**Figure 1 – Source data 1 – Gori *et al.***

**Sequences of all knockout clones**

In each case, the wild-type sequence is given on top and the mutant sequence for a particular allele is given underneath. Depending on the gene, we found between two and 4 alleles for each gene. Sequences in lower case represent mismatches to the reference sequence.

**HEK293T SMAD4 KO clone 1**

*Allele 1*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT-ACTACGAACGAGTTGTATCACCTGGAATTGAT

Allele 2

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT----ACGAACGAGTTGTATCACCTGGAATTGAT

Allele 3

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATATC-CTACGAACGAGTTGTATCACCTGGAATTGAT

**HEK293T SMAD4 KO clone 2**

*Allele 1*

379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCC----CACTACGAACGAGTTGTATCACCTGGAATTGAT

*Allele 2* and *3* not detected

**HEK293T SMAD2 KO clone 1**

*Allele 1*

 799ACTTACTCAGAACCTGCATTTTGGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCATT--GGTGTTCGATAGCATATTATGAATTAAAT

*Allele 2* not detected

**HEK293T SMAD2 KO clone 2**

*Allele 1*

 799ACTTACTCAGAACCTGCATTTTGGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCATT--GGTGTTCGATAGCATATTATGAATTAAAT

*Allele 2*

 799ACTTACTCAGAACCTGCATTTTGGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCA >400 bp insertion

**HEK293T SMAD3 KO clone 1**

*Allele 1*

 703ATCTCCTACTACGAGCTGAACCAGCG-CGTCGGGGAGACATTCCACGCC750

ATCTCCTACTACGAGCTGAACCAGCGaCGTCGGGGAGACATTCCACGCC

*Allele 2*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTC752

ATCTCCTACTACGAGCTGAACCAGCG--TCGGGGAGACATTCCACGCCTC

*Allele 3* not detected

**HEK293T SMAD3 KO clone 2**

*Allele 1*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCC750

ATCTCCTACTACGAGCTGAACCAGC------------CATTCCACGCC

*Allele 2*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCC750

--------------80 bp deletion----------ATTCCACGCC

*Allele 3*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCC750

--------------72 bp deletion------TTCCACGCC

**HEK293T SMAD2/3 double knockout clone 1**

***SMAD2***

*Allele 1*

 799ACTTACTCAGAACCTGCATTTT-GGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCATTTTTGGTGTTCGATAGCATATTATGAATTAAAT

*Allele 2* and *3* not detected

***SMAD3***

*Allele 1*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAGCT------------CGGGGAGACATTCCACGCCTCGC

*Allele 2*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAG---------------------ACATTCCACGCCTCGC

*Allele 3*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAGCTGAACCAGCG--TCGGGGAGACATTCCACGCCTCGC

**HEK293T SMAD2/3 double knockout clone 2**

***SMAD2***

*Allele 1*

 799ACTTACTCAGAACCTGCATTTTGGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCATT--GGTGTTCGATAGCATATTATGAATTAAAT

*Allele 2*

 799ACTTACTCAGAACCTGCATTTT-GGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTGCATTTTTGGTGTTCGATAGCATATTATGAATTAAAT

*Allele 3*

 799ACTTACTCAGAACCTGCATTTTGGTGTTCGATAGCATATTATGAATTAAAT849

ACTTACTCAGAACCTG--TTTTGGTGTTCGATAGCATATTATGAATTAAAT

***SMAD3***

*Allele 1*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAGCTGAACCAGCG------GGAGACATTCCACGCCTCGC

*Allele 2*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAGCTGAACCAGCGC---------------CACGCCTCGC

*Allele 3*

 703ATCTCCTACTACGAGCTGAACCAGCGCGTCGGGGAGACATTCCACGCCTCGC754

ATCTCCTACTACGAGCTGAACCAGCG--TCGGGGAGACATTCCACGCCTCGC

**HaCaT SMAD4 KO clone 1**

*Allele 1*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT-------AACGAGTTGTATCACCTGGAATTGAT

*Allele 2*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT-insertion 34-bp

*Allele 3*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT----ACGAACGAGTTGTATCACCTGGAATTGAT

*Allele 4*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT-insertion 158 bp

**HaCaT SMAD4 KO clone 2**

*Allele 1*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATATC--TACGAACGAGTTGTATCACCTGGAATTGAT

*Allele 2*

 379TGTGTGAATCCATATCACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATAT-ACTACGAACGAGTTGTATCACCTGGAATTGAT

*Allele 3*

 379TGTGTGAATCCATAT-CACTACGAACGAGTTGTATCACCTGGAATTGAT426

TGTGTGAATCCATATACACTACGAACGAGTTGTATCACCTGGAATTGAT

*Allele 4* not detected

**HaCaT SMAD4 KO clone 3**

*Allele 1*

 1474GTTGATGACCTTCGTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

GTTGATGACCTTCG--GCTTATGCATACTCAGGATGAGTTTTGTGAAA

*Allele 2*

 1474GTTGATGACCTTCGTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

GTTGATGACCTT--TCGCTTATGCATACTCAGGATGAGTTTTGTGAAA

*Allele 3*

 1474GTTGATGACCTTCGT-CGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

GTTGATGACCTTCGTTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA

*Allele 4* not detected

**HaCaT SMAD4 KO clone 4**

*Allele 1*

 1474GTTGATGACCTTCGTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

-------------------TATGCATACTCAGGATGAGTTTTGTGAAA

*Allele 2*

 1474GTTGATGACCTTCGTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

GTTGATGACCTTCG---CTTATGCATACTCAGGATGAGTTTTGTGAAA

*Allele 3*

 1474GTTGATGACCTTCGTCGCTTATGCATACTCAGGATGAGTTTTGTGAAA1521

GTTGATGACCTTCG-insertion 211 bp

*Allele 4* not detected