_HUMAN	K.YLIVVTDGHPLEGYKEPCGGLEDAVNEAK.H	6.2	3	1
	1680	523.802	46.6796	4.96E-11	P12109|CO6A1 HUMAN	R.VPSYQALLR.G	2.6	2	15
	2219	479.289	41.724	1.10E-09	P12109|CO6A1 HUMAN	R.IALVITDGR.S	2.7	2	12
	2528	794.391	57.8891	1.31E-05	P12109|CO6A1 HUMAN	K.YLIVVTDGHPLEGYKEPCGGLEDAVNEAK.H	5.2	4	4
	9614	645.345	37.4598	7.23E-09	P12109|CO6A1 HUMAN	R.LSIIATDHTYR.R	2.9	2	3
	6426	791.426	51.4583	2.18E-06	P12109|CO6A1_HUMAN	K.VFSVAITPDHLEPR.L	3.5	2	1
Collagen alpha-2(I) chain	9849	1053.51	34.43	1.53E-12	P02465|CO1A2_BOVIN	K.DYEVDATLK.S	2.1	1	6
	1914	986.106	62.6236	1.47E-06	P02465|CO1A2 BOVIN	R.LSHPEWSSGYYWIDPNQGCTMDAIK.V	5.7	3	2
	1184	695.338	47.8083	2.72E-09	P02465|CO1A2 BOVIN	R.FTYTVLVDGCSK.K	3.8	2	5
	2302	657.675	50.2298	8.49E-07	P02465|CO1A2 BOVIN	K.AVILQGSNDVELVAEGNSR.F	4.1	3	2
	753	886.962	60.1004	1.30E-06	P02465|CO1A2 BOVIN	K.SLNNQIETLLTPEGSR.K	3.8	2	3
	651	886.461	60.1004	4.35E-06	P02465|CO1A2_BOVIN	K.SLNNQIETLLTPEGSR.K	3.8	2	6
	350	757.925	49.5259	9.52E-07	P02465|CO1A2 BOVIN	K.GAAGLPGVAGAPGLPGPR.G	3.3	2	6
	15855	757.925	50.7883	1.10E-06	P02465|CO1A2 BOVIN	K.GAAGLPGVAGAPGLPGPR.G	2.6	2	3
	363	599.29	50.3332	1.69E-05	P02465|CO1A2 BOVIN	K.EMATQLAFMR.L	2.7	2	5
	563	804.344	39.2281	3.03E-07	P02465|CO1A2 BOVIN	K.VYCDFSTGETCIR.A	4.1	2	7
	18927	804.343	40.5039	1.65E-06	P02465|CO1A2_BOVIN	K.VYCDFSTGETCIR.A	4.0	2	2
	6242	599.291	51.6141	1.40E-05	P02465|CO1A2 BOVIN	K.EMATQLAFMR.L	2.6	2	5
	1271	721.343	34.43	3.98E-05	P02465|CO1A2 BOVIN	R.GDGGPPGATGFPGAAGR.T	4.1	2	6
	17001	800.414	38.2296	2.37E-04	P02465|CO1A2 BOVIN	K.GELGPVGNPGPAGPAGPR.G	3.8	2	3
	8101	1058	27.9491	2.03E-04	P08123|CO1A2_HUMAN	R.GAPGPDGNNGAQGPPGPQGVQGGK.G	4.5	2	7
	3522	793.905	37.1143	1.82E-03	P08123|CO1A2 HUMAN	R.AQPENIPAKNWYR.S	2.8	2	9
	1282	857.411	37.7693	1.62E-03	P08123|CO1A2_HUMAN	K.NSIAYMDEETGNLKK.A	4.4	2	3
	4211	1018.5	38.3398	1.89E-03	P08123|CO1A2 HUMAN	R.GEVGPAGPNGFAGPAGAAGQPGAK.G	5.6	2	4
	1099	856.909	37.8193	6.45E-04	P08123|CO1A2 HUMAN	K.NSIAYMDEETGNLKK.A	4.3	2	10
	4234	873.759	37.1664	9.87E-09	P08123|CO1A2 HUMAN	R.GSPGERGEVGPAGPNGFAGPAGAAGQPGAK.G	6.6	3	1
	1856	759.386	43.7841	5.73E-13	P08123|CO1A2 HUMAN	R.FTYTVLVDGCSKK.T	3.5	2	8
	1343	695.338	47.8083	9.99E-13	P08123|CO1A2_HUMAN	R.FTYTVLVDGCSK.K	3.5	2	12
	2423	657.675	50.2298	2.76E-07	P08123|CO1A2 HUMAN	K.AVILQGSNDVELVAEGNSR.F	4.1	3	6
	4579	568.3	33.7372	8.20E-04	P08123|CO1A2 HUMAN	R.GHNGLDGLKGQPGAPGVK.G	3.8	3	13
	9795	568.313	33.5115	1.40E-01	P08123|CO1A2 HUMAN	R.GHNGLDGLKGQPGAPGVK.G	3.8	3	9
Collagen alpha-2(V) chain	3789	576.289	39.2281	4.18E-05	P05997|CO5A2_HUMAN	K.SLSSQIETMR.S	2.8	2	4
	7958	926.491	53.0736	7.75E-04	P05997|CO5A2 HUMAN	K.SGLGSQVGLMPGSVGPVGPR.G	3.3	2	3
	9807	651.326	34.7666	7.37E-04	P12110|CO6A2 HUMAN	R.DIASTPHELYR.N	2.8	2	4
Decorin (Bone proteoglycan II)	8018	965.153	74.802	2.11E-04	P07585|PGS2_BOVIN	K.KASYSGVSLFSNPVQYWEIQPSTFR.C	4.8	3	2
	7238	964.817	74.8451	3.68E-03	P07585|PGS2 BOVIN	K.KASYSGVSLFSNPVQYWEIQPSTFR.C	4.6	3	5
	5240	779.418	39.7325	1.25E-03	P07585|PGS2 HUMAN	R.VVQCSDLGLDKVPK.D	3.8	2	4
	5748	646.888	46.6285	2.47E-13	P21793|PGS2 BOVIN	K.NLHTLILINNK.I	3.4	2	4
	8715	833.935	55.1522	6.51E-06	P21793|PGS2 BOVIN	K.DLPPDTALLDLQNNK.I	3.0	2	3
	3883	663.309	37.1143	3.71E-04	P21793|PGS2 BOVIN	K.SSGIENGAFQGMK.K	3.4	2	3
Extracellular matrix protein 1	15021	1116.5	39.7325	1.54E-12	Q16610|ECM1_HUMAN	R.FCEAEFSVK.T	2.3	1	1
	771	558.753	39.7798	3.36E-09	Q16610|ECM1_HUMAN	R.FCEAEFSVK.T	2.9	2	6
Fibrillin-1	20667	597.809	44.3355	6.85E-05	P98133|FBN1_BOVIN	K.EGISYLHFTK.K	2.7	2	2
	19147	760.661	34.4089	8.43E-05	P98133|FBN1 BOVIN	K.GYIGTHCGQPVCESGCLNGGR.C	4.7	3	2
Fibronectin	6123	542.581	44.3888	2.16E-07	P07589|FINC_BOVIN	K.LSCQCLGFGSGHFR.C	4.3	3	2
	6409	542.915	44.3888	4.79E-07	P07589|FINC BOVIN	K.LSCQCLGFGSGHFR.C	3.7	3	2
	476	716.392	43.1232	3.91E-06	P07589|FINC BOVIN	R.VPGTSASATLTGLTR.G	3.8	2	4
	1353	883.405	48.1948	6.18E-06	P07589|FINC BOVIN	R.TYLGSALVCTCYGGSR.G	5.2	2	1
	700	874.374	56.5325	1.42E-05	P07589|FINC_BOVIN	K.FGFCPMAAHEEICTTNEGVMYR.I	4.7	3	5
	3577	797.409	51.9154	3.43E-05	P07589|FINC BOVIN	R.VTDATETTITISWR.T	3.1	2	6

	5422	687.321	50.8825	4.00E-05	P07589|FINC_BOVIN	R.TFYQIGDSWEK.Y	3.1	2	3
	335	687.321	49.6277	4.20E-05	P07589|FINC_BOVIN	R.TFYQIGDSWEK.Y	3.1	2	6
	566	618.299	34.7666	4.61E-05	P07589|FINC_BOVIN	R.HTSLQTTSAGSGSFTDVR.T	3.8	3	3
	1552	772.385	43.595	5.72E-05	P07589|FINC_BOVIN	R.SYTITGLQPGTDYK.I	3.6	2	4
	13672	735.345	48.9008	7.29E-05	P07589|FINC_BOVIN	R.GEWTCVAYSQLR.D	2.9	2	2
	21306	882.906	49.6706	8.14E-05	P07589|FINC_BOVIN	R.TYLGSALVCTCYGGSR.G	4.5	2	2
	1466	642.27	29.4748	9.19E-05	P07589|FINC_BOVIN	R.WKCDPVDQCQDSETR.T	4.6	3	4
	1043	701.335	33.291	9.26E-05	P07589|FINC_BOVIN	K.HYQINQQWER.T	3.1	2	5
	1512	733.3125	34.5583	1.27E-04	P07589|FINC_BOVIN	R.QDGHLWCSTTSNYEQDQK.Y	4.9	3	8
	19908	874.376	57.8328	1.39E-04	P07589|FINC_BOVIN	K.FGFCPMAAHEEICTTNEGVMYR.I	4.0	3	1
	1425	641.936	29.4748	1.55E-04	P07589|FINC_BOVIN	R.WKCDPVDQCQDSETR.T	5.5	3	5
	14416	735.333	47.1158	2.18E-04	P07589|FINC_BOVIN	R.GEWTCVAYSQLR.D	2.9	2	3
	2391	638.309	30.2738	2.44E-04	P07589|FINC_BOVIN	K.TYHVGEQWQK.E	2.8	2	4
	984	939.899	47.2738	3.33E-04	P07589|FINC_BOVIN	K.EYLGAICSCTCFGGQR.G	4.5	2	2
	1634	731.847	46.1227	3.59E-04	P07589|FINC_BOVIN	R.GNLLQCICTGNGR.G	3.7	2	5
	618	735.345	47.6104	4.26E-04	P07589|FINC_BOVIN	R.GEWTCVAYSQLR.D	3.2	2	5
	1072	940.4	47.1673	4.31E-04	P07589|FINC_BOVIN	K.EYLGAICSCTCFGGQR.G	4.9	2	4
	3591	863.913	42.7502	5.12E-04	P07589|FINC_BOVIN	K.YSFCTDHTVLVQTR.G	4.4	2	2
	2191	831.075	44.3355	6.61E-04	P07589|FINC_BOVIN	R.TEIDKPSQMQVTDVQDNSISVR.W	6.1	3	4
	3588	864.414	42.7502	7.14E-04	P07589|FINC_BOVIN	K.YSFCTDHTVLVQTR.G	4.5	2	3
	14500	687.321	52.6265	7.14E-04	P07589|FINC_BOVIN	R.TFYQIGDSWEK.Y	3.0	2	3
	2178	662.624	36.1935	7.50E-04	P07589|FINC_BOVIN	R.IGDQWDKQHDMGHMMR.C	4.2	3	3
	16334	646.84	51.762	7.92E-04	P07589|FINC_BOVIN	R.DLQFVEVTDVK.I	3.4	2	2
	18907	1287.17	49.9756	2.85E-09	P02751|FINC_HUMAN	R.TKTETITGFQVDAVPANGQTPIQR.T	5.1	2	2
	911	678.35	47.1158	3.38E-05	P02751|FINC_HUMAN	-.IYLYTLNDNAR.-	3.3	2	5
	1095	690.355	55.3543	1.99E-04	P02751|FINC_HUMAN	K.GLAFTDVDVDSIK.I	3.4	2	6
Insulin-like growth factor-binding protein 2 (IGFBP-2)	2432	808.39	47.6104	1.06E-06	P13384|IBP2_BOVIN	R.TPCQQELDQVLER.I	4.4	2	5
	10330	569.307	43.5016	4.61E-06	P13384|IBP2_BOVIN	K.SGMKELAVFR.E	2.8	2	4
	4302	711.299	33.5685	5.93E-05	P13384|IBP2_BOVIN	R.GECWCVNPNTGK.L	3.7	2	6
	18964	631.982	52.9762	6.41E-04	P13384|IBP2_BOVIN	R.GPLEHLYSLHIPNCDK.H	3.9	3	1
Laminin subunit gamma-1	6902	721.895	61.7245	5.53E-06	P11047|LAMC1_HUMAN	R.LSAEDLVLEGAGLR.V	3.5	2	3
	18059	773.378	35.2602	1.47E-04	P11047|LAMC1_HUMAN	R.NTIEETGNLAEQAR.A	4.2	2	2
Pigment epithelium-derived factor (PEDF)	6082	780.405	55.711	6.31E-05	Q95121|PEDF_BOVIN	K.LAAAVSNFGYDLYR.V	2.6	2	7
	11487	780.904	55.7617	1.65E-04	Q95121|PEDF_BOVIN	K.LAAAVSNFGYDLYR.V	2.7	2	1
	2322	528.325	40.5441	1.44E-04	P36955|PEDF_HUMAN	K.TVQAVLTVPK.L	2.7	2	3
Serpin H	21371	612.83	33.236	9.74E-06	Q2KJH6|SERPH_BOVIN	K.GVVEVTHDLQK.H	2.9	2	1
	9482	837.411	61.7245	5.90E-04	Q2KJH6|SERPH_BOVIN	R.LYGPSSVSFAEDFVR.S	3.5	2	2
Protein S100-A4 (Metastasin)	2042	544.819	40.4056	1.14E-03	P35466|S10A4_BOVIN	K.SELKELLTR.E	2.5	2	13
	4318	624.325	44.9428	1.84E-03	P35466|S10A4_BOVIN	K.ALDVMVSTFHK.Y	2.6	2	18
SPARC (Secreted protein acidicand rich in cysteine)	5938	713.35	36.9009	1.83E-02	P09486|SPRC_HUMAN	R.APLIPMEHCTTR.F	2.6	2	5
	3767	553.813	48.244	2.07E-04	P13213|SPRC_BOVIN	K.NVLVTLYER.D	2.7	2	7
	1846	975.988	68.3591	7.99E-12	P13213|SPRC_BOVIN	K.YIPPCLDSELTEFPLR.M	2.7	2	14
	2049	975.487	68.4148	2.42E-12	P13213|SPRC_BOVIN	K.YIPPCLDSELTEFPLR.M	2.5	2	4
	944	608.312	40.5039	1.35E-05	P13213|SPRC_BOVIN	K.LHLDYIGPCK.Y	2.8	2	5
Vimentin	5	1254.57	39.5819	8.63E-03	P08670|VIME_HUMAN	R.LGDLYEEEMR.E	2.0	1	3
	7860	748.396	38.8667	2.21E-02	P08670|VIME_HUMAN	R.TYSLGSALRPSTSR.S	2.5	2	6
	599	585.36	61.5533	1.79E-07	P08670|VIME_HUMAN	K.ILLAELEQLK.G	3.3	2	22
	248	627.786	39.5819	1.92E-06	P08670|VIME_HUMAN	R.LGDLYEEEMR.E	3.3	2	21
	398	628.287	39.5656	1.83E-06	P08670|VIME_HUMAN	R.LGDLYEEEMR.E	3.3	2	1
	1114	547.266	32.7365	2.45E-05	P08670|VIME_HUMAN	K.FADLSEAANR.N	3.4	2	14
	858	767.93	58.1997	1.33E-05	P08670|VIME_HUMAN	R.KVESLQEEIAFLK.K	4.8	2	5
	726	767.429	58.1997	8.72E-06	P08670|VIME_HUMAN	R.KVESLQEEIAFLK.K	4.7	2	16
	1081	538.754	47.0218	1.03E-04	P08670|VIME_HUMAN	R.DNLAEDIMR.L	2.8	2	9
	1266	512.288	58.258	4.11E-05	P08670|VIME_HUMAN	R.KVESLQEEIAFLK.K	4.5	3	1
	1044	511.954	58.258	7.65E-05	P08670|VIME_HUMAN	R.KVESLQEEIAFLK.K	5.0	3	6
	712	770.457	54.4972	1.97E-06	P08670|VIME_HUMAN	K.ILLAELEQLKGQGK.S	4.0	2	12
	5487	745.879	47.8547	7.04E-06	P08670|VIME_HUMAN	R.QVQSLTCEVDALK.G	3.4	2	6
	1538	786.452	74.3836	1.92E-06	P08670|VIME_HUMAN	R.ISLPLPNFSSLNLR.E	2.8	2	9
	1398	785.951	74.3836	3.62E-06	P08670|VIME_HUMAN	R.ISLPLPNFSSLNLR.E	3.2	2	15
	1270	845.417	47.7067	8.99E-04	P08670|VIME_HUMAN	R.VEVERDNLAEDIMR.L	3.4	2	4
	1324	793.393	52.0724	8.38E-06	P08670|VIME_HUMAN	R.QVQSLTCEVDALKGTNESLER.Q	3.8	3	16
	9473	563.317	36.0881	7.35E-05	P08670|VIME_HUMAN	R.FANYIDKVR.F	2.9	2	9
	7773	1076.5	46.9283	2.02E-03	P08670|VIME_HUMAN	R.DNLAEDIMR.L	2.2	1	5
	383	563.305	36.2417	3.08E-04	P08670|VIME_HUMAN	R.FANYIDKVR.F	2.9	2	13
	1104	844.916	47.7592	1.12E-03	P08670|VIME_HUMAN	R.VEVERDNLAEDIMR.L	3.3	2	12
	458	563.947	47.6104	1.04E-03	P08670|VIME_HUMAN	R.VEVERDNLAEDIMR.L	3.9	3	5
	409	563.613	47.8083	1.74E-03	P08670|VIME_HUMAN	R.VEVERDNLAEDIMR.L	4.3	3	20
	3961	868.411	42.5848	5.33E-03	P08670|VIME_HUMAN	R.LQDEIQNMKEEMAR.H	4.5	2	1
	4214	867.909	42.5848	5.14E-03	P08670|VIME_HUMAN	R.LQDEIQNMKEEMAR.H	4.3	2	5
	5985	889.436	38.3837	1.11E-02	P08670|VIME_HUMAN	K.FADLSEAANRNNDALR.Q	2.6	2	3
	9685	826.901	51.1484	9.18E-03	P08670|VIME_HUMAN	R.LGDLYEEEMRELR.R	2.8	2	2
	2142	1093.99	53.4831	3.83E-02	P08670|VIME_HUMAN	R.EMEENFAVEAANYQDTIGR.L	4.6	2	2

TABLE III: PROTEINS PRESENT IN BOTH SMCs and SPCs

Database Set: 1 Database
Database Name: uniprot_sprot.fasta.hdr database
Taxonomy: Human, Bovine
Number of Proteins: 58868

Search Engine Set: 1 Search Engine
Search Engine: Sequest
Version: 27, rev. 12
Samples: All Samples
Fragment Tolerance: 1.00 Da (Monoisotopic)
Parent Tolerance: 0.0033 Da (Monoisotopic) (SPC_02), 0.0034 Da (Monoisotopic) (SPC_01), 0.0035 Da (Monoisotopic) (SPC_04), 0.0039 Da (Monoisotopic) (SMC_01), 0.0054 Da (Monoisotopic) (SPC_03), 0.0064 Da (Monoisotopic) (SMC_03), 0.0084 Da (Monoisotopic) (SMC_02)
Fixed Modifications: +57 on C (Carbamidomethyl)
Variable Modifications: +16 on M (Oxidation)
Database: the uniprot_sprot_humancow.fasta.hdr database (58868 entries)
Digestion Enzyme: Trypsin
Max Missed Cleavages: 2

Scaffold Version: Scaffold-01_06_19
Peptide Thresholds: 95.0% minimum
Protein Thresholds: 99.9% minimum and 2 peptides minimum

Displaying: Percentage of Total Spectra

No	Protein name	Molecular weight (AMU)	SMC SMC_01	SMC SMC_02	SMC SMC_03	SPC SPC_01	SPC SPC_02	SPC SPC_03	SPC SPC_04	SMC MEAN	SPC MEAN	T-test P-value	Fold Change	Accession numbers	Number of similar matches
1	Serum albumin(Allergen Bos d 6) (BSA) - Bos taurus (Bovine)	69276.2	5.70%	4.90%	4.60%	5.90%	5.30%	5.80%	3.90%	5.07%	5.23%	0.791	1.0	ALBU_BOVIN	1
2	Serotransferrin (Transferrin) (Siderophilin) (Beta-1-metal-binding globulin) - Bos taurus (Bovine)	77735.8	0.64%	0.53%	0.90%	1.10%	1.20%	1.40%	0.59%	0.69%	1.07%	0.123	1.6	TRFE_BOVIN	1
3	Vimentin - Homo sapiens (Human)	53634.7	0.99%	1.10%	0.88%	0.72%	0.76%	0.88%	1.70%	0.99%	1.02%	0.923	1.0	VIME_HUMAN	1
4	Collagen alpha-1(I) chain (Alpha-1 type I collagen) - Homo sapiens (Human)	138893.4	0.34%	0.43%	0.62%	1.50%	1.50%	1.60%	1.10%	0.46%	1.43%	0.001	3.1	CO1A1_HUMAN	1
5	Collagen alpha-2(I) chain (Alpha-2 type I collagen) - Homo sapiens (Human)	129270.6	0.73%	0.59%	1.30%	0.87%	0.75%	0.92%	0.89%	0.87%	0.86%	0.949	1.0	CO1A2_HUMAN	1
6	Fibronectin (FN) (Cold-insoluble globulin) (CIG) - Homo sapiens (Human)	262581	0.30%	0.33%	0.55%	0.70%	0.77%	0.81%	1.20%	0.39%	0.87%	0.018	2.2	FINC_HUMAN	1
7	Interstitial collagenase (EC 3.4.24.7) (Matrix metalloproteinase-1) (MMP-1) (Fibroblast collagenase) [Contains: 22 kDa interstitial collagenase; 27 kDa interstitial collagenase] - Homo sapiens (Human)	53989.9	2.70%	2.40%	2.00%	0.28%	0	0	0.47%	2.37%	0.19%	0.002	-12.6	MMP1_HUMAN	1
8	Basement membrane-specific heparan sulfate proteoglycan core protein (HSPG) (Perlecan) (PLC) - Homo sapiens (Human)	468787.5	1.10%	1.00%	1.30%	0.16%	0.18%	0.22%	0.28%	1.13%	0.21%	0.005	-5.4	PGBM_HUMAN	1
9	Alpha-2-HS-glycoprotein (Fetuin-A) (Asialofetuin) - Bos taurus (Bovine)	38399.4	0.99%	0.81%	0.88%	0.90%	0.74%	1.20%	0.65%	0.89%	0.87%	0.882	1.0	FETUA_BOVIN	1
10	Alpha-1-antiproteinase (Alpha-1-antitrypsin) (Alpha-1-proteinase inhibitor) - Bos taurus (Bovine)	46087.4	0.23%	0.29%	0.45%	0.44%	0.42%	0.58%	0.28%	0.32%	0.43%	0.292	1.3	A1AT_BOVIN	1
11	Actin, cytoplasmic 1 (Beta-actin) - Bos taurus (Bovine)	41719.8	0.41%	0.50%	0.47%	0.31%	0.30%	0.34%	0.44%	0.46%	0.35%	0.042	-1.3	ACTB_BOVIN,ACTB_HUMAN,A	4
12	Collagen alpha-1(VI) chain - Homo sapiens (Human)	108513	0.39%	0.29%	0.37%	0.21%	0.21%	0.18%	0.15%	0.35%	0.19%	0.019	-1.9	CO6A1_HUMAN	1
13	Fibronectin (FN) - Bos taurus (Bovine)	249532	0.05%	0.03%	0.09%	0.44%	0.36%	0.45%	0.72%	0.06%	0.49%	0.010	9.0	FINC_BOVIN	1
14	Collagen alpha-1(III) chain - Homo sapiens (Human)	138547	0.23%	0.21%	0.44%	0.25%	0.18%	0.22%	0.18%	0.29%	0.21%	0.364	-1.4	CO3A1_HUMAN	1
15	Laminin subunit gamma-1 (Laminin B2 chain) - Homo sapiens (Human)	177587.1	0.30%	0.18%	0.54%	0.08%	0.06%	0.09%	0.19%	0.34%	0.10%	0.148	-3.3	LAMC1_HUMAN	1
16	Biglycan (Bone/cartilage proteoglycan I) (PG-S1) (Leucine-rich PG I) - Bos taurus (Bovine)	41574.2	0.09%	0	0	0.34%	0.31%	0.34%	0.36%	0.03%	0.34%	0.005	11.0	PGS1_BOVIN	1
17	Fibrillin-1 - Homo sapiens (Human)	312283	0.21%	0.29%	0.48%	0	0	0	0.41%	0.33%	0.10%	0.146	-3.2	FBN1_HUMAN	1
18	Alpha-fetoprotein (Alpha-fetoglobulin) (Alpha-1-fetoprotein) - Bos taurus (Bovine)	68570.1	0.05%	0.07%	0.11%	0.21%	0.27%	0.28%	0.04%	0.07%	0.20%	0.099	2.7	FETA_BOVIN	1
19	Follistatin-related protein 1 (Follistatin-like 1) - Homo sapiens (Human)	34967.3	0.14%	0.15%	0.31%	0.07%	0.09%	0.06%	0.18%	0.20%	0.10%	0.197	-2.0	FSTL1_HUMAN	1
20	SPARC (Secreted protein acidic and rich in cysteine) (Osteonectin) (ON) (Basement-membrane protein 40) (BM-40) - Homo sapiens (Human)	34613.9	0.16%	0.20%	0.25%	0.16%	0.14%	0.12%	0.13%	0.20%	0.14%	0.116	-1.5	SPRC_HUMAN	1
21	Laminin subunit beta-1 (Laminin B1 chain) - Homo sapiens (Human)	198045.3	0.21%	0.18%	0.38%	0.05%	0.02%	0.03%	0.06%	0.26%	0.04%	0.072	-6.3	LAMB1_HUMAN	1
22	Filamin-A (Alpha-filamin) (Filamin-1) (Endothelial actin-binding protein) (Actin-binding protein 280) (ABP-280) (Nonmuscle filamin) - Homo sapiens (Human)	280711.4	0	0.07%	0.09%	0.08%	0.14%	0.09%	0.33%	0.05%	0.16%	0.158	3.2	FLNA_HUMAN	1
23	Fetuin-B - Bos taurus (Bovine)	42645.5	0.02%	0.05%	0.14%	0.26%	0.12%	0.21%	0.06%	0.07%	0.16%	0.167	2.3	FETUB_BOVIN	1
24	Tubulin beta chain (Tubulin beta-5 chain) - Homo sapiens (Human)	49652.6	0.25%	0.13%	0.20%	0.03%	0.07%	0.10%	0.18%	0.19%	0.10%	0.098	-2.0	TBB5_HUMAN	1
25	Growth-regulated protein alpha (CXCL1) (Melanoma growth stimulatory activity) (MGSA) (Neutrophil-activating protein 3) (NAP-3) (GRO-alpha(1-73)) [Contains: GRO-alpha(4-73); GRO-alpha(5-73); GRO-alpha(6-73)] - Homo sapiens (Human)	11283.7	0.67%	0.58%	0.40%	0.07%	0	0	0.18%	0.55%	0.06%	0.011	-9.0	GROA_HUMAN	1
26	Heat shock cognate 71 kDa protein (Heat shock 70 kDa protein 8) - Homo sapiens (Human)	70881.8	0.14%	0.12%	0.23%	0	0.07%	0.05%	0.24%	0.16%	0.09%	0.291	-1.8	HSP7C_HUMAN	1
27	72 kDa type IV collagenase (EC 3.4.24.24) (72 kDa gelatinase) (Matrix metalloproteinase-2) (MMP-2) (Gelatinase A) (TBE-1) - Homo sapiens (Human)	73867.1	0.16%	0.09%	0.20%	0.08%	0.11%	0.10%	0.09%	0.15%	0.10%	0.228	-1.6	MMP2_HUMAN	1
28	Pyruvate kinase isozymes M1/M2 (EC 2.7.1.40) (Pyruvate kinase muscle isozyme) (Pyruvate kinase 2/3) (Cytosolic thyroid hormone-binding protein) (CTHBP) (THBP1) - Homo sapiens (Human)	57919.5	0.12%	0.19%	0.11%	0.03%	0.05%	0.05%	0.25%	0.14%	0.09%	0.469	-1.5	KPYM_HUMAN	1
29	Collagen alpha-2(V) chain - Homo sapiens (Human)	144891.6	0.07%	0.10%	0.10%	0.11%	0.18%	0.18%	0.13%	0.09%	0.15%	0.035	1.7	CO5A2_HUMAN	1
30	Alpha-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hydro-lyase) (Non-neural enolase) (NNE) (Enolase 1) (Phosphopyruvate hydratase) (C-myc promoter-binding protein) (MBP-1) (MPB-1) (Plasminogen-binding protein) - Homo sapiens (Human)	47152.2	0.09%	0.11%	0.13%	0.05%	0.07%	0.06%	0.19%	0.11%	0.09%	0.634	-1.2	ENOA_HUMAN	1
31	Alpha-1-acid glycoprotein (Orosomucoid) (OMD) - Bos taurus (Bovine)	23165.2	0.05%	0.06%	0.09%	0.21%	0.18%	0.21%	0.06%	0.06%	0.16%	0.060	2.6	A1AG_BOVIN	1
32	Annexin A2 (Annexin II) (Lipocortin II) (Calpactin I heavy chain) (Chromobindin-8) (p36) (Protein I) (Placental anticoagulant protein IV) (PAP-IV) - Homo sapiens (Human)	38588.1	0.14%	0.16%	0.27%	0.08%	0.11%	0	0.07%	0.19%	0.07%	0.070	-2.9	ANXA2_HUMAN	1
33	Insulin-like growth factor-binding protein 7 (IGFBP-7) (IBP-7) (IGF-binding protein 7) (MAC25 protein) (Prostacyclin-stimulating factor) (PGI2-stimulating factor) (IGFBP-rP1) - Homo sapiens (Human)	29111.8	0.32%	0.22%	0.24%	0.03%	0.03%	0.05%	0.07%	0.26%	0.05%	0.013	-5.7	IBP7_HUMAN	1
34	Collagen alpha-2(VI) chain - Homo sapiens (Human)	108562.8	0.07%	0.08%	0.13%	0.11%	0.08%	0.16%	0.06%	0.09%	0.10%	0.746	1.1	CO6A2_HUMAN	1
35	Metalloproteinase inhibitor 1 (TIMP-1) (Erythroid-potentiating activity) (EPA) (Tissue inhibitor of metalloproteinases) (Fibroblast collagenase inhibitor) (Collagenase inhibitor) - Homo sapiens (Human)	23153.1	0.41%	0.26%	0.35%	0.02%	0	0	0.06%	0.34%	0.02%	0.012	-18.1	TIMP1_HUMAN	1
36	Fructose-bisphosphate aldolase A (EC 4.1.2.13) (Muscle-type aldolase) (Lung cancer antigen NY-LU-1) - Homo sapiens (Human)	39402.6	0.16%	0.11%	0.11%	0.03%	0.03%	0.05%	0.18%	0.13%	0.07%	0.241	-1.7	ALDOA_HUMAN	1
37	78 kDa glucose-regulated protein (GRP 78) (Heat shock 70 kDa protein 5) (Immunoglobulin heavy chain-binding protein) (BiP) (Endoplasmic reticulum lumenal Ca(2+)-binding protein grp78) - Homo sapiens (Human)	72316.7	0.12%	0.09%	0.10%	0.07%	0.09%	0.05%	0.12%	0.10%	0.08%	0.264	-1.3	GRP78_HUMAN	1
38	Collagen alpha-1(V) chain - Homo sapiens (Human)	183544.7	0.05%	0.01%	0.03%	0.18%	0.14%	0.15%	0.09%	0.03%	0.14%	0.005	4.9	CO5A1_HUMAN	1
39	Tropomyosin alpha-4 chain (Tropomyosin-4) (TM30p1) - Homo sapiens (Human)	28504.4	0.02%	0.08%	0.10%	0.03%	0.02%	0.06%	0.13%	0.07%	0.06%	0.888	-1.1	TPM4_HUMAN	1
40	Myosin light polypeptide 6 (Myosin light chain alkali 3) (Myosin light chain 3) (MLC-3) (LC17) - Bos taurus (Bovine)	16911.8	0.12%	0.10%	0.09%	0.10%	0.06%	0.09%	0.16%	0.10%	0.10%	0.964	1.0	MYL6_BOVIN,MYL6_HUMAN	2
41	Vitamin D-binding protein (DBP) (Group-specific component) (Gc-globulin) (VDB) - Bos taurus (Bovine)	53325.1	0.02%	0.02%	0.04%	0.11%	0.14%	0.09%	0.04%	0.03%	0.10%	0.040	3.3	VTDB_BOVIN	1
42	Moesin (Membrane-organizing extension spike protein) - Homo sapiens (Human)	67803.8	0.09%	0.09%	0.09%	0.02%	0.04%	0.02%	0.10%	0.09%	0.04%	0.102	-2.1	MOES_HUMAN	1
43	Protein disulfide-isomerase A3 (EC 5.3.4.1) (Disulfide isomerase ER-60) (ERp60) (58 kDa microsomal protein) (p58) (ERp57) (58 kDa glucose-regulated protein) - Homo sapiens (Human)	56766.6	0.12%	0.10%	0.07%	0.05%	0.05%	0.02%	0.09%	0.10%	0.05%	0.075	-1.9	PDIA3_HUMAN	1
44	Collagen alpha-2(I) chain (Alpha-2 type I collagen) - Bos taurus (Bovine)	129046.7	0	0	0.03%	0.20%	0.16%	0.18%	0.13%	0.01%	0.17%	0.000	17.9	CO1A2_BOVIN	1
45	Galectin-1 (Lectin galactoside-binding soluble 1) (Beta-galactoside-binding lectin L-14-I) (Lactose-binding lectin 1) (S-Lac lectin 1) (Galaptin) (14 kDa lectin) (HPL) (HBL) (Putative MAPK-activating protein MP12) - Homo sapiens (Human)	14697.8	0.07%	0.11%	0.13%	0.02%	0.05%	0.03%	0.07%	0.10%	0.04%	0.052	-2.5	LEG1_HUMAN	1
46	Extracellular matrix protein 1 (Secretory component p85) - Homo sapiens (Human)	60655.4	0.09%	0.03%	0.07%	0.05%	0.06%	0.08%	0.07%	0.07%	0.06%	0.914	1.0	ECM1_HUMAN	1
47	Myosin-9 (Myosin heavy chain 9) (Myosin heavy chain, nonmuscle IIa) (Nonmuscle myosin heavy chain IIa) (NMMHC II-a) (NMMHC-IIA) (Cellular myosin heavy chain, type A) (Nonmuscle myosin heavy chain-A) (NMMHC-A) - Homo sapiens (Human)	226519.5	0.02%	0.03%	0.06%	0.02%	0.05%	0.03%	0.13%	0.04%	0.06%	0.540	1.5	MYH9_HUMAN	1
48	Tubulin alpha-ubiquitous chain (Alpha-tubulin ubiquitous) (Tubulin K-alpha-1) - Homo sapiens (Human)	50133.7	0.05%	0.02%	0.09%	0.05%	0.10%	0.02%	0.09%	0.05%	0.06%	0.667	1.2	TBAK_HUMAN	1
49	Decorin (Bone proteoglycan II) (PG-S2) (PG40) - Homo sapiens (Human)	39730.2	0.09%	0.13%	0.14%	0.02%	0.02%	0.03%	0.02%	0.12%	0.02%	0.016	-6.3	PGS2_HUMAN	1
50	Metalloproteinase inhibitor 2 (TIMP-2) (Tissue inhibitor of metalloproteinases 2) (CSC-21K) - Homo sapiens (Human)	24381.9	0.09%	0.08%	0.07%	0.07%	0.06%	0.08%	0.07%	0.08%	0.07%	0.214	-1.2	TIMP2_HUMAN	1
51	Procollagen C-endopeptidase enhancer 1 (Procollagen COOH-terminal proteinase enhancer 1) (Procollagen C-proteinase enhancer 1) (PCPE-1) (Type I procollagen COOH-terminal proteinase enhancer) (Type 1 procollagen C-proteinase enhancer protein) - H	47954.5	0.07%	0.06%	0.18%	0.03%	0.02%	0.05%	0.06%	0.10%	0.04%	0.245	-2.7	PCOC1_HUMAN	1
52	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor 1 A-1) (eEF1A-1) (Elongation factor Tu) (EF-Tu) - Bos taurus (Bovine)	50123.2	0.07%	0.08%	0.06%	0.07%	0.04%	0.06%	0.09%	0.07%	0.06%	0.742	-1.1	EF1A1_BOVIN,EF1A1_HUMAN	2
53	Histone H4 (H4.1) - Bos taurus (Bovine)	11349.7	0.02%	0.01%	0.03%	0.02%	0.03%	0.03%	0.22%	0.02%	0.07%	0.350	3.6	H4_BOVIN,H4_HUMAN	2
54	Transgelin-2 (SM22-alpha homolog) - Homo sapiens (Human)	22373.9	0.02%	0.05%	0.07%	0.02%	0.05%	0.06%	0.10%	0.05%	0.06%	0.682	1.2	TAGL2_HUMAN	1
55	Complement C3 [Contains: Complement C3 beta chain; Complement C3 alpha chain; C3a anaphylatoxin; Complement C3b alpha' chain; Complement C3c alpha' chain fragment 1; Complement C3dg fragment; Complement C3g fragment; Complement C3d fra	187237.1	0	0.01%	0.01%	0.05%	0.08%	0.10%	0.02%	0.01%	0.06%	0.063	7.3	CO3_BOVIN	1
56	Elongation factor 2 (EF-2) - Bos taurus (Bovine)	95352.2	0.02%	0.05%	0.09%	0.03%	0.02%	0.02%	0.09%	0.05%	0.04%	0.635	-1.3	EF2_BOVIN,EF2_HUMAN	2
57	Interleukin-8 (IL-8) (CXCL8) (Monocyte-derived neutrophil chemotactic factor) (MDNCF) (T-cell chemotactic factor) (Neutrophil-activating protein 1) (NAP-1) (Protein 3-10C) (Granulocyte chemotactic protein 1) (GCP-1) (Monocyte-derived neutrophil-activating p	11080.4	0.21%	0.13%	0.11%	0.02%	0	0	0.03%	0.15%	0.01%	0.039	-13.0	IL8_HUMAN	1
58	Protein disulfide-isomerase (EC 5.3.4.1) (PDI) (Prolyl 4-hydroxylase subunit beta) (Cellular thyroid hormone-binding protein) (p55) - Homo sapiens (Human)	57100.1	0.02%	0.06%	0.07%	0.02%	0	0.02%	0.13%	0.05%	0.04%	0.784	-1.2	PDIA1_HUMAN	1
59	Calumenin (Crocalbin) (IEF SSP 9302) - Homo sapiens (Human)	37089.6	0.02%	0.01%	0.04%	0.03%	0.06%	0.03%	0.03%	0.03%	0.04%	0.311	1.5	CALU_HUMAN	1
60	EMILIN-1 (Elastin microfibril interface-located protein 1) (Elastin microfibril interfacer 1) - Homo sapiens (Human)	106676.7	0.05%	0.03%	0.14%	0	0.01%	0.02%	0.02%	0.07%	0.01%	0.196	-7.7	EMIL1_HUMAN	1
61	Latent-transforming growth factor beta-binding protein, isoform 1S (LTBP-1) (Transforming growth factor beta-1-binding protein 1) (TGF-beta1-BP-1) - Homo sapiens (Human)	152767.2	0	0%	0.23%	0	0	0	0.04%	0.08%	0.01%	0.483	-7.0	LTB1S_HUMAN	1
62	Histone H2B type 1-C/E/F/G/I (H2B.a/g/h/k/l) (H2B.1 A) (H2B/a) (H2B/g) (H2B/h) (H2B/k) (H2B/l) - Homo sapiens (Human)	13801.5	0%	0.02%	0.04%	0.02%	0.03%	0.05%	0.12%	0.02%	0.05%	0.282	2.5	H2B1C_HUMAN,H2B1D_HUMA	7
63	Serpin H1 (Collagen-binding protein) (Colligin) (47 kDa heat shock protein) (Rheumatoid arthritis-related antigen RA-A47) (Arsenic-transactivated protein 3) (AsTP3) (Proliferation-inducing gene 14 protein) - Homo sapiens (Human)	46424	0.02%	0.03%	0.03%	0	0.05%	0	0.10%	0.03%	0.04%	0.742	1.3	SERPH_HUMAN	1
64	Lysyl oxidase homolog 2 (EC 1.4.3.-) (Lysyl oxidase-like protein 2) (Lysyl oxidase-related protein 2) (Lysyl oxidase-related protein WS9-14) - Homo sapiens (Human)	86705.1	0.02%	0.05%	0.03%	0.05%	0.05%	0.05%	0.03%	0.03%	0.04%	0.247	1.3	LOXL2_HUMAN	1
65	14-3-3 protein zeta/delta (Protein kinase C inhibitor protein 1) (KCIP-1) (Factor activating exoenzyme S) (FAS) - Bos taurus (Bovine)	27727.9	0.09%	0.05%	0.06%	0.02%	0.02%	0.02%	0.04%	0.06%	0.02%	0.079	-2.8	1433Z_BOVIN	1
66	Histone H2A type 1-D (H2A.3) - Homo sapiens (Human)	14090	0.05%	0.02%	0.01%	0.07%	0.06%	0.06%	0.12%	0.03%	0.08%	0.046	2.8	H2A1D_HUMAN,H2A1H_HUMA	6
67	Cofilin-1 (Cofilin, non-muscle isoform) (18 kDa phosphoprotein) (p18) - Homo sapiens (Human)	18485.2	0.05%	0.03%	0.07%	0.03%	0.02%	0	0.07%	0.05%	0.03%	0.395	-1.5	COF1_HUMAN	1
68	Alpha-actinin-1 (Alpha-actinin cytoskeletal isoform) (Non-muscle alpha-actinin-1) (F-actin cross-linking protein) - Bos taurus (Bovine)	102965.9	0.02%	0.03%	0	0.02%	0	0.02%	0.10%	0.02%	0.03%	0.609	1.7	ACTN1_BOVIN	1
69	Triosephosphate isomerase (EC 5.3.1.1) (TIM) (Triose-phosphate isomerase) - Homo sapiens (Human)	26651.1	0.14%	0.09%	0.06%	0	0.04%	0.02%	0	0.10%	0.01%	0.063	-6.9	TPIS_HUMAN	1
70	Profilin-1 (Profilin I) - Homo sapiens (Human)	15036.3	0.09%	0.08%	0.04%	0%	0.02%	0%	0.04%	0.07%	0.02%	0.040	-4.7	PROF1_HUMAN	1
71	Amyloid beta A4 protein (APP) (ABPP) (Alzheimer disease amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-A	86863.1	0.02%	0.05%	0.07%	0.02%	0.04%	0	0.04%	0.05%	0.03%	0.285	-1.9	A4_CAVPO,A4_HUMAN,A4_MA	6
72	Apolipoprotein A-I (Apo-AI) (ApoA-I) - Bos taurus (Bovine)	30258.8	0	0.01%	0.01%	0.05%	0.05%	0.08%	0.03%	0.01%	0.05%	0.014	6.1	APOA1_BOVIN	1
73	Collagen alpha-1(I) chain (Alpha-1 type I collagen) - Bos taurus (Bovine)	138920.7	0	0	0.03%	0.11%	0.10%	0.12%	0.06%	0.01%	0.10%	0.003	10.4	CO1A1_BOVIN	1
74	Laminin subunit alpha-5 - Homo sapiens (Human)	399725.1	0.02%	0.02%	0.01%	0.03%	0.02%	0.05%	0.03%	0.02%	0.03%	0.158	1.6	LAMA5_HUMAN	1
75	Insulin-like growth factor-binding protein 6 (IGFBP-6) (IBP-6) (IGF-binding protein 6) - Homo sapiens (Human)	25303.8	0.09%	0.02%	0.07%	0%	0.01%	0.03%	0.02%	0.06%	0.01%	0.135	-4.7	IBP6_HUMAN	1
76	Phosphoglycerate mutase 1 (EC 5.4.2.1) (EC 5.4.2.4) (EC 3.1.3.13) (Phosphoglycerate mutase isozyme B) (PGAM-B) (BPG-dependent PGAM 1) - Homo sapiens (Human)	28786.8	0	0.02%	0.04%	0.03%	0.02%	0.02%	0.06%	0.02%	0.03%	0.583	1.4	PGAM1_HUMAN	1
77	Nucleoside diphosphate kinase B (EC 2.7.4.6) (NDK B) (NDP kinase B) (nm23-H2) (C-myc purine-binding transcription factor PUF) - Homo sapiens (Human)	17280.3	0.05%	0.09%	0.04%	0	0.02%	0	0.03%	0.06%	0.01%	0.070	-5.2	NDKB_HUMAN	1
78	Kininogen-1 (Kininogen I) (Thiol proteinase inhibitor) [Contains: Kininogen-1 heavy chain; Bradykinin (Kallidin I); Lysyl-bradykinin (Kallidin II); Kininogen-1 light chain] - Bos taurus (Bovine)	68871.6	0	0	0.01%	0.05%	0.08%	0.05%	0.02%	0.00%	0.05%	0.043	10.1	KNG1_BOVIN	1
79	Alpha-S1-casein - Bos taurus (Bovine)	24511.4	0.02%	0.03%	0.04%	0.03%	0.02%	0.03%	0.03%	0.03%	0.03%	0.574	-1.1	CASA1_BOVIN	1
80	Phosphoglycerate kinase 1 (EC 2.7.2.3) (Primer recognition protein 2) (PRP 2) (Cell migration-inducing gene 10 protein) - Homo sapiens (Human)	44597.3	0.05%	0.06%	0.07%	0	0	0	0.06%	0.06%	0.01%	0.056	-3.9	PGK1_HUMAN	1
81	Beta-2-microglobulin [Contains: Beta-2-microglobulin variant pI 5.3] - Homo sapiens (Human)	13696.9	0.14%	0.10%	0.10%	0	0	0	0.03%	0.11%	0.01%	0.005	-15.1	B2MG_HUMAN	1
82	Pigment epithelium-derived factor (PEDF) (Serpin-F1) (EPC-1) - Homo sapiens (Human)	46326.4	0	0	0.03%	0.03%	0.05%	0.03%	0.03%	0.01%	0.04%	0.090	3.8	PEDF_HUMAN	1
83	Plasminogen activator inhibitor 1 (PAI-1) (Endothelial plasminogen activator inhibitor) (PAI) - Homo sapiens (Human)	45042.3	0.09%	0.02%	0.06%	0.02%	0	0.02%	0	0.06%	0.01%	0.131	-7.3	PAI1_HUMAN	1
84	Inter-alpha-trypsin inhibitor heavy chain H4 (ITI heavy chain H4) (Inter-alpha-inhibitor heavy chain 4) - Bos taurus (Bovine)	101496.8	0	0	0.01%	0.03%	0.05%	0.05%	0	0.00%	0.03%	0.088	6.8	ITIH4_BOVIN	1
85	Plasminogen activator inhibitor 1 (PAI-1) (Endothelial plasminogen activator inhibitor) (PAI) - Bos taurus (Bovine)	45354	0.09%	0.02%	0	0.02%	0.02%	0.02%	0	0.04%	0.01%	0.475	-2.8	PAI1_BOVIN	1
86	Thioredoxin (Trx) - Bos taurus (Bovine)	11794.4	0	0	0.01%	0.02%	0.04%	0.03%	0.03%	0.00%	0.03%	0.016	6.2	THIO_BOVIN	1
87	60 kDa heat shock protein, mitochondrial (Hsp60) (60 kDa chaperonin) (CPN60) (Heat shock protein 60) (HSP-60) (Mitochondrial matrix protein P1) (P60 lymphocyte protein) (HuCHA60) - Homo sapiens (Human)	61037.7	0.07%	0.02%	0.01%	0.02%	0.03%	0.02%	0.02%	0.04%	0.02%	0.464	-1.8	CH60_HUMAN	1
88	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 (EC 1.14.11.4) (Lysyl hydroxylase 1) (LH1) - Bos taurus (Bovine)	83471.6	0	0.02%	0.03%	0%	0.06%	0.02%	0.02%	0.02%	0.02%	0.756	1.3	PLOD1_BOVIN	1
89	Coactosin-like protein - Bos taurus (Bovine)	15992.2	0.02%	0.01%	0	0.02%	0.02%	0%	0.06%	0.01%	0.02%	0.466	2.0	COTL1_BOVIN,COTL1_HUMAN	2
90	Inter-alpha-trypsin inhibitor heavy chain H2 (ITI heavy chain H2) (Inter-alpha-inhibitor heavy chain 2) (Inter-alpha-trypsin inhibitor complex component II) (Serum-derived hyaluronan-associated protein) (SHAP) - Homo sapiens (Human)	106420.5	0	0	0.01%	0.03%	0.03%	0.03%	0.04%	0.00%	0.03%	0.007	7.4	ITIH2_HUMAN	1
91	Nucleobindin-1 - Bos taurus (Bovine)	54964.9	0.02%	0	0	0.02%	0.04%	0.03%	0.03%	0.01%	0.03%	0.087	3.8	NUCB1_BOVIN	1
92	Nidogen-2 (NID-2) (Osteonidogen) - Homo sapiens (Human)	151376.5	0	0.01%	0.01%	0%	0.02%	0.03%	0	0.01%	0.01%	0.592	1.6	NID2_HUMAN	1
93	Thrombospondin-1 - Homo sapiens (Human)	129628.7	0	0.01%	0.04%	0	0	0.03%	0.04%	0.02%	0.02%	0.962	1.0	TSP1_HUMAN	1
94	Heat shock protein HSP 90-beta (HSP 84) (HSP 90) - Homo sapiens (Human)	83249.3	0%	0.02%	0.03%	0	0.03%	0	0.02%	0.02%	0.01%	0.687	-1.4	HS90B_HUMAN	1
95	Alpha-actinin-4 (Non-muscle alpha-actinin 4) (F-actin cross-linking protein) - Homo sapiens (Human)	104839.2	0.02%	0.02%	0.04%	0	0.08%	0	0	0.03%	0.02%	0.693	-1.5	ACTN4_HUMAN	1
96	14-3-3 protein beta/alpha (Protein kinase C inhibitor protein 1) (KCIP-1) - Bos taurus (Bovine)	28064.1	0	0.02%	0	0.02%	0	0	0.10%	0.01%	0.03%	0.442	4.0	1433B_BOVIN,1433B_HUMAN	2
97	Collagen alpha-2(IV) chain [Contains: Canstatin] - Homo sapiens (Human)	167539.6	0.07%	0.01%	0.04%	0	0.01%	0.02%	0.02%	0.04%	0.01%	0.200	-4.3	CO4A2_HUMAN	1
98	Nidogen-1 (Entactin) - Homo sapiens (Human)	136433.8	0.02%	0.01%	0.04%	0.02%	0.01%	0.02%	0	0.03%	0.01%	0.219	-2.6	NID1_HUMAN	1
99	AMBP protein [Contains: Alpha-1-microglobulin; Inter-alpha-trypsin inhibitor light chain (ITI-LC) (Bikunin) (HI-30) (BI-14) (Cumulus extracellular matrix-stabilizing factor) (ESF)] - Bos taurus (Bovine)	39217.2	0	0	0.01%	0	0.04%	0.05%	0.02%	0.00%	0.03%	0.153	5.4	AMBP_BOVIN	1
100	Tropomyosin beta chain (Tropomyosin 2) (Beta-tropomyosin) - Homo sapiens (Human)	32833.7	0	0	0.01%	0.03%	0	0	0	0.00%	0.01%	0.722	1.8	TPM2_HUMAN	1

TABLE IV: PROTEINS PREDOMINANTLY IN SMCs

Displaying:Percentage of Total Spectra Protein name	Molecular weight (AMU)	SMC SMC_01	SMC SMC_02	SMC SMC_03	SPC SPC_01	SPC SPC_02	SPC SPC_03	SPC SPC_04	SMC MEAN	SPC MEAN	T-test P-value	Fold Change	Accession numbers	Number of similar matches
Laminin subunit alpha-4 - Homo sapiens (Human)	202512.4	0.32%	0.25%	0.35%	0	0	0	0.02%	0.31%	0.00%	0.009	SMC	LAMA4_HUMAN	1
Thrombospondin-2 - Homo sapiens (Human)	129934.9	0.12%	0.12%	0.47%	0.02%	0	0	0	0.24%	0.00%	0.184	SMC	TSP2_HUMAN	1
Versican core protein (Large fibroblast proteoglycan) (Chondroitin sulfate proteoglycan core protein 2) (PG-M) (Glial hyaluronate-binding protein) (GHAP) -	372794.6	0.32%	0.29%	0.27%	0.02%	0	0	0	0.29%	0.00%	0.001	SMC	CSPG2_HUMAN	1
Transforming growth factor-beta-induced protein ig-h3 (Beta ig-h3) (Kerato-epithelin) (RGD-containing collagen-associated protein) (RGD-CAP) - Homo sa	74664.9	0.07%	0.17%	0.24%	0	0	0	0.02%	0.16%	0.00%	0.087	SMC	BGH3_HUMAN	1
Collagen alpha-3(VI) chain - Homo sapiens (Human)	343532.2	0.18%	0.21%	0.17%	0	0	0	0	0.19%	0.00%	0.004	SMC	CO6A3_HUMAN	1
Tissue factor pathway inhibitor 2 (TFPI-2) (Placental protein 5) (PP5) - Homo sapiens (Human)	26916.9	0.16%	0.16%	0.28%	0	0	0	0.02%	0.20%	0.00%	0.038	SMC	TFPI2_HUMAN	1
Complement C3 [Contains: Complement C3 beta chain; Complement C3 alpha chain; C3a anaphylatoxin; Complement C3b alpha' chain; Complement C3	187131.1	0.02%	0.06%	0.37%	0	0	0	0	0.15%	0.00%	0.309	SMC	CO3_HUMAN	1
Sushi repeat-containing protein SRPX - Homo sapiens (Human)	51554.9	0.14%	0.17%	0.16%	0	0	0	0	0.16%	0.00%	0.003	SMC	SRPX_HUMAN	1
Peptidyl-prolyl cis-trans isomerase A (EC 5.2.1.8) (PPIase A) (Rotamase A) (Cyclophilin A) (Cyclosporin A-binding protein) - Homo sapiens (Human)	17994.9	0.12%	0.13%	0.13%	0	0	0	0	0.13%	0.00%	0.001	SMC	PPIA_HUMAN	1
Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12) (GAPDH) - Homo sapiens (Human)	36035.3	0.12%	0.15%	0.10%	0	0	0	0	0.12%	0.00%	0.014	SMC	G3P_HUMAN	1
C-type lectin domain family 11 member A (Stem cell growth factor) (Lymphocyte secreted C-type lectin) (p47) (C-type lectin superfamily member 3) - Homo	35676.4	0.14%	0.09%	0.10%	0	0	0.02%	0	0.11%	0.00%	0.016	SMC	CLC11_HUMAN	1
Nucleobindin-1 (CALNUC) - Homo sapiens (Human)	53861.6	0.02%	0.05%	0.11%	0.02%	0	0	0	0.06%	0.00%	0.166	SMC	NUCB1_HUMAN	1
Biglycan (Bone/cartilage proteoglycan I) (PG-S1) - Homo sapiens (Human)	41637.9	0.09%	0.08%	0.11%	0	0	0	0	0.09%	0.00%	0.010	SMC	PGS1_HUMAN	1
Pentraxin-related protein PTX3 (Pentaxin-related protein PTX3) (Tumor necrosis factor-inducible protein TSG-14) - Homo sapiens (Human)	42001.9	0.02%	0.05%	0.10%	0	0	0	0	0.06%	0.00%	0.133	SMC	PTX3_HUMAN	1
Macrophage inflammatory protein 2-beta (MIP2-beta) (CXCL3) (Growth-regulated protein gamma) (GRO-gamma) (GRO-gamma(1-73)) [Contains: GRO-g	11324.6	0.07%	0.07%	0.09%	0	0	0	0	0.07%	0.00%	0.006	SMC	MIP2B_HUMAN	1
Small inducible cytokine B5 (CXCL5) (Epithelial-derived neutrophil-activating protein 78) (Neutrophil-activating peptide ENA-78) (ENA-78(1-78)) [Contains:	11954.5	0.12%	0.10%	0.07%	0	0	0	0	0.10%	0.00%	0.021	SMC	SCYB5_HUMAN	1
Cadherin-2 (Neural-cadherin) (N-cadherin) (CD325 antigen) (CDw325) - Homo sapiens (Human)	99793.8	0.07%	0.05%	0.09%	0	0	0	0	0.07%	0.00%	0.029	SMC	CADH2_HUMAN	1
Latent-transforming growth factor beta-binding protein 2 (LTBP-2) - Homo sapiens (Human)	195038.5	0.05%	0.03%	0.06%	0	0.01%	0	0	0.05%	0.00%	0.014	SMC	LTBP2_HUMAN	1
Small inducible cytokine B6 (CXCL6) (Granulocyte chemotactic protein 2) (GCP-2) (Chemokine alpha 3) (CKA-3) [Contains: Small inducible cytokine B6, N	11879.5	0.02%	0.03%	0.10%	0	0	0	0.02%	0.05%	0.00%	0.176	SMC	SCYB6_HUMAN	1
Stanniocalcin-1 (STC-1) - Homo sapiens (Human)	27603.3	0.07%	0.05%	0.10%	0	0	0	0.02%	0.07%	0.00%	0.043	SMC	STC1_HUMAN	1
Insulin-like growth factor-binding protein 4 (IGFBP-4) (IBP-4) (IGF-binding protein 4) - Homo sapiens (Human)	27915.7	0.05%	0.06%	0.07%	0	0	0	0	0.06%	0.00%	0.016	SMC	IBP4_HUMAN	1
Small inducible cytokine A2 (CCL2) (Monocyte chemotactic protein 1) (MCP-1) (Monocyte chemoattractant protein 1) (Monocyte chemotactic and activating	11007.3	0.07%	0.02%	0.03%	0	0	0	0	0.04%	0.00%	0.115	SMC	CCL2_HUMAN	1
Sulfhydryl oxidase 1 (EC 1.8.3.2) (Quiescin Q6) (hQSOX) - Homo sapiens (Human)	82560.7	0%	0.05%	0.11%	0	0	0	0	0.05%	0.00%	0.247	SMC	QSCN6_HUMAN	1
Peroxiredoxin-1 (EC 1.11.1.15) (Thioredoxin peroxidase 2) (Thioredoxin-dependent peroxide reductase 2) (Proliferation-associated gene protein) (PAG) (Na	22092.9	0.02%	0.06%	0.03%	0	0.02%	0	0	0.04%	0.00%	0.075	SMC	PRDX1_HUMAN	1
Endoplasmin (Heat shock protein 90 kDa beta member 1) (94 kDa glucose-regulated protein) (GRP94) - Bos taurus (Bovine)	92411.4	0.02%	0.06%	0.06%	0	0	0	0.02%	0.05%	0.00%	0.052	SMC	ENPL_BOVIN,ENPL_HUMAN,ENF	3
CD59 glycoprotein (Membrane attack complex inhibition factor) (MACIF) (MAC-inhibitory protein) (MAC-IP) (Protectin) (MEM43 antigen) (Membrane inhibit	14159.2	0.02%	0.01%	0.07%	0	0	0	0.02%	0.04%	0.00%	0.227	SMC	CD59_HUMAN	1
L-lactate dehydrogenase A chain (EC 1.1.1.27) (LDH-A) (LDH muscle subunit) (LDH-M) (Proliferation-inducing gene 19 protein) (Renal carcinoma antigen N	36671.2	0.07%	0.05%	0.06%	0	0	0	0	0.06%	0.00%	0.015	SMC	LDHA_HUMAN	1
Lumican (Keratan sulfate proteoglycan lumican) (KSPG lumican) - Homo sapiens (Human)	38413.5	0.02%	0.07%	0.03%	0	0	0	0	0.04%	0.00%	0.106	SMC	LUM_HUMAN	1
EGF-containing fibulin-like extracellular matrix protein 1 (Fibulin-3) (FIBL-3) (Fibrillin-like protein) (Extracellular protein S1-5) - Homo sapiens (Human)	54621.1	0.02%	0.03%	0.09%	0	0	0	0	0.05%	0.00%	0.131	SMC	FBLN3_HUMAN	1
Peptidyl-prolyl cis-trans isomerase B (EC 5.2.1.8) (PPIase) (Rotamase) (Cyclophilin B) (S-cyclophilin) (SCYLP) (CYP-S1) - Homo sapiens (Human)	22724.9	0.02%	0.01%	0.09%	0	0.02%	0	0	0.04%	0.00%	0.258	SMC	PPIB_HUMAN	1
Complement C1r subcomponent (EC 3.4.21.41) (Complement component 1, r subcomponent) [Contains: Complement C1r subcomponent heavy chain; Cc	80156.7	0.07%	0.03%	0.06%	0	0	0	0	0.05%	0.00%	0.035	SMC	C1R_HUMAN	1
Endosialin (Tumor endothelial marker 1) (CD248 antigen) - Homo sapiens (Human)	80839.7	0.02%	0.01%	0.06%	0	0	0	0	0.03%	0.00%	0.156	SMC	CD248_HUMAN	1
Integrin beta-1 (Fibronectin receptor subunit beta) (Integrin VLA-4 subunit beta) (CD29 antigen) - Homo sapiens (Human)	88447.1	0.02%	0.03%	0.04%	0	0	0	0	0.03%	0.00%	0.027	SMC	ITB1_HUMAN	1
Ribonuclease 4 (EC 3.1.27.-) (RNase 4) (Ribonuclease BL4) - Bos taurus (Bovine)	13722.9	0	0.02%	0.04%	0	0	0	0.02%	0.02%	0.00%	0.281	SMC	RNAS4_BOVIN,RNAS4_HUMAN	2
Testican-1 (Protein SPOCK) - Homo sapiens (Human)	49106.7	0	0.03%	0.06%	0	0.01%	0	0	0.03%	0.00%	0.226	SMC	TICN1_HUMAN	1
Complement factor H (H factor 1) - Homo sapiens (Human)	139052.1	0	0.01%	0.04%	0	0	0	0	0.02%	0.00%	0.295	SMC	CFAH_HUMAN	1
Annexin A1 (Annexin I) (Lipocortin I) (Calpactin II) (Chromobindin-9) (p35) (Phospholipase A2 inhibitory protein) - Homo sapiens (Human)	38697.9	0	0.01%	0.06%	0	0	0	0	0.02%	0.00%	0.322	SMC	ANXA1_HUMAN	1
Pappalysin-1 (EC 3.4.24.79) (Pregnancy-associated plasma protein-A) (PAPP-A) (Insulin-like growth factor-dependent IGF-binding protein 4 protease) (IGF	181119.7	0	0.02%	0.04%	0	0	0	0	0.02%	0.00%	0.221	SMC	PAPP1_HUMAN	1

TABLE V: PROTEINS PREDOMINANTLY IN SPCs

Displaying:Percentage of Total Spectra Protein name	Molecular weight (AMU)	SMC SMC_01	SMC SMC_02	SMC SMC_03	SPC SPC_01	SPC SPC_02	SPC SPC_03	SPC SPC_04	SMC MEAN	SPC MEAN	T-test P-value	Fold Change	Accession numbers	Number of similar matches
Fibrillin-1 (MP340) - Bos taurus (Bovine)	312221.1	0	0	0	0.16%	0.18%	0.19%	0.04%	0.00%	0.14%	0.024	SPC	FBN1_BOVIN	1
Decorin (Bone proteoglycan II) (PG-S2) - Bos taurus (Bovine)	39862.5	0	0	0	0.16%	0.16%	0.15%	0.21%	0.00%	0.17%	0.001	SPC	PGS2_BOVIN	1
Lamin-A/C (70 kDa lamin) (Renal carcinoma antigen NY-REN-32) - Homo sapiens (Human)	74122.7	0	0	0	0.07%	0.09%	0.10%	0.30%	0.00%	0.14%	0.085	SPC	LMNA_HUMAN	1
Latent-transforming growth factor beta-binding protein 2 (LTBP-2) - Bos taurus (Bovine)	198383.4	0	0	0	0.13%	0.10%	0.15%	0.13%	0.00%	0.13%	0.001	SPC	LTBP2_BOVIN	1
Peptidyl-prolyl cis-trans isomerase A (EC 5.2.1.8) (PPIase A) (Rotamase A) (Cyclophilin A) (Cyclosporin A-binding protein) - Bos taurus (Bovine)	17851.8	0	0	0	0.11%	0.09%	0.06%	0.22%	0.00%	0.12%	0.042	SPC	PPIA_BOVIN	1
Periostin (PN) (Osteoblast-specific factor 2) (OSF-2) - Homo sapiens (Human)	93300	0	0	0	0.02%	0.08%	0.02%	0.27%	0.00%	0.10%	0.212	SPC	POSTN_HUMAN	1
Insulin-like growth factor-binding protein 2 (IGFBP-2) (IBP-2) (IGF-binding protein 2) - Bos taurus (Bovine)	33996.5	0	0	0	0.08%	0.13%	0.10%	0.13%	0.00%	0.11%	0.003	SPC	IBP2_BOVIN	1
Plectin-1 (PLTN) (PCN) (Hemidesmosomal protein 1) (HD1) (Plectin-11) - Homo sapiens (Human)	531707.9	0	0	0	0.03%	0.04%	0.03%	0.19%	0.00%	0.07%	0.157	SPC	PLEC1_HUMAN	1
Collagen alpha-1(XIV) chain (Undulin) - Homo sapiens (Human)	193498.1	0	0	0	0.02%	0.03%	0.05%	0.09%	0.00%	0.05%	0.062	SPC	COEA1_HUMAN	1
Metalloproteinase inhibitor 1 (TIMP-1) (Embryogenin-1) (EG-1) - Bos taurus (Bovine)	23013.7	0	0	0	0.10%	0.04%	0.06%	0.03%	0.00%	0.06%	0.032	SPC	TIMP1_BOVIN	1
Protein disulfide-isomerase (EC 5.3.4.1) (PDI) (Prolyl 4-hydroxylase subunit beta) (Cellular thyroid hormone-binding protein) (p55) - Bos taurus (Bovine)	57249.7	0	0	0	0.02%	0.05%	0.02%	0.13%	0.00%	0.05%	0.149	SPC	PDIA1_BOVIN	1
Triosephosphate isomerase (EC 5.3.1.1) (TIM) (Triose-phosphate isomerase) - Bos taurus (Bovine)	26671.2	0	0	0	0	0.04%	0.02%	0.15%	0.00%	0.05%	0.228	SPC	TPIS_BOVIN	1
FK506-binding protein 10 (EC 5.2.1.8) (Peptidyl-prolyl cis-trans isomerase) (PPIase) (Rotamase) (65 kDa FK506-binding protein) (FKBP65) (Immunophilin FKBP65) - Ho	64227.9	0	0	0	0.08%	0.01%	0.05%	0.03%	0.00%	0.04%	0.077	SPC	FKB10_HUMAN	1
Alpha-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hydro-lyase) (Non-neural enolase) (NNE) (Enolase 1) (Phosphopyruvate hydratase) (HAP47) - Bos taurus (Bovine)	47309.1	0	0	0	0	0.04%	0.02%	0.12%	0.00%	0.04%	0.200	SPC	ENOA_BOVIN	1
Lumican (Keratan sulfate proteoglycan) (KSPG) (Corneal keratan sulfate proteoglycan 37B core protein) - Bos taurus (Bovine)	38740.8	0	0	0	0.03%	0.04%	0.03%	0.02%	0.00%	0.03%	0.011	SPC	LUM_BOVIN	1
Collagen alpha-1(III) chain - Bos taurus (Bovine)	93633.1	0	0	0	0.08%	0.09%	0.08%	0.06%	0.00%	0.08%	0.001	SPC	CO3A1_BOVIN	1
EGF-like repeat and discoidin I-like domain-containing protein 3 (EGF-like repeats and discoidin I-like domains protein 3) (Developmentally-regulated endothelial cell locu	53747	0	0	0	0.03%	0.03%	0.03%	0.03%	0.00%	0.03%	0.000	SPC	EDIL3_HUMAN	1
Serpin H1 (Collagen-binding protein) (Colligin) - Bos taurus (Bovine)	46490	0	0	0	0.03%	0.01%	0.06%	0.02%	0.00%	0.03%	0.088	SPC	SERPH_BOVIN	1
Pigment epithelium-derived factor (PEDF) (Serpin-F1) - Bos taurus (Bovine)	46213	0	0	0	0.07%	0	0.06%	0.06%	0.00%	0.05%	0.058	SPC	PEDF_BOVIN	1
Pregnancy zone protein - Homo sapiens (Human)	163816.9	0	0	0	0.08%	0.07%	0.08%	0	0.00%	0.06%	0.058	SPC	PZP_HUMAN	1
Rho GDP-dissociation inhibitor 1 (Rho GDI 1) (Rho-GDI alpha) - Bos taurus (Bovine)	23403.8	0	0	0	0	0%	0.02%	0.07%	0.00%	0.02%	0.296	SPC	GDIR_BOVIN	1
Histone H1.2 (Histone H1d) - Homo sapiens (Human)	21347.8	0	0	0	0	0.02%	0	0.07%	0.00%	0.02%	0.255	SPC	H12_HUMAN,H13_HUMAN,	3
Transgelin (Smooth muscle protein 22-alpha) (SM22-alpha) (25 kDa F-actin-binding protein) - Bos taurus (Bovine)	22580.8	0	0	0	0	0.03%	0	0.07%	0.00%	0.03%	0.228	SPC	TAGL_BOVIN	1
Peroxiredoxin-1 (EC 1.11.1.15) - Bos taurus (Bovine)	22192.4	0	0	0	0.02%	0.02%	0.02%	0.06%	0.00%	0.03%	0.092	SPC	PRDX1_BOVIN	1
Macrophage-capping protein (Actin-regulatory protein CAP-G) - Homo sapiens (Human)	38499.9	0	0	0	0.02%	0.02%	0.02%	0.04%	0.00%	0.02%	0.049	SPC	CAPG_HUMAN	1
Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12) (GAPDH) - Bos taurus (Bovine)	35850	0	0	0	0.02%	0.03%	0	0.07%	0.00%	0.03%	0.151	SPC	G3P_BOVIN	1
L-lactate dehydrogenase A chain (EC 1.1.1.27) (LDH-A) - Bos mutus grunniens (Wild yak) (Bos grunniens)	36668	0	0	0	0	0.02%	0.03%	0.04%	0.00%	0.02%	0.076	SPC	LDHA_BOSMU,LDHA_BOVI	2
Annexin A2 (Annexin II) (Lipocortin II) (Calpactin I heavy chain) (Chromobindin-8) (p36) (Protein I) (Placental anticoagulant protein IV) (PAP-IV) - Bos taurus (Bovine)	38596	0	0	0	0.02%	0	0.08%	0.02%	0.00%	0.03%	0.208	SPC	ANXA2_BOVIN	1
Plasminogen (EC 3.4.21.7) [Contains: Plasmin heavy chain A; Activation peptide; Plasmin heavy chain A, short form; Plasmin light chain B] - Bos taurus (Bovine)	91197.2	0	0	0	0	0.03%	0.05%	0	0.00%	0.02%	0.191	SPC	PLMN_BOVIN	1
Tropomyosin-1 alpha chain (Alpha-tropomyosin) - Bos taurus (Bovine)	32678	0	0	0	0.03%	0.01%	0	0	0.00%	0.01%	0.281	SPC	TPM1_BOVIN	1
Epididymal secretory protein E1 (Niemann Pick type C2 protein homolog) (16 kDa secretory protein) - Sus scrofa (Pig)	16269.5	0	0	0	0	0.04%	0.02%	0	0.00%	0.01%	0.241	SPC	NPC2_PIG	1
Complement factor B (EC 3.4.21.47) (C3/C5 convertase) (EC-VMFB) [Contains: Complement factor B Ba fragment; Complement factor B Bb fragment] - Bos taurus (Bov	85349.6	0	0	0	0	0.02%	0.02%	0	0.00%	0.01%	0.198	SPC	CFAB_BOVIN	1

TABLE VI: PIVOTAL TABLES HIGHLIGHTING HUMAN AND BOVINE-SPECIFIC PEPTIDES

Protein accession numbers	MS/MS sample name	FNALQYLR	ISNIPDEYFK	LKEDAVSAAFK	NNQIDHTDDK	NNQIDHTDEK	RFNALQYLR	SLVDLQLTNNK	SLVDLQLTNNKISK	SVPMVPPGIK	VANEVTLN
LUM_BOVIN	SPC_01		95%					95%			
	SPC_02		95%		95%			95%			
	SPC_03		95%					95%			
	SPC_04								95%	50%	
LUM_HUMAN	SMC_01					95%					81%
	SMC_02	95%		95%			95%				63%
	SMC_03	95%				95%					
	SPC_04									50%	

Protein accession numbers	MS/MS sample name	AVPKEISPDTTLLDLQNNDISELR	AVPKEISPDTTLLDLQNNDISELRK	AYYNGISLFNNPVPYYWEVQPATFR	DDFKGLQHLYALVLVNNK	DDFKGLQHLYALVLVNNKISK	DLPETLNELHLDHNK	EISPDTTLLDLQNNDISELR	EISPDTTLLDLQNNDISELRK	ELHLDNNKLSR	GLQHLYALVLVNNK	GLQHLYALVLVNNKISK	IQAIELEDLLR	LAIQPGNYK	LAIQPGNYKK	LGLGHNQIR	LTGIPK	MIENGSLSFLPTLR	NHLVEIPPNLPSSLVELR	NMNCIEMGGNPLENSGFEPPGAFDGLK	NMNCIEMGGNPLENSGFEPPGAFDGLKLNYL	RAYYNGISLFNNPVPYYWEVQPATFR	VGVNDFCPMGFGVKR	VGVNDFCPVGFGVK	VGVNDFCPVGFGVKR	VPAGLPDLK	VVQCSDLGLK
PGS1_BOVIN	SMC_01													95%		95%											95%
	SMC_02													95%		95%											95%
	SMC_03			95%	95%	95%								95%		95%											95%
	SPC_01			95%	95%		95%		95%		95%			95%	95%	95%						95%		95%		95%	95%	95%
	SPC_02	95%	95%	95%	95%		95%	95%	95%	95%	95%			95%	95%	95%						95%	95%	95%		95%	95%	95%
	SPC_03	95%		95%	95%	95%			95%		95%	95%		95%		95%		95%	63%				95%	95%		95%	95%	95%
	SPC_04			95%	95%	95%			95%		56%	95%	95%	95%	77%	95%		95%	63%			95%	95%	95%		95%	95%	95%
PGS1_HUMAN	SMC_01													95%		95%											95%
	SMC_02													95%		95%								88%			95%
	SMC_03			95%	95%	95%								95%		95%				95%				95%			95%
	SPC_01			95%	95%									95%		95%											95%
	SPC_02			95%	95%									95%		95%											95%
	SPC_03			95%	95%	95%								95%		95%			63%								95%
	SPC_04			95%	95%	95%								95%		95%											95%

Protein accession numbers	MS/MS sample name	ASYSGVSLFSNPVQYWEIQPSTFR	DLPPDTALLDLQNNK	DLPPDTALLDLQNNKITEIKDGDFK	ELPEKMPK	ISPGAFAPLVK	ITEIKDGDFK	KASYSGVSLFSNPVQYWEIQPSTFR	LYLSKNQLK	NLHALILVNNK	NLHTLILINNK	NLHTLILINNKISK	NQLKELPEK	NQLKELPEKMPK	SAIQLGNYK	SSGIENGAFQGMK	SSGIENGAFQGMKK	TLQELRAHENEITK	TLQELRVHENEITK	VDAASLKGLNNLAK	VHENEITKVR	VSPGAFTPLVK	VVQCSDLGLDKVPK
PGS2_BOVIN	SMC_01							95%	95%					74%						95%			
	SMC_02							95%	48%					90%		95%				95%			
	SMC_03	95%						95%						95%						95%			
	SPC_01	95%				95%	95%	95%			95%		94%	95%		95%							
	SPC_02		95%	95%		95%	95%	95%			95%		95%	95%		95%							
	SPC_03	95%				95%	85%	95%	50%		95%		95%	95%		95%	95%						
	SPC_04	95%			23%	95%		95%			95%	95%		95%			95%		95%	95%	95%		
PGS2_HUMAN	SMC_01							95%	95%					74%	95%					95%		89%	
	SMC_02							95%	48%					90%	95%	95%				95%		95%	
	SMC_03	95%						95%		95%				95%	95%			95%		95%		95%	95%
	SPC_01	95%					95%	95%					94%	95%	95%	95%							
	SPC_02						95%	95%					95%	95%	95%	95%							
	SPC_03	95%					85%	95%	50%				95%	95%	95%	95%	95%						95%
	SPC_04	95%			23%			95%						95%	95%		95%			95%			

Table VII. Cytokines profiles from SMCs, SPCs and EACs

Cytokines	SMCs (n=3)	SPCs (n=3)	EACs (n=4)
IL-1beta	58.2 ± 7.0	0.0 ± 0.0	0.0 ± 0.0
IL-2Ra	11.6 ± 0.9	0.0 ± 0.0	12.2 ± 6.6
IL-2	2.2 ± 0.1	0.0 ± 0.0	0.0 ± 0.0
IL-4	24.8 ± 1.5	0.1 ± 0.1	1.5 ± 0.0
IL-5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
IL-6	46,111.0 ± 2,445.9	0.0 ± 0.0	18.6 ± 13.6
IL-7	7.8 ± 0.3	0.0 ± 0.0	0.1 ± 0.0
IL-8	299,085.5 ± 29,618.2	0.2 ± 0.0	3,336.0 ± 1,048.9
IL-9	24.0 ± 2.2	0.0 ± 0.0	63.3 ± 20.7
IL-10	18.7 ± 1.9	0.2 ± 0.0	2.6 ± 0.2
IL-12	2.3 ± 0.4	0.0 ± 0.0	0.0 ± 0.0
IL-13	0.1 ± 0.0	0.0 ± 0.0	0.4 ± 0.2
IL-15	0.5 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
IL-17	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Eotaxin	882.4 ± 263.5	0.0 ± 0.0	1.8 ± 0.4
FGF basic	10.1 ± 0.6	3.8 ± 1.3	1.2 ± 0.2
GCSF	311,987.3 ± 52,348.2	0.0 ± 0.0	0.9 ± 0.5
GMCSF	9.4 ± 0.7	0.0 ± 0.0	0.0 ± 0.0
INFgamma	313.0 ± 15.8	0.2 ± 0.1	7.1 ± 1.4
IP-10	48.3 ± 19.8	0.0 ± 0.0	1,096.5 ± 289.5
MCP-1	17,703.9 ± 3,412.4	15.0 ± 1.6	19,589.2 ± 9,949.0
MIP-1alpha	2.4 ± 0.0	0.1 ± 0.0	0.0 ± 0.0
MIP-1beta	0.0 ± 0.0	0.0 ± 0.0	4.1 ± 0.8
PDGF-BB	116.2 ± 3.3	99.6 ± 25.8	3,173.0 ± 228.6
RANTES	2.4 ± 0.7	3.2 ± 1.7	88.2 ± 40.2
TNFalpha	14.9 ± 1.8	0.4 ± 0.2	1.0 ± 0.7
VEGF	7,658.9 ± 521.5	90.2 ± 6.6	381.0 ± 19.9

SMCs denotes human aortic smooth muscle cells; SPCs, late-outgrowth smooth muscle progenitors; EAC, peripheral-blood derived early angiogenic cells. Cytokine concentrations (pg/ml) are given as mean ± S.E.