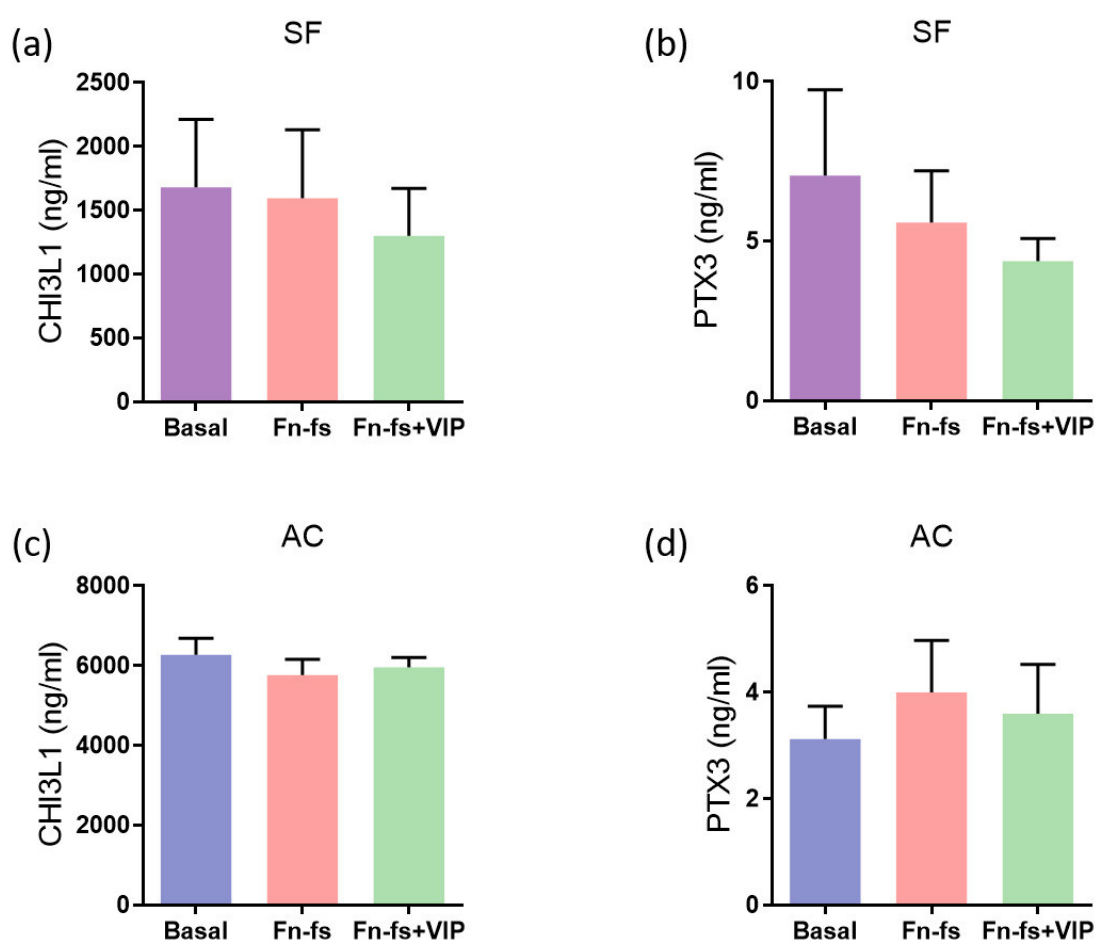
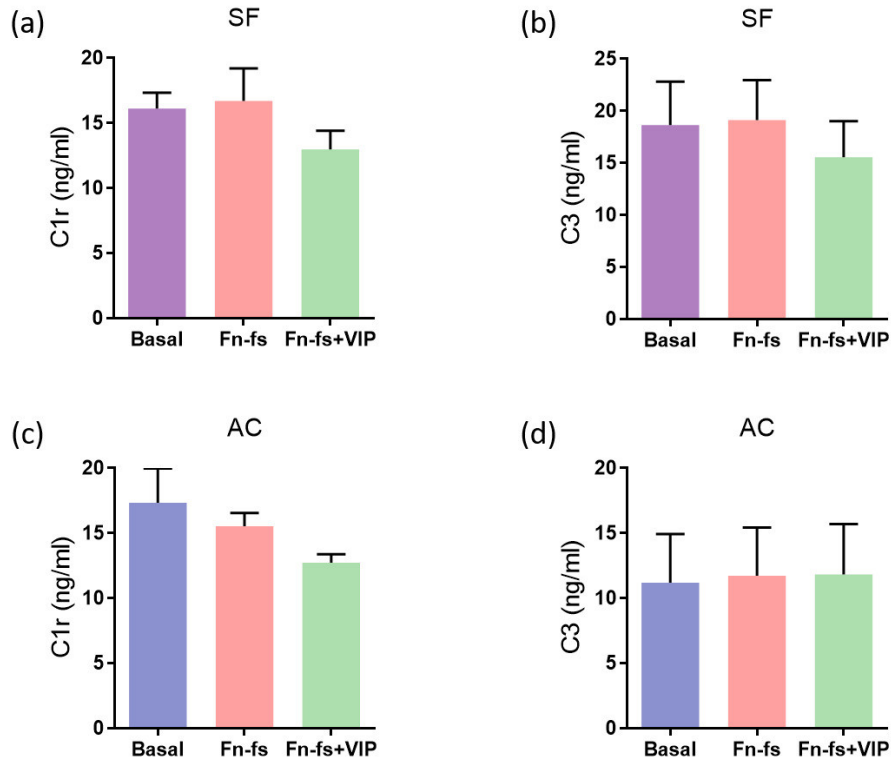


# Proteomic Analysis of Synovial Fibroblasts and Articular Chondrocytes Co-Cultures Reveals Valuable VIP-Modulated Inflammatory and Degradative Proteins in Osteoarthritis

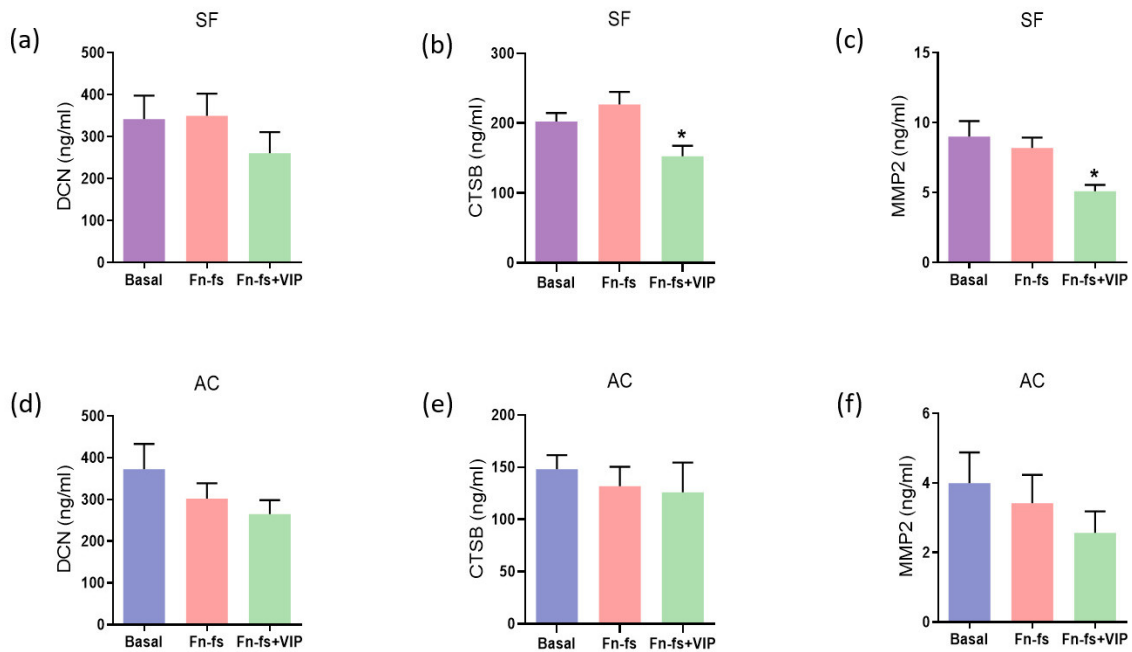
Selene Pérez-García <sup>1</sup>, Valentina Calamia <sup>2</sup>, Tamara Hermida-Gómez <sup>2</sup>, Irene Gutiérrez-Cañas <sup>1</sup>, Mar Carrión <sup>1</sup>, Raúl Villanueva-Romero <sup>1</sup>, David Castro <sup>1</sup>, Carmen Martínez <sup>1</sup>, Yasmina Juarranz <sup>1</sup>, Francisco J. Blanco <sup>2</sup> and Rosa P. Gomariz <sup>1,\*</sup>



**Figure S1.** VIP-modulated inflammatory proteins. Protein secretion of (a),(c) CHI3L1 and (b),(d) PTX3 were determined by ELISA and Multiplex, respectively, in (a),(b) SF and (c),(d) AC cultures secretomes at 48 hours of treatment with and without 10 nM 45 kDa Fn-fs in the presence and absence of 10 nM VIP (n = 5). Data are presented as mean  $\pm$  SEM of duplicate determinations.



**Figure S2.** VIP-modulated complement pathway proteins. Protein secretion of (a),(c) C1R and (b),(d) C3 were determined by ELISA and Multiplex, respectively, in (a),(b) SF and (c),(d) AC cultures secretomes at 48 hours of treatment with and without 10 nM 45 kDa Fn-fs in the presence and absence of 10 nM VIP (n = 5). Data are presented as mean  $\pm$  SEM of duplicate determinations.



**Figure S3.** VIP-modulated ECM degradation proteins. Protein secretion of (a),(d) DCN, (b),(e) CTSSB, and (c),(f) MMP2 were determined by ELISA and Multiplex, respectively, in (a),(b),(c) SF and (d),(e),(f) AC cultures secretomes at 48 hours of treatment with and without 10 nM 45 kDa Fn-fs in the presence and absence of 10 nM VIP (n = 5). Data are presented as mean  $\pm$  SEM of duplicate determinations. \* $p < 0.05$  Fn-fs+VIP vs Fn-fs.

**Table S1.** Proteins identified by SILAC analysis in the Fn-fs-stimulated secretome of OA SF-AC co-cultures with or without VIP treatment.

**Forward**

Acc No <sup>a</sup>	Protein Symbol	Protein Name	Peptides (95%) <sup>b</sup>	Ratio <sup>c</sup>	PVal <sup>d</sup>	EF <sup>e</sup>
P63261	ACTG	Actin, cytoplasmic 2	10	1.217	0.472	1.796 4
P12814	ACTN1	Alpha-actinin-1	3	1.992	0.049	EF > 2
P04075	ALDO A	Fructose-bisphosphate aldolase A	2	1.111	0.850	EF > 2
P15144	AMPN	Aminopeptidase N	1	0.779	0.861	EF > 2
P01008	ANT3	Antithrombin-III	2			
P27695	APEX1	DNA-(apurinic or apyrimidinic site) lyase	1	1.995		
Q15582	BGH3	Transforming growth factor-beta-induced protein ig-h3	5	0.686	0.109	1.645 8
P00736	C1R	Complement C1r subcomponent	7	0.666	0.072	1.574 3
P09871	C1S	Complement C1s subcomponent	5	0.939	0.824	1.886 5
P40121	CAPG	Macrophage-capping protein	3	0.684	0.411	EF > 2
P07858	CATB	Cathepsin B	7	0.660	0.041	1.542 6
P07339	CATD	Cathepsin D	1	0.950	0.990	EF > 2
P07711	CATL1	Cathepsin L1	3	0.698	0.220	EF > 2
P16070	CD44	CD44 antigen	1	1.174		
P00751	CFAB	Complement factor B	7	0.695	0.067	1.486
P08603	CFAH	Complement factor H	1	0.933		
P36222	CH3L1	Chitinase-3-like protein 1	46	0.481	0.000	1.32
P10909	CLUS	Clusterin	3	0.507	0.015	1.528
Q8N137	CNTRB	Centrobin	1			
P08123	CO1A2	Collagen alpha-2(I) chain	10	0.585	0.012	1.487 2
P01024	CO3	Complement C3	1	0.545	0.022	1.477 9
P12109	CO6A1	Collagen alpha-1(VI) chain	4	0.654	0.007	1.298 3
P49747	COMP	Cartilage oligomeric matrix protein	4	0.665	0.041	1.471 7
Q14019	COTL1	Coactin-like protein	2	1.558	0.141	EF > 2
O94985	CSTN1	Calsynenin-1	1	0.709		
P13639	EF2	Elongation factor 2	2	1.745	0.187	EF > 2
P06733	ENOA	Alpha-enolase	7	1.640	0.001	1.242 9
Q12805	FBLN3	EGF-containing fibulin-like extracellular matrix protein 1	1	0.414		
P02751	FINC	Fibronectin	11	0.552	0.552	EF > 2
Q06828	FMOD	Fibromodulin	2	0.595	0.147	EF > 2
P06744	G6PI	Glucose-6-phosphate isomerase	1	1.833		
P07093	GDN	Glia-derived nexin	5	0.804	0.218	1.473 1
P28161	GSTM2	Glutathione S-transferase Mu 2	1			
P09211	GSTP1	Glutathione S-transferase P	3	1.248	0.678	EF > 2
P02042	HBD	Hemoglobin subunit delta	1	0.010		
P11142	HSP7C	Heat shock cognate 71 kDa protein	1	2.408	0.076	EF > 2

P04792	HSPB1	Heat shock protein beta-1	2	1.586	0.505	EF > 2
P17936	IBP3	Insulin-like growth factor-binding protein 3	1	0.489	0.437	EF > 2
P22692	IBP4	Insulin-like growth factor-binding protein 4	2			
P24592	IBP6	Insulin-like growth factor-binding protein 6	1	0.684	0.185	EF > 2
Q16270	IBP7	Insulin-like growth factor-binding protein 7	2	1.291	0.235	EF > 2
P05155	IC1	Plasma protease C1 inhibitor	1	0.710		
P0DOX7	IGK	Immunoglobulin kappa light chain	1			
P05231	IL6	Interleukin-6	3	1.221	0.423	1.987 5
P13645	K1C10	Keratin, type I cytoskeletal 10	3			
P35527	K1C9	Keratin, type I cytoskeletal 9	2			
P04264	K2C1	Keratin, type II cytoskeletal 1	11	76.42 7		
P14618	KPYM	Pyruvate kinase PKM	5	1.389	0.158	1.646 5
P00338	LDHA	L-lactate dehydrogenase A chain	2	2.175	0.351	EF > 2
P17931	LEG3	Galectin-3	1	1.097	0.981	EF > 2
P51884	LUM	Lumican	10	0.536	0.008	1.511 3
P40925	MDHC	Malate dehydrogenase, cytoplasmic	1	3.158		
P03956	MMP1	Interstitial collagenase	17	0.967	0.888	1.671 8
P08253	MMP2	72 kDa type IV collagenase	10	0.672	0.031	1.419
P08254	MMP3	Stromelysin-1	7	1.386	0.725	EF > 2
P26038	MOES	Moesin	5	1.419	0.695	EF > 2
Q96TA1	NIBL1	Niban-like protein 1	1	1.167		
P05121	PAI1	Plasminogen activator inhibitor 1	1	0.620	0.143	EF > 2
Q15113	PCOC1	Procollagen C-endopeptidase enhancer 1	1	0.556		
P30101	PDIA3	Protein disulfide-isomerase A3	2	1.243	0.489	EF > 2
P18669	PGAM1	Phosphoglycerate mutase 1	2	1.324	0.340	EF > 2
P00558	PGK1	Phosphoglycerate kinase 1	1	1.083	0.834	EF > 2
P07585	PGS2	Decorin	14	0.582	0.008	1.454 3
P62937	PPIA	Peptidyl-prolyl cis-trans isomerase A	2	2.017	0.090	EF > 2
P23284	PPIB	Peptidyl-prolyl cis-trans isomerase B	1	1.653	0.377	EF > 2
Q06830	PRDX1	Peroxiredoxin-1	2	1.948	0.020	1.505 8
P30041	PRDX6	Peroxiredoxin-6	1	76.42 7		
P07737	PROF1	Profilin-1	1	1.033	0.969	EF > 2
P49721	PSB2	Proteasome subunit beta type-2	1	2.914		
Q9UL46	PSME2	Proteasome activator complex subunit 2	2	1.799	0.196	EF > 2
P26022	PTX3	Pentraxin-related protein 3	5	0.451	0.021	1.827 5
O00391	QSOX1	Sulfhydryl oxidase 1	6	0.610	0.003	1.302 3
P55017	S12A3	Solute carrier family 12 member 3	1			
P50454	SERPH	Serpin H1	1	1.368	0.379	EF > 2
P04179	SODM	Superoxide dismutase [Mn], mitochondrial	1	2.812		
P09486	SPRC	SPARC	3	0.526	0.031	1.644 1
P42224	STAT1	Signal transducer and activator of transcription 1- alpha/beta	2			
P23381	SYWC	Tryptophan--tRNA ligase, cytoplasmic	1	0.667	0.153	EF > 2

P68363	TBA1B	Tubulin alpha-1B chain	7	1.907	0.005	EF > 2
P07437	TBB5	Tubulin beta chain	5	2.630	0.012	1.909 8
P01033	TIMP1	Metalloproteinase inhibitor 1	1	0.566	0.270	EF > 2
P16035	TIMP2	Metalloproteinase inhibitor 2	1	0.608		
P29401	TKT	Transketolase	4	1.511	0.170	EF > 2
P60174	TPIS	Triphosphate isomerase	2	0.806	0.530	EF > 2
P02788	TRFL	Lactotransferrin	1			
P19971	TYPH	Thymidine phosphorylase	1	0.909		
P22314	UBA1	Ubiquitin-like modifier-activating enzyme 1	1	1.076	0.601	EF > 2
Q6EMK4	VASN	Vasorin	1	0.429	0.077	EF > 2
P08670	VIME	Vimentin	16	1.758	0.402	EF > 2
P02774	VTDB	Vitamin D-binding protein	1			
P04004	VTNC	Vitronectin	1			
Q5GH72	XKR7	XK-related protein 7	1			

## Reverse

Acc No <sup>a</sup>	Protein Symbol	Protein Name	Peptides (95%) <sup>b</sup>	Ratio <sup>c</sup>	PVal <sup>d</sup>	EF <sup>e</sup>
P01023	A2MG	Alpha-2-macroglobulin	2			
P63261	ACTG	Actin, cytoplasmic 2	8	1.022	0.780	1.194
P12814	ACTN1	Alpha-actinin-1	4	1.462	0.143	1.842 4
P02768	ALBU	Serum albumin	25			
P04075	ALDOA	Fructose-bisphosphate aldolase A	1	1.250		
P15144	AMPN	Aminopeptidase N	1	0.589		
P27695	APEX1	DNA-(apurinic or apyrimidinic site) lyase	1	1.084		
Q9PIU1	ARP3B	Actin-related protein 3B	1	1.202		
P61769	B2MG	Beta-2-microglobulin	1	0.823		
Q15582	BGH3	Transforming growth factor-beta-induced protein ig-h3	7	0.410	0.000	1.329 5
P00736	C1R	Complement C1r subcomponent	8	0.649	0.007	1.331 7
P09871	C1S	Complement C1s subcomponent	9	0.531	0.040	1.815 4
P40121	CAPG	Macrophage-capping protein	2	1.816	0.120	EF > 2
P07858	CATB	Cathepsin B	8	0.516	0.000	1.171 2
P07339	CATD	Cathepsin D	1	0.615	0.183	EF > 2
P07711	CATL1	Cathepsin L1	4	0.692	0.079	1.606 7
P16070	CD44	CD44 antigen	1	0.604		
P00751	CFAB	Complement factor B	10	0.591	0.191	EF > 2
P08603	CFAH	Complement factor H	1	1.419		
P36222	CH3L1	Chitinase-3-like protein 1	60	0.559	0.002	1.419 7

P10909	CLUS	Clusterin	5	0.880	0.907	EF > 2
P08123	CO1A2	Collagen alpha-2(I) chain	10	1.000	1.000	1.651 2
P01024	CO3	Complement C3	1	0.346	0.064	EF > 2
P12109	CO6A1	Collagen alpha-1(VI) chain	3	0.886	0.465	1.429 6
P12111	CO6A3	Collagen alpha-3(VI) chain	2	0.593	0.016	1.471
Q99715	COCA 1	Collagen alpha-1(XII) chain	1	0.623		
P49747	COMP	Cartilage oligomeric matrix protein	9	1.222	0.508	1.662 2
Q14019	COTL1	Coactin-like protein	2	1.314	0.253	EF > 2
P02511	CRYA B	Alpha-crystallin B chain	1	3.606		
O94985	CSTN1	Calsyntenin-1	1	0.839		
P13639	EF2	Elongation factor 2	1	1.514	0.181	EF > 2
P06733	ENOA	Alpha-enolase	5	1.133	0.589	1.709 1
Q12805	FBLN3	EGF-containing fibulin-like extracellular matrix protein 1	1	0.373		
P02751	FINC	Fibronectin	12	0.568	0.013	1.513 7
Q06828	FMOD	Fibromodulin	2	0.818	0.631	EF > 2
P04406	G3P	Glyceraldehyde-3-phosphate dehydrogenase	1	1.292	0.235	EF > 2
P06744	G6PI	Glucose-6-phosphate isomerase	1	1.369		
P50395	GDIB	Rab GDP dissociation inhibitor beta	1	1.459	0.829	EF > 2
P07093	GDN	Glia-derived nexin	9	0.431	0.005	1.650 8
P09211	GSTP1	Glutathione S-transferase P	2	1.880	0.099	EF > 2
P57053	H2BFS	Histone H2B type F-S	1	2.068		
P02042	HBD	Hemoglobin subunit delta	1			
P04792	HSPB1	Heat shock protein beta-1	1	1.729	0.221	EF > 2
P17936	IBP3	Insulin-like growth factor-binding protein 3	2	1.003	0.995	EF > 2
P22692	IBP4	Insulin-like growth factor-binding protein 4	2	1.057	0.704	EF > 2
P24592	IBP6	Insulin-like growth factor-binding protein 6	1	0.576		
Q16270	IBP7	Insulin-like growth factor-binding protein 7	2	0.787	0.249	EF > 2
P0DOX 7	IGK	Immunoglobulin kappa light chain	1			
P05231	IL6	Interleukin-6	4	0.424	0.032	EF > 2
P13645	K1C10	Keratin, type I cytoskeletal 10	2			
P35527	K1C9	Keratin, type I cytoskeletal 9	2			
P35908	K22E	Keratin, type II cytoskeletal 2 epidermal	3	0.010		
P04264	K2C1	Keratin, type II cytoskeletal 1	10	0.010		

P14618	KPYM	Pyruvate kinase PKM	4	1.204	0.522	1.996 6
P00338	LDHA	L-lactate dehydrogenase A chain	3	1.515	0.466	EF > 2
P51884	LUM	Lumican	16	0.632	0.253	EF > 2
P33908	MA1A 1	Mannyl-oligaccharide 1,2-alpha-mannidase IA	1	0.589		
P14174	MIF	Macrophage migration inhibitory factor	2	0.775		
P03956	MMP1	Interstitial collagenase	18	0.322	0.014	EF > 2
P08253	MMP2	72 kDa type IV collagenase	10	0.541	0.003	1.400 1
P08254	MMP3	Stromelysin-1	10	0.414	0.082	EF > 2
P26038	MOES	Moesin	5	1.344	0.206	1.686 5
P22392	NDKB	Nucleide diphphate kinase B	2	1.949	0.135	EF > 2
Q96TA1	NIBL1	Niban-like protein 1	1	2.583		
P05121	PAI1	Plasminogen activator inhibitor 1	1	0.542	0.105	EF > 2
Q15113	PCOC1	Procollagen C-endopeptidase enhancer 1	1	0.366		
P30101	PDIA3	Protein disulfide-isomerase A3	4	2.090	0.003	1.352 6
Q15084	PDIA6	Protein disulfide-isomerase A6	1			
P18669	PGAM 1	Phosphoglycerate mutase 1	2	1.994	0.112	EF > 2
P21810	PGS1	Biglycan	1	0.554	0.106	EF > 2
P07585	PGS2	Decorin	13	0.540	0.022	1.665
O60664	PLIN3	Perilipin-3	1	2.891		
P62937	PPIA	Peptidyl-prolyl cis-trans isomerase A	2	1.573	0.145	EF > 2
P23284	PPIB	Peptidyl-prolyl cis-trans isomerase B	1	1.110	0.852	EF > 2
Q06830	PRDX1	Peroxiredoxin-1	1	1.725	0.393	EF > 2
P30041	PRDX6	Peroxiredoxin-6	1	1.014		
Q92954	PRG4	Proteoglycan 4	2	0.831	0.737	EF > 2
P49721	PSB2	Proteasome subunit beta type-2	1	1.289		
Q9UL46	PSME2	Proteasome activator complex subunit 2	2	2.023	0.296	EF > 2
P26022	PTX3	Pentraxin-related protein 3	5	0.628	0.069	1.783 1
O00391	QSOX1	Sulfhydryl oxidase 1	6	0.474	0.001	1.415 6
P50454	SERPH	Serpin H1	2	1.497	0.161	EF > 2
Q9H299	SH3L3	SH3 domain-binding glutamic acid-rich-like protein 3	1	2.518		
P04179	SODM	Superoxide dismutase [Mn], mitochondrial	2	0.853		
P09486	SPRC	SPARC	5	0.551	0.239	EF > 2
P23381	SYWC	Tryptophan--tRNA ligase, cytoplasmic	1	0.914		

P68363	TBA1B	Tubulin alpha-1B chain	8	1.511	0.017	1.379 9
Q13509	TBB3	Tubulin beta-3 chain	4	1.841	0.532	EF > 2
P07437	TBB5	Tubulin beta chain	4	1.598	0.717	EF > 2
P24821	TENA	Tenascin	1	0.635	0.274	EF > 2
P01033	TIMP1	Metalloproteinase inhibitor 1	4	0.654	0.023	1.403
P16035	TIMP2	Metalloproteinase inhibitor 2	1	0.753	0.214	EF > 2
P29401	TKT	Transketolase	3	1.398	0.050	1.553 7
P60174	TPIS	Triphosphate isomerase	3	1.600	0.195	EF > 2
P02787	TRFE	Serotransferrin	2	0.010		
Q8NBS 9	TXND 5	Thioredoxin domain-containing protein 5	2	1.343	0.210	EF > 2
P19971	TYPH	Thymidine phosphorylase	1	1.039		
P22314	UBA1	Ubiquitin-like modifier-activating enzyme 1	1	2.945		
O60701	UGDH	UDP-glucose 6-dehydrogenase	1	5.006	0.145	EF > 2
Q6EMK 4	VASN	Vasorin	1	0.717	0.335	EF > 2
P08670	VIME	Vimentin	11	1.230	0.275	1.48
P18206	VINC	Vinculin	2	1.776		
P04004	VTNC	Vitronectin	1			

<sup>a</sup>Protein accession number according to the SwissProt and TrEMBL databases. <sup>b</sup>Number of unique peptides (Pept) used for protein identification at 95% confidence. <sup>c</sup>SILAC ratios that represent the relative protein abundance in Fn-fs+VIP versus Fn-fs treated SF-AC co-cultures at the same time point (48 h) (n = 4). <sup>d</sup>p-value of the corresponding SILAC ratios. <sup>e</sup>Error factor calculated by Protein Pilot 4.0 software for quantification accuracy. SILAC, stable isotope labelling by amino acids in cell culture; OA SF-AC, osteoarthritic synovial fibroblasts-articular chondrocytes.



**Table S2.** Proteins identified by SILAC analysis in the secretome of OA Fn-fs-stimulated SF-AC co-cultures and normal IL-1 $\beta$ -stimulated AC.

Acc No <sup>a</sup>	Protein Symbol	Protein name	Fn-fs stimulated SF-AC <sup>b</sup>	IL-1 $\beta$ stimulated AC <sup>c</sup>
P01009	A1AT	Alpha-1-antitrypsin		x
P01023	A2MG	Alpha-2-macroglobulin	x	
P63261	ACTG	Actin, cytoplasmic 2	x	
P12814	ACTN1	Alpha-actinin-1	x	
P04075	ALDOA	Fructose-bisphosphate aldolase A	x	
P15144	AMPN	Aminopeptidase N	x	
P01008	ANT3	Antithrombin-III	x	
P07355	ANXA2	Annexin A2		x
P27695	APEX1	DNA-(apurinic or apyrimidinic site) lyase	x	
Q9P1U1	ARP3B	Actin-related protein 3B	x	
P61769	B2MG	Beta-2-microglobulin	x	x
Q15582	BGH3	Transforming growth factor-beta-induced protein ig-h3	x	x
P00736	C1R	Complement C1r subcomponent	x	x
P09871	C1S	Complement C1s subcomponent	x	x
P40121	CAPG	Macrophage-capping protein	x	
P07858	CATB	Cathepsin B	x	x
P07339	CATD	Cathepsin D	x	
P07711	CATL1	Cathepsin L1	x	
Q76M96	CCD80	Coiled-coil domain-containing protein 80		x
P13500	CCL2	C-C motif chemokine 2b		x
P80075	CCL8	C-C motif chemokine 8b		x
P16070	CD44	CD44 antigen	x	
P00751	CFAB	Complement factor B	x	x
P08603	CFAH	Complement factor H	x	
P36222	CH3L1	Chitinase-3-like protein 1	x	x
Q15782	CH3L2	Chitinase-3-like protein 2b		x
P10909	CLUS	Clusterin	x	x
Q8N137	CNTRB	Centrobilin	x	
P08123	CO1A2	Collagen alpha-2(I) chain	x	x
P01024	CO3	Complement C3	x	x
P02461	CO3A1	Collagen alpha-1(III) chain		x
P12109	CO6A1	Collagen alpha-1(VI) chain	x	x
P12111	CO6A3	Collagen alpha-3(VI) chain	x	
Q99715	COCA1	Collagen alpha-1(XII) chain	x	x
P49747	COMP	Cartilage oligomeric matrix protein	x	
Q14019	COTL1	Coactin-like protein	x	
P02511	CRYAB	Alpha-crystallin B chain	x	
P09603	CSF1	Macrophage colony-stimulating factor 1b		x
O94985	CSTN1	Calsynenin-1	x	
P19876	CXCL3	C-X-C motif chemokine 3b		x
P42830	CXCL5	C-X-C motif chemokine 5b		x
P80162	CXCL6	C-X-C motif chemokine 6b		x
P01034	CYTC	Cystatin-C		x

P15924	DESP	Desmoplakinb		x
P13639	EF2	Elongation factor 2	x	
P06733	ENOA	Alpha-enolase	x	
P23142	FBLN1	Fibulin-1		x
Q12805	FBLN3	EGF-containing fibulin-like extracellular matrix protein 1	x	x
P02751	FINC	Fibronectin	x	x
Q06828	FMOD	Fibromodulin	x	
Q12841	FSTL1	Follistatin-related protein 1		x
P04406	G3P	Glyceraldehyde-3-phosphate dehydrogenase	x	
P06744	G6PI	Glucose-6-phosphate isomerase	x	
P50395	GDIB	Rab GDP dissociation inhibitor beta	x	
P07093	GDN	Glia-derived nexin	x	x
P09341	GROA	Growth-regulated alpha protein		x
P28161	GSTM2	Glutathione S-transferase Mu 2	x	
P09211	GSTP1	Glutathione S-transferase P	x	
P57053	H2BFS	Histone H2B type F-S	x	
P02042	HBD	Hemoglobin subunit delta	x	
P11142	HSP7C	Heat shock cognate 71 kDa protein	x	
P04792	HSPB1	Heat shock protein beta-1	x	
P17936	IBP3	Insulin-like growth factor-binding protein 3	x	x
P22692	IBP4	Insulin-like growth factor-binding protein 4	x	x
P24593	IBP5	Insulin-like growth factor-binding protein 5		x
P24592	IBP6	Insulin-like growth factor-binding protein 6	x	x
Q16270	IBP7	Insulin-like growth factor-binding protein 7	x	x
P05155	IC1	Plasma protease C1 inhibitor	x	x
P0DOX7	IGK	Immunoglobulin kappa light chain	x	
P05231	IL6	Interleukin-6	x	x
P10145	IL8	Interleukin-8		x
P13645	K1C10	Keratin, type I cytoskeletal 10	x	x
P02533	K1C14	Keratin, type I cytoskeletal 14b		x
P08779	K1C16	Keratin, type I cytoskeletal 16b		x
P35527	K1C9	Keratin, type I cytoskeletal 9	x	x
P04264	K2C1	Keratin, type II cytoskeletal 1	x	x
P04259	K2C6B	Keratin, type II cytoskeletal 6Bb		x
P14618	KPYM	Pyruvate kinase PKM	x	
P00338	LDHA	L-lactate dehydrogenase A chain	x	
P17931	LEG3	Galectin-3	x	
P51884	LUM	Lumican	x	x
P33908	MA1A1	Mannyl-oligaccharide 1,2-alpha-mannidase IA	x	
P40925	MDHC	Malate dehydrogenase, cytoplasmic	x	
Q08431	MFGM	Lactadherin		x
P14174	MIF	Macrophage migration inhibitory factor	x	
P03956	MMP1	Interstitial collagenase	x	x
P08253	MMP2	72 kDa type IV collagenase	x	x
P08254	MMP3	Stromelysin-1	x	x
P26038	MOES	Moesin	x	

P22392	NDKB	Nucleide diphphate kinase B	x	
Q96TA1	NIBL1	Niban-like protein 1	x	
Q8N130	NPT2C	Sodium-dependent phosphate transport protein 2Cb		x
P05121	PAI1	Plasminogen activator inhibitor 1	x	
Q15113	PCOC1	Procollagen C-endopeptidase enhancer 1	x	x
P30101	PDIA3	Protein disulfide-isomerase A3	x	
Q15084	PDIA6	Protein disulfide-isomerase A6	x	
P18669	PGAM1	Phosphoglycerate mutase 1	x	
P00558	PGK1	Phosphoglycerate kinase 1	x	
P21810	PGS1	Biglycan	x	x
P07585	PGS2	Decorin	x	x
O60664	PLIN3	Perilipin-3	x	
P55058	PLTP	Phospholipid transfer protein		x
A5A3E0	POTEF	POTE ankyrin domain family member Fb		x
P62937	PPIA	Peptidyl-prolyl cis-trans isomerase A	x	
P23284	PPIB	Peptidyl-prolyl cis-trans isomerase B	x	
Q06830	PRDX1	Peroxiredoxin-1	x	
P30041	PRDX6	Peroxiredoxin-6	x	
Q92954	PRG4	Proteoglycan 4	x	x
P07737	PROF1	Profilin-1	x	
P49721	PSB2	Proteasome subunit beta type-2	x	
Q9UL46	PSME2	Proteasome activator complex subunit 2	x	
P26022	PTX3	Pentraxin-related protein 3	x	x
O00391	QSOX1	Sulfhydryl oxidase 1	x	x
P05109	S10A8	Protein S100-A8b		x
P06702	S10A9	Protein S100-A9b		x
P55017	S12A3	Solute carrier family 12 member 3	x	
P07602	SAP	Proactivator polypeptideb		x
P31431	SDC4	Syndecan-4		x
P50454	SERPH	Serpin H1	x	
Q9H299	SH3L3	SH3 domain-binding glutamic acid-rich-like protein 3	x	
P04179	SODM	Superoxide dismutase [Mn], mitochondrial	x	
P09486	SPRC	SPARC	x	x
P42224	STAT1	Signal transducer and activator of transcription 1-alpha/beta	x	
P23381	SYWC	Tryptophan--tRNA ligase, cytoplasmic	x	
Q7Z7G0	TARSH	Target of Nesh-SH3		x
P68363	TBA1B	Tubulin alpha-1B chain	x	
Q13509	TBB3	Tubulin beta-3 chain	x	
P07437	TBB5	Tubulin beta chain	x	
P24821	TENA	Tenascin	x	x
P05452	TETN	Tetranectin		x
P01033	TIMP1	Metalloproteinase inhibitor 1	x	x
P16035	TIMP2	Metalloproteinase inhibitor 2	x	x
P29401	TKT	Transketolase	x	

P60174	TPIS	Triphosphate isomerase	x	
P02787	TRFE	Serotransferrin	x	
P02788	TRFL	Lactotransferrin	x	
Q8NH M4	TRY6	Putative trypsin-6b		x
P98066	TSG6	TNF-inducible gene 6 protein		x
P07996	TSP1	Thrombospondin-1		x
Q8NBS 9	TXND5	Thioredoxin domain-containing protein 5	x	
P19971	TYPH	Thymidine phosphorylase	x	
P22314	UBA1	Ubiquitin-like modifier-activating enzyme 1	x	
O60701	UGDH	UDP-glucose 6-dehydrogenase	x	
Q6EMK 4	VASN	Vasorin	x	x
P19320	VCAM1	Vascular cell adhesion protein 1		x
P08670	VIME	Vimentin	x	
P18206	VINC	Vinculin	x	
P02774	VTDB	Vitamin D-binding protein	x	
P04004	VTNC	Vitronectin	x	
Q5GH7 2	XKR7	XK-related protein 7	x	

<sup>a</sup>Protein accession number according to the SwissProt and TrEMBL databases. <sup>b</sup>Proteins identified by SILAC analysis in the present study. <sup>c</sup>Proteins identified by SILAC analysis in the previous study [32]. SILAC, stable isotope labelling by amino acids in cell culture; OA, osteoarthritis; Fn-fs, fibronectin fragments; SF, synovial fibroblasts; AC, articular chondrocytes; IL-1 $\beta$ , interleukin-1 $\beta$ .