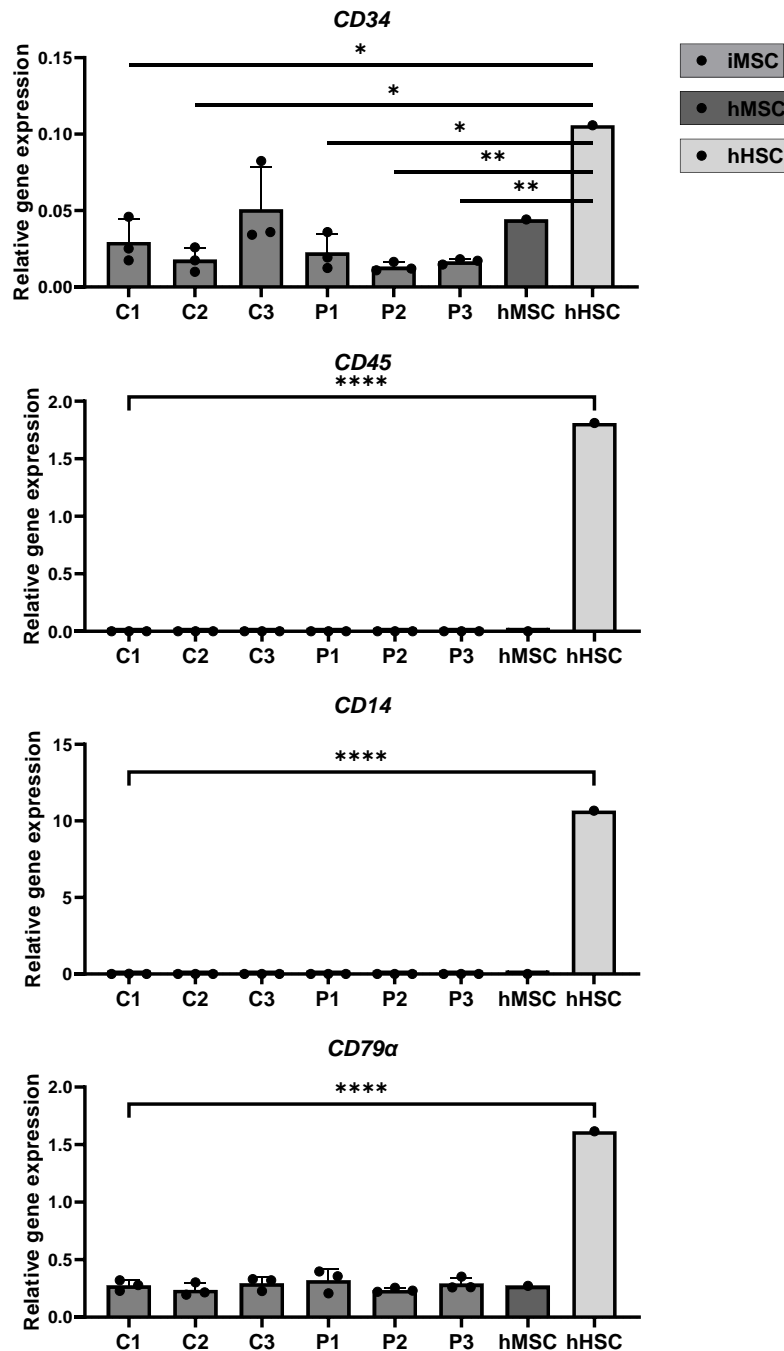
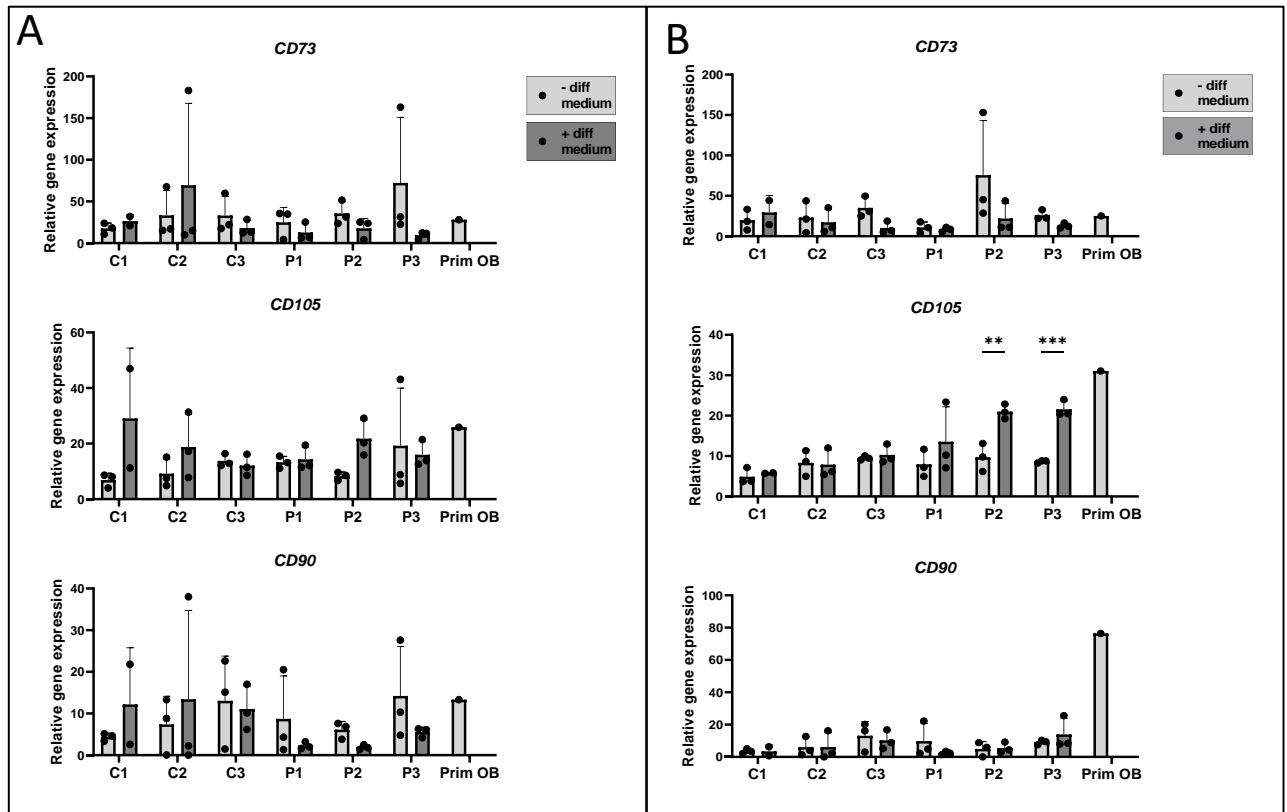


## Supplemental Figures and Tables



**Figure S1**

Relative gene expression of hematopoietic stem cell (hHSC) markers *CD45*, *CD34*, *CD14* and *CD79α* in healthy controls (C1, C2, C3), OI patients (P1, P2 and P3), primary bone marrow mesenchymal stem cells (hMSC) and primary hematopoietic stem cells (hHSC). Relative gene expression was normalized against *TBP*. Standard deviation (SD) is shown per cell line (n=3), no SD is present for hHSC and hMSC (n=1). Statistical significance is indicated on the graphs (P-values  $\leq 0.05$  (\*),  $\leq 0.01$  (\*\*),  $\leq 0.0001$  (\*\*\*\*)).



**Figure S2**

Relative gene expression of mesenchymal stem cell markers *CD73*, *CD90* and *CD105* in osteogenic induced and not induced healthy control iMSC (C1, C2, C3), OI patient iMSCs (P1, P2 and P3) and not induced primary osteoblasts (Prim OB) on day 21 (A) and day 28 (B). Relative gene expression was normalized against *TBP*. Standard deviation (SD) is shown per cell line (n=3), no SD is present for Prim OB (n=1). Statistical significance is indicated on the graphs (P-values ≤ 0.01 (\*\*), ≤ 0.001 (\*\*\*)).

**Table S1**

Information about healthy control iPSC (C1, C2, C3) and OI patient iPSC (P1, P2 and P3) cell lines.

Line	Name	Genotype	Pathogenic variant	Sex	Age	Reprogramming method	Reference	Characterizations
C1	Hvs228	Control	NA	F	19 y	Lentivirus	Nadadur, A. G. <i>et al</i> <sup>46</sup>	Karyotyping, PCR
C2	Hvs420A	Control	NA	M	21 y	Lentivirus	VUi036-A	Staining of OCT3/4, SSEA4, AP, TRA-1-60 and TRA-1-81
C3	Hvs451A	Control	NA	M	19 y	Sendai	VUi032-A	Staining of OCT3/4, SSEA4, TRA-1-60 and TRA-1-81, PCR Sendai and karyotyping
P1	Hvs492A	HI OI type I	COL1A1: c.279del T	M	38 y	Sendai	VUi043-A	Staining of OCT3/4, SSEA4, TRA-1-60 and TRA-1-81, and 3 germ layer test (PCR)
P2	Hvs459	DN OI type 3	COL1A1: c.2299G>A	F	0y	Sendai	VUi045-A	Staining of OCT3/4, SSEA4, AP, TRA-1-60 and TRA-1-81, PCR Sendai and 3 germ layer test (staining)
P3	Hvs460	DN OI type 4	COL1A1: c.1678G>A	F	0y	Sendai	VUi046-A	Staining of OCT3/4, SSEA4, TRA-1-60 and TRA-1-81, PCR Sendai and 3 germ layer test (staining)

**Table S2**

Qualitative analysis of alkaline phosphatase (ALP) and Alizarid Red (AR) staining on day 21 and day 28 after osteogenic induction in healthy controls iMSC (C1, C2, C3), OI patients iMSCs (P1, P2 and P3) and hMSCs. ALP and AR stainings were rated by + (some cells are stained), ++ (most/all cells are stained), – (no cells are stained) and x (no cells present).

<b>Osteoblast differentiation</b>				
<b>Cell line</b>	<b>ALP D21</b>	<b>ALP D28</b>	<b>AR D21</b>	<b>AR D28</b>
<b>C1</b>	+	+	+	+
<b>C1</b>	++	++	+	+
<b>C1</b>	++	++	+	++
<b>C2</b>	++	++	+	+
<b>C2</b>	+	+	+	++
<b>C2</b>	+	+	-	-
<b>C3</b>	++	++	-	-
<b>C3</b>	++	++	-	++
<b>C3</b>	++	x	-	x
<b>P1</b>	++	-	-	-
<b>P1</b>	++	++	-	-
<b>P1</b>	++	++	+	+
<b>P2</b>	+	+	+	+
<b>P2</b>	++	x	+	x
<b>P2</b>	x	++	+	x
<b>P3</b>	+	++	-	+
<b>P3</b>	++	x	+	x
<b>P3</b>	+	++	+	-
<b>hMSC</b>	++	++	++	++

**Table S3**

Qualitative analysis of Sudan III staining after adipogenic induction in healthy control iMSC (C1, C2, C3), OI patient iMSCs (P1, P2 and P3) and hMSCs. Morphology is rated by + (large cells with normal nucleus), ++ (large cells with big nucleus) and – (spindle-like cells), while the presence of vesicles is rated by + (some vesicles are present, small), ++ (a lot of vesicles are present, small), +++ (many vesicles are present, big) and – (no vesicles are present).

<b>Adipogenic differentiation</b>		
<b>Cell line</b>	<b>Morphology</b>	<b>Vesicles</b>
<b>C1</b>	++	+
<b>C1</b>	++	+
<b>C1</b>	++	+
<b>C2</b>	++	-
<b>C2</b>	++	++
<b>C2</b>	+	-
<b>C3</b>	++	++
<b>C3</b>	++	++
<b>C3</b>	++	++
<b>P1</b>	++	++
<b>P1</b>	++	++
<b>P1</b>	++	++
<b>P2</b>	++	++
<b>P2</b>	++	++
<b>P2</b>	++	+++
<b>P3</b>	++	-
<b>P3</b>	++	-
<b>P3</b>	++	++
<b>hMSC</b>	++	+++

**Table S4**

Qualitative analysis of Alcian blue staining in healthy controls iMSC (C1, C2, C3) and OI patient iMSCs (P1, P2 and P3) after chondrogenic induction. Staining was rated by + (lightly blue), ++ (blue) and – (no staining). The presence of cell monolayer outgrowth was also noted by + (present) and – (absent).

	Alcian blue staining	Cell monolayer outgrowth
<b>C1</b>	+	-
<b>C1</b>	++	-
<b>C1</b>	++	-
<b>C2</b>	+++	-
<b>C2</b>	++	-
<b>C2</b>	+	-
<b>C3</b>	++	-
<b>C3</b>	++	-
<b>C3</b>	++	-
<b>P1</b>	+	-
<b>P1</b>	++	-
<b>P1</b>	++	-
<b>P2</b>	++	-
<b>P2</b>	++	-
<b>P2</b>	+	-
<b>P3</b>	+	-
<b>P3</b>	++	-
<b>P3</b>	++	-

**Table S5**

(a) RT-qPCR analysis qPCR programme

	T <sub>m</sub> (°C)	Time(s)	Ramp rate (°C/s)	Cycli	Analysis Mode
Preheat	95	10 min	4.8	1 ×	None
PCR	95 60 72 78	10 5 10 5	4.8 2.5 4.8 4.8	45x	Quantification
Melting-curve	95  60 95	1  1	4.8  2,2 0,03	  1x	Melting curves
Cooling	40	30	1,5	1×	None

(B) List of primers used in RT-qPCR analysis to measure the relative mRNA expression levels.

Gene	Forward	Reverse	Product length (bp)
<i>ACAN</i>	GCACCTTTCAGTGTCATTCC	GTGGTCATAGTTCACCTTGAAGA	258
<i>ALP</i>	AGGGACATTGACGTGATCAT	CCTGGCTCGAAGAGACC	242
<i>CD105</i>	CACCACAGCGGAAAAAGGTG	GCCGGTTTTGGGTATGGGTA	335
<i>CD73</i>	CTCCTCTCAATCATGCCGCT	CCCAGGTAATTGTGCCATTGT	182
<i>CD90</i>	TCCCGAACCAACTTCACCAG	ATGCCCTCACACTTGACCAG	173
<i>COL10A1</i>	GGGCAGAGGAAGCTTCAGAAA	TCTCAGATGGATTCTGCGTGC	73
<i>COL1A1</i>	GTGCTAAAGGTGCCAATGGT	ACCAGGTTACCGCTGTTAC	128
<i>COL2A1</i>	AGGATGGCTGCACGAAACAT	GCCATTCAGTGCAGAGTCCT	255
<i>FABP4</i>	TGACGAAGTCACTGCAGATG	GAACCTCAGTCCAGGTCAAC	217

<i>HNK-1/B3GAT1</i>	TGGGTTGTGAGTGCTGGTAA	GTGATGAGCAGAGTCCAGGG	116
<i>NANOG</i>	AATGGTGTGACGCAGAAGGC	TGCACCAGGTCTGAGTGTC	196
<i>NGFR/p75NT R</i>	GATCCCTGGCCGTTGGATTA	TTGCAGCTGTTCCACCTCTG	267
<i>OCN/BGLAP</i>	CACCGAGACACCATGAGAGC	CTGCTTGGACACAAAGGCTGC	132
<i>OCT4</i>	CCCACACTGCAGCAGATCA	ACCACACTCGGACCACATCC	70
<i>OPN</i>	TTCCAAGTAAGTCCAACGAAAG	GTGACCAGTTCATCAGATTCAT	181
<i>PAX6</i>	AGGTCAGGCTTCGCTAATGG	TGCTGATTGGTGATGGCTCA	97
<i>PPAR<math>\gamma</math></i>	CGACCAGCTGAATCCAGAGT	GATGCGGATGGCCACCTCTT	241
<i>RUNX2</i>	CGTGGCCTTCAAGGTGGTAG	GAGGCATTCCGGAGCTCAG	105
<i>SOX2</i>	ATGGGTTCGGTGGTCAAGTC	CTGATCATGTCCCGGAGGTC	107
<i>SOX9</i>	GGCAAGCTCTGGAGACTTCTG	CCCGTTCTTCACCGACTTCC	138
<i>TBP</i>	AGTTCTGGGATTGTACCGCA	TCCTCATGATTACCGCAGCA	139
<i>TFAP2A</i>	GACCTCTCGATCCACTCCTTAC	GAGACGGCATTGCTGTTGGACT	137

**Table S6**

List of antibodies and stainings used during flow cytometry analysis of healthy control iNCC (C1, C2, C3) and OI patient iNCC (P1, P2 and P3) cell lines.

<b>Name</b>	<b>Fluorophore</b>	<b>Company</b>	<b>Catalogue number</b>	<b>Concentration</b>	<b>Clone</b>
Anti-p75 NGF Receptor antibody [NGFR5]	PE-Cy7	Abcam	ab234270	1:100	NGFR5
CD57 Antibody	FITC	Miltenyi Biotec	130-122-935	1:100	TB03
PAX-6 Antibody, REAfinity™	APC	Miltenyi Biotec	130-123-328	1:100	REA507



Fixable Viability Dye	eFluor780	eBioscience, ThermoFisher Scientific	65-0865-14	1:1000	-
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APC allophycocyanin, FITC fluorescein isothiocyanate, PE R-phycoerthrin.