

Supplement Table 1. Demographic characteristic of studied populations.

Sample	Characteristics	Control		RA
		10 OA	10 AS	10
Synovium	No. subjects	10 OA	10 AS	10
	Female/male	6/4	3/7	7/3
	Age	41 to 77 (mean 60)	28 to 54 (mean 35)	23 to 70 (mean 50)
	CRP	-	-	30–100 mg/l
	anti-CCP	-	-	300–3000 u/ml
Peripheral blood	RF	-	-	160–2560 u/ml
	Cohort I	n/female	160/58	267/183
		Age	23 to 70 (mean 48)	22 to 71 (mean 51.7)
	Cohort II	n/female	1056/792	1151/863
	Age	20 to 75 (mean 56)	21 to 75 (mean 57)	

RA: rheumatoid arthritis; OA: osteoarthritis; AS: ankylosing spondylitis.

Supplementary Table 2. Downregulated genes in siRNA-PCSK6 RASF.

Accession No.	Gene Symbol	Gene Description	Fold Change (si 1/Mock)	GO Molecular Function Term	p
NM_001128635	<i>RIMBP3B</i>	RIMS binding protein 3B	0.352258396	Oxidoreductase activity	0.00109
NM_001828	<i>CLC</i>	Charcot-Leyden crystal protein	0.360919	Lysophospholipase activity // sugar binding // hydrolase activity //	0.001
NM_001190706	<i>MTRNR2L9</i>	MT-RNR2-like 9	0.387046283	---	0.00156
NM_001123375	<i>HIST2H3D</i>	Histone cluster 2, H3d	0.392534945	DNA binding // protein binding	0.00745
BC030554	<i>TARP</i>	TCR gamma alternate reading frame protein	0.39323428	---	0.00857
XR_113625	<i>LOC100505937</i>	Hypothetical LOC100505937	0.411953099	---	0.01088
BC039116	<i>TRGC2</i>	T cell receptor gamma constant 2	0.412056764	Transmembrane receptor activity	0.0274
NM_152997	<i>C4orf7</i>	Chromosome 4 open reading frame 7	0.412929101	---	0.04
NM_001168221	<i>ALS2CR11</i>	Amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	0.424658785	---	0.034
NM_006273	<i>CCL7</i>	Chemokine (C-C motif) ligand 7	0.429194948	Chemokine activity // heparin binding // chemokine activity	0.01
NM_025189	<i>ZNF430</i>	Zinc finger protein 430	0.430173632	DNA binding // zinc ion binding // metal ion binding //	0.0039
ENST00000390331	<i>IGLC7</i>	Immunoglobulin lambda constant 7	0.430693961	Antigen binding // antigen binding	0.0325
NM_080748	<i>ROMO1</i>	Reactive oxygen species modulator 1	0.440564147	Molecular function	0.0322
NM_024733	<i>ZNF665</i>	Zinc finger protein 665	0.457570199	DNA binding // zinc ion binding // metal ion binding	0.00515
BC104224	<i>DCAF4L1</i>	DDB1 and CUL4 associated factor 4-like 1	0.466438571	---	0.002
AF210649	<i>NAG20</i>	NAG20	0.481154458	---	0.003

ENST00000423958	<i>AKR1B15</i>	Aldo-keto reductase family 1, member B15	0.481154458	Oxidoreductase activity	00.022
NM_033273	<i>ZNF479</i>	Zinc finger protein 479	0.482096546	DNA binding // zinc ion binding // metal ion binding	0.045
NM_003540	<i>HIST1H4F</i>	Histone cluster 1, H4f	0.482563934	Protein binding // DNA binding // transcription initiation factor activity	0.001
NM_130467	<i>PAGE5</i>	P antigen family, member 5 (prostate associated)	0.486418498	---	0.0001
NM_001004739	<i>OR5L2</i>	Olfactory receptor, family 5, subfamily L, member 2	0.494285675	Receptor activity // olfactory	0.004
NM_001039724.3	<i>NOSTIN</i>	Nitric oxide synthase trafficker	0.5	Endocytosis	0.035
NM_020130	<i>C10orf116</i>	Chromosome 8 open reading frame 4	0.5	Apoptosis	0.0149
NM_004994.2	<i>MMP-9</i>	Matrix metalloproteinase 9	0.5	Local proteolysis of the extracellular matrix	0.032
NM_201280	<i>TXNDC5</i>	Thioredoxin domain containing 5	0.5	Vesicle-mediated transport // otolith morphogenesis // developmental pigmentation	0.0385
NM_001530	<i>HIF1alpha</i>	Hypoxia inducible factor 1	0.5	Response to hypoxia	0.021
NM_018402	<i>IL-26</i>	Interleukin 26	0.5	Cell-cell signaling	0.0313
NM_002416.1	<i>CXCL9</i>	Chemokine (C-X-C motif) ligand 9	0.565356583	---	0.0475

siRNA: small interfering RNA; PCSK6: proprotein convertase subtilisin/kexin type 6; RASF: rheumatoid arthritis synovium fibroblasts.

Supplementary Table 3. Upregulated genes in siRNA-PCSK6 RASF.

Accession number	Gene Symbol	Gene Description	Fold Change (si 1/Mock)	GO Molecular Function Term	p
NM_001001915	<i>OR2G2</i>	olfactory receptor, family 2, subfamily G, member 2	2.008291933	Receptor activity // olfactory receptor activity /	0.005
AK128852	<i>NFE2L2</i>	nuclear factor (erythroid-derived 2)-like 2	2.042291784	---	0.019
NM_006900	<i>IFNA13</i>	interferon, alpha 13	2.065373928	Cytokine activity // interferon-alpha/beta receptor binding //	0.00476
BC031588	<i>LOC100508869</i>	hypothetical LOC100508869	2.075190816	---	0.0147
AK125454	<i>LOC100128300</i>	hypothetical LOC100128300	2.081702637	---	0.036
ENST00000482608	<i>C8orf46</i>	chromosome 8 open reading frame 46	2.082297207	---	0.00825
AK125343	<i>SRXN1</i>	sulfiredoxin 1	2.086056163	Nucleotide binding // DNA binding // ATP binding // antioxidant activity // oxidoreductase activity,	0.0192
NM_001004450	<i>OR1B1</i>	olfactory receptor, family 1, subfamily B, member 1	2.090469508	Receptor activity // olfactory receptor activity	0.014
AK097518	<i>C1orf49</i>	chromosome 1 open reading frame 49	2.097727092	---	0.011
NM_199336	<i>FAHD2B</i>	fumarylacetoacetate hydrolase domain containing 2B	2.118050518	Hydrolase activity // metal ion binding /	0.0026
NM_178523	<i>ZNF616</i>	zinc finger protein 616	2.121438712	DNA binding // zinc ion binding // metal ion binding /	0.031
DQ341454	<i>TRBJ2-6</i>	T cell receptor beta joining 2-6	2.143905031	---	0.0017
ENST00000400206	<i>CSNK1E</i>	casein kinase 1, epsilon	2.150467011	Nucleotide binding // protein kinase activity // protein serine/threonine kinase activity // // nucleotide binding // ATP binding	0.005
NM_152418	<i>DCAF4L2</i>	DDB1 and CUL4 associated factor 4-like 2	2.156560216	---	0.025

NM_001105569	<i>MSGN1</i>	mesogenin 1	2.160240595	DNA binding // transcription regulator activity	0.014
NM_018974	<i>UNC93A</i>	unc-93 homolog A (C. elegans)	2.193799989	Molecular function	0.0312
NM_001004744	<i>OR5R1</i>	olfactory receptor, family 5, subfamily R, member 1	2.194507195	Receptor activity // olfactory receptor activity /	0.0115
AK123595	<i>LOC100216546</i>	hypothetical LOC100216546	2.198666822	---	0.0073
BC040288	<i>LOC100130428</i>	IGYY565	2.206648746	---	0.0226
ENST00000390578	<i>IGHD2-15</i>	immunoglobulin heavy diversity 2-15	2.505643215	---	0.015
NM_001039361	<i>PRAMEF10</i>	PRAME family member 10	2.519362989	---	0.02
XM_001713850	<i>LOC730268</i>	anaphase-promoting complex subunit 1-like	2.524497065	---	0.01
NM_002722	<i>PPY</i>	pancreatic polypeptide	2.541700428	G-protein-coupled receptor binding // receptor binding // hormone activity //	0.014
NM_176887	<i>TAS2R46</i>	taste receptor, type 2, member 46	2.717855962	Receptor activity // G-protein coupled	0.03
ENST00000449138	<i>LOC100510554</i>	hypothetical protein LOC100510554	3.173381564	---	0.015

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