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Supplementary Table S1: Source and primer sequences of riboprobes used to validate gene expression by whole mount *in situ* hybridization.

Gene Symbol	IMAGE ID	Vector	Primers
1810019J16Rik	3599314	pCMV-SPORT-6	Fwd: 5’-AAGACCAGCATGGGCAGCAGCTT-3’ Rev: 5’TAATACGACTCACTATAGGGAATATAGCAAGTGGGCACTGCCCACA-3’
B4galt6	4037384	pCMV-SPORT-6	Fwd: 5’-TTGATGAAGTCCATCAGCTCTTCTCC-3’ Rev: 5’-TAATACGACTCACTATAGGGTTCTTCACTTCCAGTCCCAAGCAA-3’
Rbm47	4240441	pCMV-SPORT-6	M13 forward and reverse
Capn6	6517565	pCMV-SPORT-6.1	Fwd: 5’-AGGACAGAGGTGATCAAGGCCAA-3’ Rev: 5’-TAATACGACTCACTATAGGGTTTGTAAGCAGTGTGGCAAAGG-3’
Cldn4	876728	pT7T3D-PacI	Fwd: 5’-TTTTCGGATTGAGCTCATAACAGCC-3’ Rev: 5’-TAATACGACTCACTATAGGGACAAAACAAGAAACCACAGAGAAGGC-3’
Igfbp5	2648602	pCMV-SPORT-6	M13 forward and reverse
Rhou	3964150	pCMV-SPORT-6	M13 forward and reverse

Supplementary Table S2: Top 100 genes that are preferentially expressed in the foregut endoderm relative to the cranial mesoderm and ectoderm tissues.

Symbol	Probe ID	Fold change mean	Selected GO biological process
Pax9	1442229_at	479.87	organ morphogenesis
Tmem27	1435064_a_at	100.74	proteolysis
Masp1	1425985_s_at	92.72	complement activation, lectin pathway
Gm10664	1436287_at	80.98	---
T	1419304_at	62.01	mesoderm development
Tmprss2	1458347_s_at	54.45	proteolysis
Foxa1	1418496_at	52.78	pattern specification
Afp	1436879_x_at	51.45	liver development, transport
Ttr	1454608_x_at	38.41	transport
Spink3	1415938_at	34.57	negative regulation of peptidase activity
Hoxa1	1420565_at	32.00	anterior/posterior pattern specification
Cpm	1429413_at	30.32	proteolysis
Dpp4	1459973_x_at	25.12	response to hypoxia, cell-cell adhesion
Tbx1	1425779_a_at	24.78	pharyngeal system development
Endod1	1426541_a_at	24.14	phosphodiester bond hydrolysis
Arg1	1419549_at	24.04	liver development
Macc1	1457044_at	21.32	---
Mpzl2	1416236_a_at	21.32	cell adhesion
Cdh1	1448261_at	20.68	cell adhesion
Tbx3	1448029_at	20.38	organ morphogenesis
Tgfb2	1450923_at	18.56	morphogenesis
Shh	1436869_at	18.14	pattern specification
Stx3	1425530_a_at	17.15	neurotransmitter transport
Cldn9	1439427_at	17.00	---
Slco4c1	1437870_at	16.72	ion transport
Foxa2	1422833_at	16.07	endoderm development
1810019J16Rik	1417797_a_at	15.93	---
Cldn11	1416003_at	15.67	cell adhesion
Krt18	1448169_at	15.37	tumor necrosis factor-mediated signaling pathway
Col11a1	1418599_at	15.29	cartilage condensation
Gbx2	1420337_at	15.16	tube morphogenesis
St14	1418076_at	15.16	cell migration
Cldn4	1418283_at	15.07	calcium-independent cell-cell adhesion
Hoxb1	1453501_at	14.62	anterior/posterior pattern specification
Slc35f3	1456764_at	14.43	transport

Crb3	1434851_s_at	14.41	cell-cell junction organization
Dsg2	1439476_at	14.13	homophilic cell adhesion
Ces1d	1435370_a_at	13.46	lipid catabolic process
Airn	1456139_at	13.31	regulation of gene expression by genetic imprinting
Kctd12b	1442368_at	13.18	G-protein coupled receptor signaling pathway
Gramd1b	1435229_at	13.13	---
Limch1	1435321_at	12.49	actomyosin structure organization
Moxd1	1422643_at	12.31	catecholamine metabolic process
Tgm2	1433428_x_at	11.83	blood vessel remodeling
Isl1	1422720_at	11.65	pharyngeal system developme
Met	1434447_at	11.63	liver development
Rbm47	1423411_at	11.26	---
Igfbp5	1452114_s_at	11.06	regulation of cell growth
Socs3	1455899_x_at	10.85	signal transduction
Has2	1449169_at	10.71	hyaluronan biosynthetic process
Cldn6	1417845_at	10.51	calcium-independent cell-cell adhesion
Frem1	1455280_at	10.46	cell adhesion
Ap1s3	1455735_at	10.42	vesicle-mediated transport
Inadl	1418983_at	10.42	---
Dkk3	1448669_at	10.20	Wnt receptor signaling pathway
Hhex	1423319_at	10.09	hepatic duct development
Prdm1	1420425_at	10.00	germ cell development
Scara3	1427020_at	9.93	---
Id4	1450928_at	9.89	cell proliferation
Nuak1	1438684_at	9.74	cell adhesion
Esrp1	1454681_at	9.65	regulation of RNA splicing
Rnf128	1418318_at	9.65	protein ubiquitination
Clic6	1454866_s_at	9.62	transport
Plat	1415806_at	9.61	cell-cell adhesion
Casr	1449881_a_at	9.57	signal transduction
Stx3	1425536_at	9.57	transport
Nedd9	1437132_x_at	9.52	cell adhesion
Epcam	1416579_a_at	9.46	ureteric bud development
Rhou	1449028_at	9.46	cytoskeleton organization
Ptch1	1428853_at	9.33	organ morphogenesis
Fam134b	1424683_at	9.23	sensory perception of pain
Itga3	1455158_at	9.23	cell adhesion
Sh3bgrl2	1434109_at	9.07	---
St8sia4	1419186_a_at	9.07	ganglioside biosynthetic process
Slc16a1	1415802_at	8.98	organic anion transpor
Frmd4b	1438169_a_at	8.91	establishment of epithelial cell polarity
Cldn7	1448393_at	8.88	calcium-independent cell-cell adhesion
Ctsh	1418365_at	8.71	epithelial cell migration
Slc39a8	1416832_at	8.70	ion transport

Rbp4	1426225_at	8.70	retinol transpor
Ypel2	1434277_a_at	8.64	---
Endod1	1433796_at	8.61	phosphodiester bond hydrolysis
Akap5	1436142_at	8.59	protein targeting
Dusp9	1433845_x_at	8.59	inactivation of MAPK activity
Tuba4a	1417373_a_at	8.38	microtubule-based movement
9930105H17Rik	1423071_x_at	8.36	---
Hhip	1455277_at	8.29	smoothened signaling pathway
Fam107b	1448509_at	8.28	---
Pura	1455538_at	8.28	DNA unwinding
Lifr	1454984_at	8.17	organ regeneration
Kitl	1415855_at	8.12	cell adhesion
Sowahb	1438408_at	8.12	---
Ctsh	1443814_x_at	8.12	cell migration
Plcxd1	1437842_at	8.11	lipid metabolic process
Rgs5	1417466_at	8.08	signal transduction
Serinc5	1433571_at	8.06	lipid metabolic process
Rarb	1454906_at	8.04	digestive tract development
Etv5	1428142_at	8.01	cellular response to oxidative stress
Cldn8	1449091_at	8.01	calcium-independent cell-cell adhesion
---	1460084_at	7.75	---

Supplementary S3: Foregut gene markers sequences and annealing temperature for PCR

Gene	Sequence (5'-3')	Annealing temperature
Capn6-F	5' TGCTTGTTCCAACCATGTTCCAAC	60°C
Capn6-R	5' TTGCTTGACTTTGGCAGTAGGACCA	60°C
Rbm47-F	5' TGTGACCCCTACACGTTGGCCTACT	60°C
Rbm47-R	5' TTCGATTATTTTCGGGGCTGGG	60°C
B4galt6-F	5' TTTGCAGCGAAGCTGGACAAGTACAT	60°C
B4galt6-R	5' TCAATTGGAGCTAATTCTGGCATGAG	60°C
Igfbp5-F	5' GAGCAACACAAAGGGAGAGCAAAGAA	60°C
Igfbp5-R	5' TGAGCACAGCTGACCTCCTCCGTAT	60°C
Rhou-F	5' TACATCCCTACGGCCTTCGACAAC	60°C
Rhou-R	5' TCTTCAGGCACCGGCTTCTCTTT	60°C
1810019J16Rik-F	5' ACTACCACCTGGATGAGCAAGACGC	60°C
1810019J16Rik-R	5' ACACAGAGGTCCTGGTTCCTCTCCT	60°C
Cldn4-F	5' TATGGTCATCAGCATCATCGTGGGT	60°C
Cldn4-R	5' GAGTACTTGGCCGAGTAGGGCTTGT	60°C
β-actin-F	5' AGCACCCTGTGCTGCTCA	60°C
β-actin-R	5' GTACGACCAGAGGCATACA	60°C

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Supplementary Table S4: Lists of genes for the heat maps shown in Figure 3: Expression profile of TGFβ signalling pathway components and response genes in the EpiSCs. Genes are listed in a top to bottom order for each heat map.

Figure 3 a	Figure 3 bi	Figure 3 bii	Figure 3 biii
Ep300	E2f4	Acvrl1	Rbl1
Rbl1	Eng	Tgfb2	Acvrl1
Acvrl1	Acvrl1	Id1	Ep300
Smad6	Rbl1	Eng	Eng
Eng	Ep300	Msx2	Smad3
Acvr1	Smad3	Id2	Smad5
Id2	Tgfb2	Smad3	Sp1
Smad3	Sp1	Ep300	E2f4
Tgfb2	Tgfbr2	Rbl1	Thbs1
Id1	Thbs1	Smad1	Crebbp
Msx2	Smad5	Sp1	Smad1
Sp1	Id3	Acvr1	Tgfbr2
Smad1	Smad1	Crebbp	Smad6
Thbs1	Crebbp	Smad6	Id2
E2f4	Msx2	Tgfbr2	Id1
Id3	Smad6	Id3	Msx2
Smad5	Acvr1	Thbs1	Acvr1
Crebbp	Id1	E2f4	Id3
Tgfbr2	Id2	Smad5	Tgfb2

Figure 3 d	Figure 3 ei	Figure 3 eii	Figure 3 eiii
Ephb2	Brd2	Tnfsf10	Myod1
Mbd1	Gtf2i	Atf4	Agt
Bcl2l1	Bach1	Bhlhe40	Nfkbia
Klf10	Vegfa	Klf10	Snai1
Cdkn1b	Acta2	Ar	Acta2
S100a8	Cryab	Cryab	Atf4
Atf4	Cebpb	Cdc6	Gadd45b
Emp1	Ephb2	Pthlh	Ctnnb1
Rhoa	Serpine1	Nfkbia	Nfib
Creb1	Sox4	Fn1	Rhoa
Bhlhe40	Dnaja1	Hmox1	Bach1
Nfkbia	Fos	Plg	Creb1
Ctnnb1	Mapk8	Mmp2	Dnaja1
Nfib	Ifrd1	Furin	Furin
Gadd45b	Rara	Ifrd1	Ptgs2
Rhob	Mapk14	Herpud1	S100a8
Tnfsf10	Mmp2	Nfib	Sox4
Herpud1	Runx1	Gadd45b	Brd2
Aipl1	Shh	Rhoa	Map3k7
Rara	Pthlh	Snai1	Ppara
Snail1	Il10	Myod1	Gtf2i
Myod1	Bdnf	pdgfa	Ptk2
Pdgfa	Ppara	Aipl1	Shh
Agt	Map3k7	Rhob	Mapk14
Wfs1	Atf3	Srebf2	Bcl2l1
Bach1	Hey1	Ephb2	Mbd1
Srebf2	Myc	Wfs1	Cdkn1b
Ptgs2	Aipl1	Rara	Hes1
Furin	Hmox1	Agt	Rhob
Rad21	Gadd45b	Emp1	Atf3
Ptk2	Wfs1	Cdkn1b	Emp1
Pthlh	Nfib	Ctnnb1	Ar
Plg	Ar	Bcl2l1	Bhlhe40
Myc	Rhoa	Creb1	Cebpb
Fos	Furin	S100a8	Fn1
	Bhlhe40	Ptk2	Plg
	Gli2	Sox4	Rad21

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Hmox1	Myod1	Cebpb	Mapk8
Ar	Ctnnb1	Gli2	Runx1
Fn1	Klf10	Atf3	Mmp2
Mmp2	Creb1	Mapk14	Hey1
Brd2	Hes1	Serpine1	Il10
Shh	Nfkbia	Mapk8	Rara
Hes1	Rhob	Acta2	Tnfsf10
Serpine1	Cdkn1b	Rad21	Myc
Acta2	Plg	Il10	Gli2
Vegfa	Cdc6	Ptgs2	Serpine1
Atf3	Emp1	Shh	Srebf2
Cdc6	Agt	Gtf2i	Ifrd1
Runx1	Fn1	Ppara	Bdnf
Ppara	Snai1	Dnaja1	Fos
Sox4	S100a8	Brd2	Cdc6
Hey1	Tnfsf10	Map3k7	Pthlh
Dnaja1	Atf4	Bdnf	Vegfa
Gtf2i	Bcl2l1	Myc	Hmox1
Mapk14	Pdgfa	Fos	Klf10
Mapk8	Mbd1	Vegfa	Herpud1
Ifrd1	Ptgs2	Hes1	Wfs1
Cryab	Rad21	Runx1	Cryab
Il10	Ptk2	Bach1	Aipl1
Cebpb	Herpud1	Hey1	Pdgfa
Map3k7	Serbf2	Mbd1	
Bdnf			
Gli2			