Supplementary Table S1. RNA Quality Control

Control		FOP	
Sample	**RIN^e value**	**Sample**	**RIN^e value**
Con1−ActA	8.3	FOP1−ActA	8.6
Con1+ActA	8.0	FOP1+ActA	9.3
Con2−ActA	7.9	FOP2−ActA	1.8
Con2+ActA	8.4	FOP2+ActA	9.0
Con3−ActA	7.8	FOP3−ActA	8.0
Con3+ActA	1.0	FOP3+ActA	8.5
Con4−ActA	8.4	FOP4−ActA	8.4
Con4+ActA	9.1	FOP4+ActA	8.9
Con5−ActA	8.7	FOP5−ActA	7.6
Con5+ActA	8.2	FOP5+ActA	7.6
Con6−ActA	8.3	FOP6−ActA	8.2
Con6+ActA	9.0	FOP6+ActA	9.0

Supplementary Table S1. RNA integrity number (RIN) values were determined on RNA isolated from CD14-positive monocytes from a group of FOP patients and a group of healthy controls treated with (+ActA) or without (−ActA) Activin-A.

Supplementary Table S2. Most significantly upregulated genes

ENSEMBL ID	Gene name	*p*(adj)-value	Log2 fold change
ENSG00000173391	*OLR1*	3,79E-77	4,30
ENSG00000204252	*HLA-DOA*	1,76E-53	4,20
ENSG00000179583	*CIITA*	2,34E-53	3,15
ENSG00000011201	*ANOS1*	5,05E-46	2,12
ENSG00000197093	*GAL3ST4*	4,42E-45	5,61
ENSG00000166033	*HTRA1*	3,53E-42	2,17
ENSG00000072422	*RHOBTB1*	5,50E-41	2,07
ENSG00000151117	*TMEM86A*	7,76E-35	2,26
ENSG00000102996	*MMP15*	3,70E-34	2,20
ENSG00000134508	*CABLES1*	8,39E-34	4,04
ENSG00000166927	*MS4A7*	4,61E-33	3,05
ENSG00000116774	*OLFML3*	1,40E-32	5,21
ENSG00000198286	*CARD11*	2,95E-32	3,01
ENSG00000124225	*PMEPA1*	6,07E-32	2,92
ENSG00000169116	*PARM1*	4,71E-31	4,59
ENSG00000182985	*CADM1*	4,66E-30	2,70

ENSG00000182578	*CSF1R*	1,04E-29	2,01
ENSG00000145284	*SCD5*	5,80E-28	3,60
ENSG00000102221	*JADE3*	2,35E-26	2,41
ENSG00000232629	*HLA-DQB2*	1,11E-25	2,65
ENSG00000179715	*PCED1B*	3,20E-25	2,99
ENSG00000184588	*PDE4B*	3,74E-25	2,54
ENSG00000163995	*ABLIM2*	4,94E-25	2,95
ENSG00000137642	*SORL1*	7,87E-25	2,72
ENSG00000188070	*C11ORF95*	8,51E-25	2,13
ENSG00000120708	*TGFBI*	1,00E-24	3,31
ENSG00000196664	*TLR7*	2,77E-24	3,09
ENSG00000134042	*MRO*	6,46E-24	3,48
ENSG00000204174	*NPY4R*	6,46E-24	5,05
ENSG00000164176	*EDIL3*	7,46E-24	4,32
ENSG00000148400	*NOTCH1*	9,59E-24	2,32
ENSG00000164171	*ITGA2*	1,98E-23	4,22
ENSG00000213420	*GPC2*	4,49E-23	2,99
ENSG00000223865	*HLA-DPB1*	4,73E-23	2,54
ENSG00000273415	*LINC02725*	8,63E-23	2,67
ENSG00000104059	*FAM189A1*	2,04E-22	4,10
ENSG00000164037	*SLC9B1*	2,15E-22	3,49
ENSG00000106976	*DNM1*	5,99E-22	3,56
ENSG00000183019	*MCEMP1*	6,24E-22	4,36

Supplementary Table S2. Most significantly upregulated genes present in the 100 most significantly differentially expressed genes sorted on p(adj) value

Supplementary Table S3. Most significantly downregulated genes

ENSEMBL ID	**Gene name**	***p*(adj)-value**	**Log2 fold change**
ENSG00000271856	*LINC01215*	9,23E-54	-4,18
ENSG00000174370	*C11ORF45*	1,53E-39	-3,01
ENSG00000180509	*KCNE1*	2,46E-39	-2,36
ENSG00000151704	*KCNJ1*	5,09E-38	-3,70
ENSG00000118971	*CCND2*	1,44E-37	-2,79

ENSG00000111859	*NEDD9*	1,10E-34	-3,66
ENSG00000168350	*DEGS2*	3,37E-34	-3,14
ENSG00000036672	*USP2*	9,74E-34	-2,33
ENSG00000075340	*ADD2*	1,23E-33	-4,20
ENSG00000243742	*RPLP0P2*	7,24E-33	-2,93
ENSG00000117586	*TNFSF4*	9,50E-33	-2,44
ENSG00000181634	*TNFSF15*	1,40E-32	-3,15
ENSG00000245248	*USP2-AS1*	6,07E-32	-3,59
ENSG00000166501	*PRKCB*	6,27E-32	-2,84
ENSG00000286872	*AC024270.4*	1,31E-30	-2,53
ENSG00000170485	*NPAS2*	2,27E-30	-4,25
ENSG00000129451	*KLK10*	4,45E-30	-4,48
ENSG00000147509	*RGS20*	5,60E-30	-2,96
ENSG00000147168	*IL2RG*	5,77E-30	-2,13
ENSG00000203685	*C1ORF95*	9,06E-30	-3,77
ENSG00000256508	*MRGPRF-AS1*	5,70E-29	-4,18
ENSG00000254740	*AP003396.3*	3,75E-28	-3,66
ENSG00000156011	*PSD3*	5,49E-28	-2,73
ENSG00000152413	*HOMER1*	5,80E-28	-2,92
ENSG00000276289	*KCNE1B*	7,98E-28	-2,47
ENSG00000232453	*LOC105378753*	3,52E-27	-3,99
ENSG00000073712	*FERMT2*	5,46E-27	-2,95
ENSG00000157470	*FAM81A*	6,61E-27	-3,26
ENSG00000147231	*CXORF57*	8,03E-27	-2,44
ENSG00000172575	*RASGRP1*	1,13E-26	-2,15
ENSG00000232258	*TMEM114*	4,20E-26	-3,18
ENSG00000162551	*ALPL*	5,17E-26	-4,24
ENSG00000119866	*BCL11A*	9,93E-26	-2,59
ENSG00000175175	*PPM1E*	1,08E-25	-2,85
ENSG00000077782	*FGFR1*	2,20E-25	-2,34
ENSG00000176928	*GCNT4*	3,18E-25	-2,80
ENSG00000162896	*PIGR*	6,60E-25	-3,61
ENSG00000175356	*SCUBE2*	7,21E-25	-3,45

ENSG00000155886	*SLC24A2*	1,16E-24	-5,53
ENSG00000228486	*LINC01125*	1,36E-24	-3,05
ENSG00000188613	*NANOS1*	1,57E-24	-3,20
ENSG00000163803	*PLB1*	1,89E-24	-2,10
ENSG00000117245	*KIF17*	2,59E-24	-2,79
ENSG00000185022	*MAFF*	4,36E-24	-2,33
ENSG00000107736	*CDH23*	4,64E-24	-3,09
ENSG00000234572	*LOC101927438*	4,71E-24	-4,14
ENSG00000011347	*SYT7*	4,83E-24	-3,97
ENSG00000263325	*AC003965.2*	5,01E-24	-3,52
ENSG00000111371	*SLC38A1*	9,23E-24	-4,07
ENSG00000166949	*SMAD3*	1,59E-23	-2,96
ENSG00000284240	*LINC02801*	1,67E-23	-3,82
ENSG00000076706	*MCAM*	4,74E-23	-4,13
ENSG00000180720	*CHRM4*	7,51E-23	-4,52
ENSG00000000938	*FGR*	1,08E-22	-2,16
ENSG00000135525	*MAP7*	2,00E-22	-2,58
ENSG00000162894	*FCMR*	2,15E-22	-3,11
ENSG00000214212	*C19ORF38*	2,23E-22	-2,15
ENSG00000102003	*SYP*	2,56E-22	-3,18
ENSG00000155893	*PXYLP1*	2,58E-22	-2,07
ENSG00000196395	*AC244505.1*	4,78E-22	-2,75
ENSG00000172935	*MRGPRF*	4,81E-22	-3,33

Supplementary Table S3. Most significantly downregulated genes present in the 100 most significantly differentially expressed genes sorted on p(adj) value

Supplementary Table S4. Upregulated genes per cellular process during cell fusion

Differentiation	Actin Organization	Chemotaxis	Adhesion	Fusion
APLP1	*ACTN2*	*ANGPT1*	*ADAM19*	*ACTN2*
AXL	*ASAP3*	*CALCR*	*CARD11*	*ADAM12*

CALCR	*CADM1*	*CCL18*	*CD244*	*ADCY1*
CNGB1	*CDC42EP5*	*CMKLR1*	*CDH5*	*ADGRB1*
CSF1R	*CDH5*	*CSF1R*	*EFNB3*	*CHRNA6*
DNM1	*CLDN4*	*CXCL12*	*GRAP2*	*CST3*
F2	*CSF1R*	*CXCR3*	*HLA-DPA1*	*CXCL1*
GAS6	*CTNNA2*	*EXT1*	*HLA-DPB1*	*CXCL12*
GIPR	*CTNND2*	*FFAR4*	*HLA-DRA*	*DGKI*
HLA-DRA	*CXCL12*	*FLT4*	*IGF1*	*DNM1*
IL2RA	*DGKI*	*GAS6*	*IL2RA*	*EHD2*
IL6	*EPHA2*	*GPBAR1*	*IL6*	*F5*
IL7R	*ESPNL*	*IL6*	*IL7R*	*FPR1*
ITGB3	*EXT1*	*ITGA2*	*KIF26B*	*FUCA1*
PDE4B	*F2*	*ITGB3*	*NOTCH1*	*GAS6*
PPEF1	*F2R*	*JAM3*	*PLEKHA7*	*HGF*
RGS10	*F2RL2*	*NOTCH1*	*SPTA1*	*HPSE*
RGS4	*GJA1*	*P2RY6*	*WNT5A*	*IGF1*
ROR2	*GPBAR1*	*PDGFD*		*ITGB3*
SLC9B2	*GPR35*	*PTN*		*LCN2*
	GRIP1	*ROR2*		*LRRC7*
	ID1	*S1PR1*		*MCEMP1*
	IGF1	*SELL*		*NCAM1*
	IL6	*THBS1*		*NOTCH1*
	ITGB3	*TRPV4*		*OLR1*
	JAM3	*WNT5A*		*PFN2*
	MAP1A			*PRSS12*
	MARCKSL1			*RAB3B*
	MARVELD3			*RETN*
	MID1			*RNASE2*
	MYO1B			*RNASE3*
	NET1			*SCGB3A1*
	NLGN4X			*SELL*
	NOTCH1			*SYT3*
	P2RY8			*TCN1*

PEAK3	*THBS1*
PFN2	
PLEKHA7	
PMP22	
PROX1	
PTN	
RASAL1	
RGS4	
RHOBTB1	
S1PR1	
SEMA3E	
SEMA4D	
SLC39A12	
SPTA1	
SYT3	
TRPV4	
WASF3	
WNT5A	
ZNF664-RFLNA	

Supplementary Table S4. Significantly upregulated genes with cut- off values of p(adj)<0.01 and Log2Fold change ≥ 2, divided into the different stages of cell fusion they are associated with.

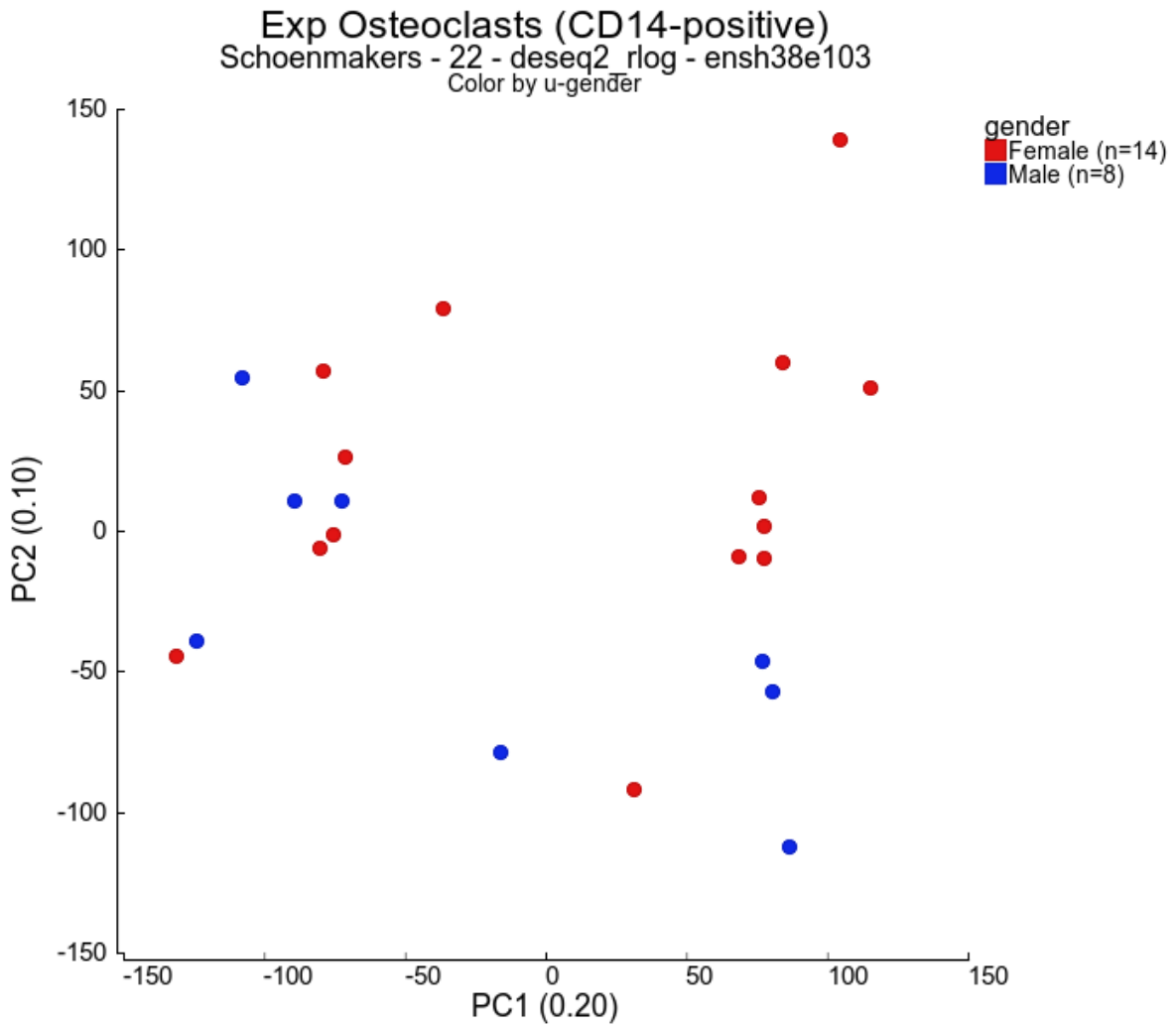


Figure S1 **PCA plot depicting inter-gender variability. Control and FOP female donors (both – and + Activin-A) depicted in red, Control and FOP male donors (both – and + Activin-A) depicted in blue.**