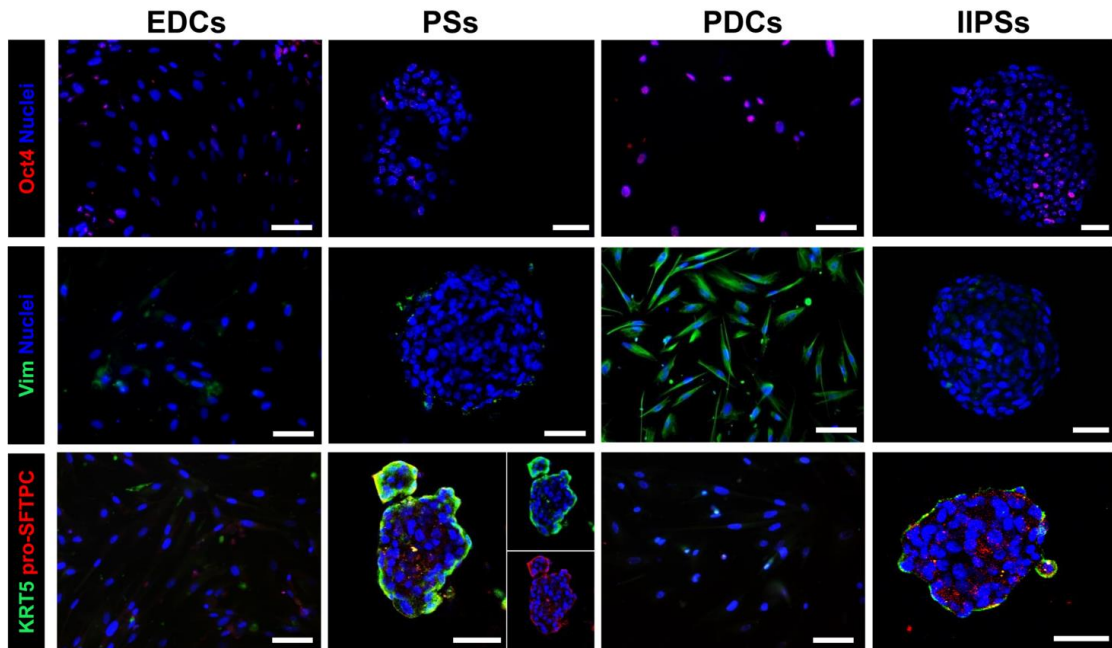


2

3 SUPPLEMENTAL FIGURES.

4



5

6 **Figure S1. Immunofluorescence stainings at various cell culture stages.** Oct4, vimentin (VIM),

6

7 cytokeratin 5 (KRT5) and pro-surfactant C (pro-SFTPC) stainings at the explant-derived cells (EDCs),

7

8 pneumospheres (PSs), PS-derived cells (PDCs) and secondary PSs (IIPsSs) stages. Oct4+ cells were enriched

8

9 after the EDC stage, and particularly at the PDC stage. A clear on/off switch was detectable for vimentin

9

10 (VIM) expression in PDCs, while the opposite regulation was observed for the epithelial markers KRT5 and

10

11 pro-SFTPC in PSs and IIPsSs. Scale bars = 50µm.

11

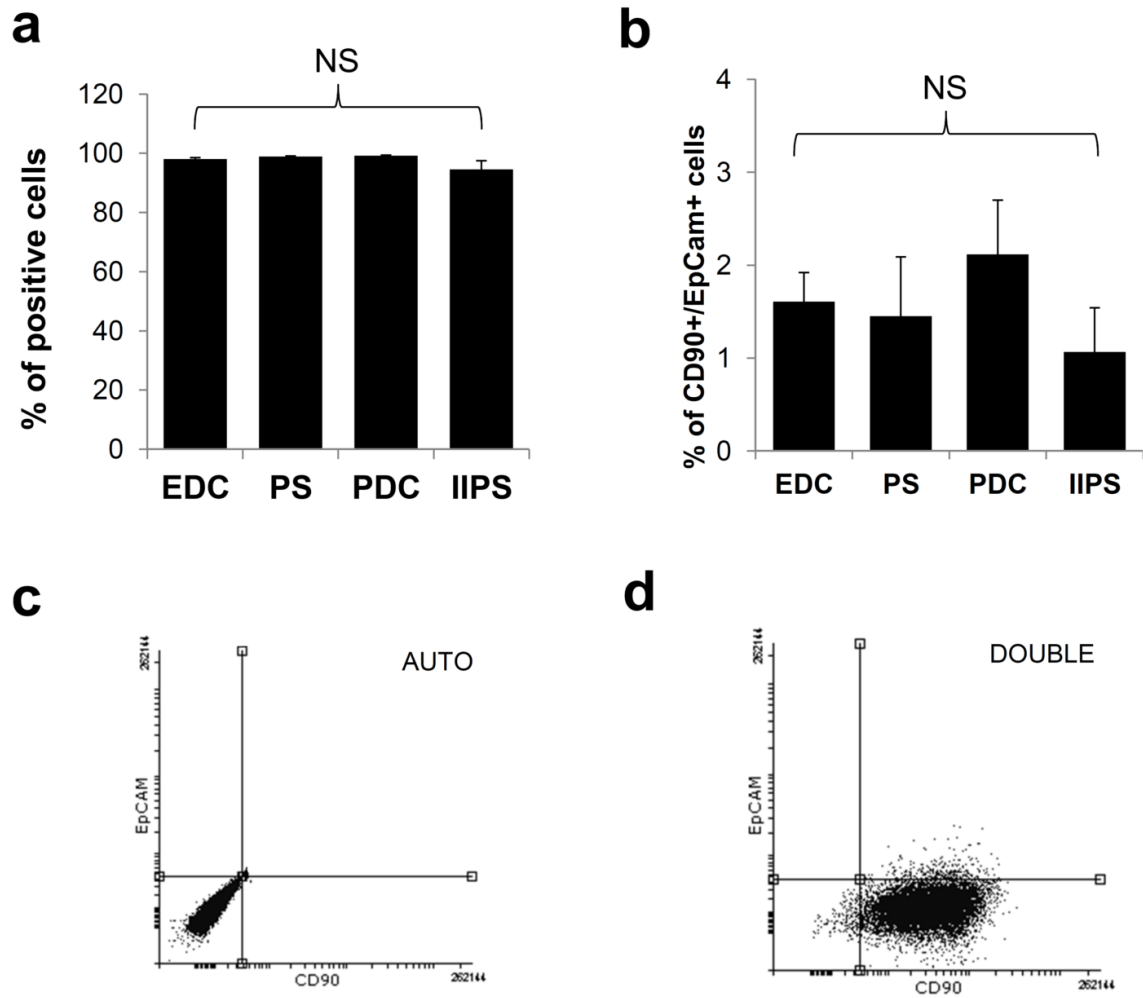
12

13

14

15

16



17

18

19

20

21

22

23

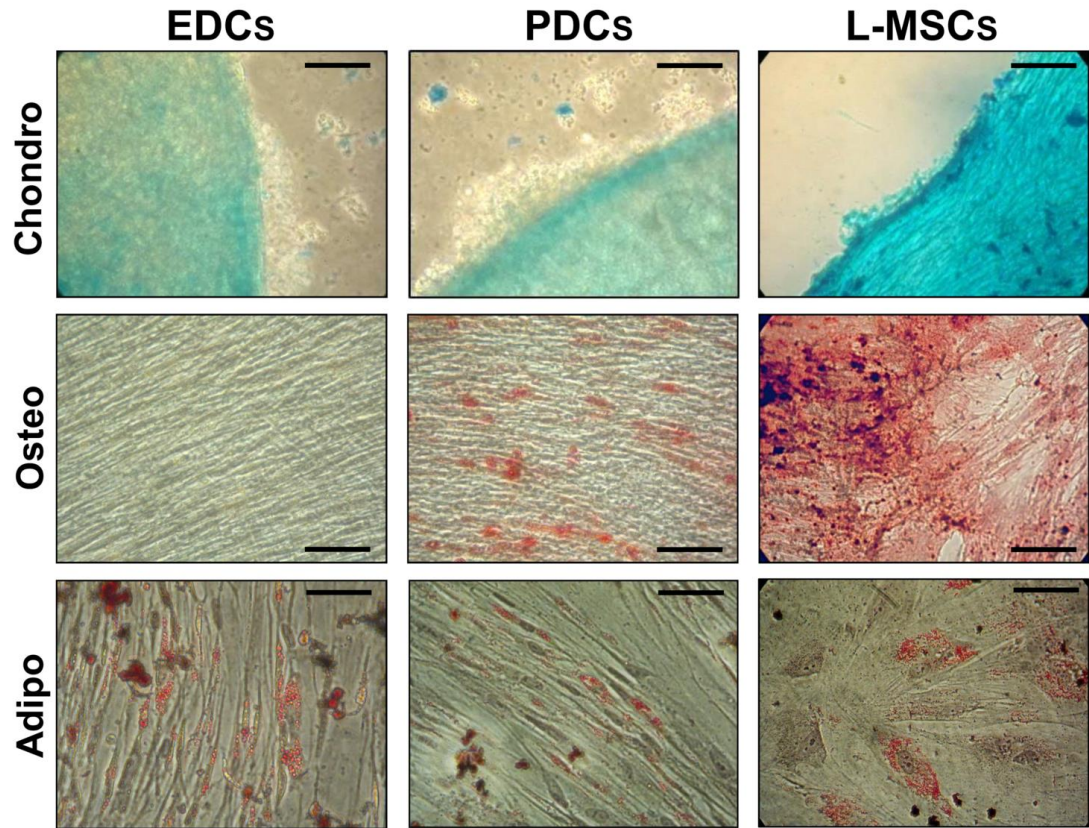
24

25

26

27

Figure S2. Immunophenotype at different stages of culture. The proportion of CD90+ cells (a) was constant at all culture stages (EDC, PS, PDC, IIPS), as it was the small subpopulation of EpCam+/CD90+ double positive cells. Representative dot-plot panels for the analysis of autofluorescence (c) and double staining (d). NS: not significant.



28

29

30

31

32

33

34

35

36

37

38

39

40

41

Figure S3. Transdifferentiation assays of EDCs and PDCs for mesenchymal lineages. Chondrogenic, osteogenic and adipogenic transdifferentiation potential of EDCs and PDCs was assessed. The mesenchymal potential of EDCs was not complete, since osteogenic differentiation was not detectable. Conversely, PDCs clearly contained a subpopulation with complete multi-lineage potential, although such potential was dramatically lower than pure lung mesenchymal stem cells (L-MSCs) isolated from lung parenchyma. Scale bars = 50 μ m.

42 SUPPLEMENTAL TABLES

43 Table S1. Primers sequence for realtime PCR.

Target	Sequence	Tm (°C)	Size[bp]	Other names
TTF-1 fw	ACCAGGACACCATGAGGAAC	59,8	116	Nkx2.1
TTF-1 rv	GCTCATGTTCATGCCGCT	60,9		
SFTPA1 fw	ATCCCTGGAGAGTGTGGAGA	59,6	102	
SFTPA1 rv	AAAGTCGTGGAGTGTGGCTT	59,7		
SFTPA2 fw	CTGGAGAGCGTGGAGAGAAG	60,2	98	
SFTPA2 rv	GAAGTCGTGGAGTGTGGCTT	60,3		
SFTPC fw	AGCAAAGAGGTCCTGATGGA	59,8	103	
SFTPC rv	CGATAAGAAGGCGTTTCAGG	59,8		
SCGB1A1 fw	ATGAAACTCGCTGTCACCCT	59,7	114	CCSP
SCGB1A1 rv	TGTGTCCATGAGGAGGGTTT	60,3		
TP73L fw	CCACCCTACAGTACTGCCCT	59,1	114	p63
TP73L rv	TTGTCTGTGTGCTCTGGGAC	59,9		
NGFR fw	CTGCTGCTGTTGCTGCTTCT	62	98	p75
NGFR rv	CAGGCTTTGCAGCACTCAC	60,7		
KRT5 fw	GGAGCTCATGAACACCAAGC	60,8	104	CK5
KRT5 rv	CTGGTCCAACCTCCTTCTCCA	60,2		

KRT14 fw	GGCCTGCTGAGATCAAAGAC	60	105	CK14
KRT14 rv	TCTGCAGAAGGACATTGGC	60		
KRT18 fw	GAGCACTTGGAGAAGAAGGG	59	126	CK18
KRT18 rv	GTCAATCTGCAGAACGATGC	59,4		
AQP1 fw	CTCTCAGGCATCACCTCCTC	59,9	109	
AQP1 rv	GGAGGGTCCCGATGATCT	59,8		
AQP5 fw	TGGCATCCTCTACGGTGTG	60,6	119	
AQP5 rv	GCTGGAAGGTCAGAATCAGC	59,9		
Oct4 fw	GTGGAGGAAGCTGACAACAA	58,9	118	
Oct4 rv	TCTCCAGGTTGCCTCTCACT	60		
TGFBR2 fw	CTGCACATCGTCCTGTGG	59,8	110	
TGFBR2 rv	GGAAACTTGACTGCACCGTT	60,1		
CTNNB1 fw	AGGTCTGAGGAGCAGCTTCA	60,2	142	beta-catenin
CTNNB1 rv	ATTGTCCACGCTGGATTTTC	59,9		
Snail fw	CTTCTCTAGGCCCTGGCTG	59	134	
Snail rv	CATCTGAGTGGGTCTGGAGG	59		
Vim fw	ACCCACTCAAAAAGGACACTTC	59	88	
Vim rv	GGTCATCGTGATGCTGAGAA	59		

44 Tm: melting temperature.

45

46 **Table S2. Complete panel of proteins screened by protein array in conditioned media.**

POS	POS	POS	POS	NEG	NEG	ENA-78	GCSF	GM-CSF	GRO	GRO- α
I-309	IL-1 α	IL-1 β	IL-2	IL-3	IL-4	IL-5	IL-6	IL-7	IL-8	IL-10
IL-12	IL-13	IL-15	IFN- γ	MCP-1	MCP-2	MCP-3	MCSF	MDC	MIG	MIP-1 β
MIP-1 δ	RANTES	SCF	SDF-1	TARC	TGF- β 1	TNF- α	TNF- β	EGF	IGF-1	Angiogenin
Oncostatin M	Thrombopoietin	VEGF	PDGF-BB	Leptin	BDNF	BLC	CCL3	Eotaxin	Eotaxin-2	Eotaxin-3
FGF-4	FGF-6	FGF-7	FGF-9	Flt-3 ligand	Fractalkine	GCP-2	GDNF	HGF	IGFBP-1	IGFBP-2
IGFBP-3	IGFBP-4	IL-16	IP-10	LIF	LIGHT	MCP-4	MIF	MIP-3 α	NAP-2	NT-3
NT-4	Osteopontin	Osteoprotegerin	PARC	PLGF	TGF- β 2	TGF- β 3	TIMP-1	TIMP-2	POS	POS

47

48

49

50

51

52

53