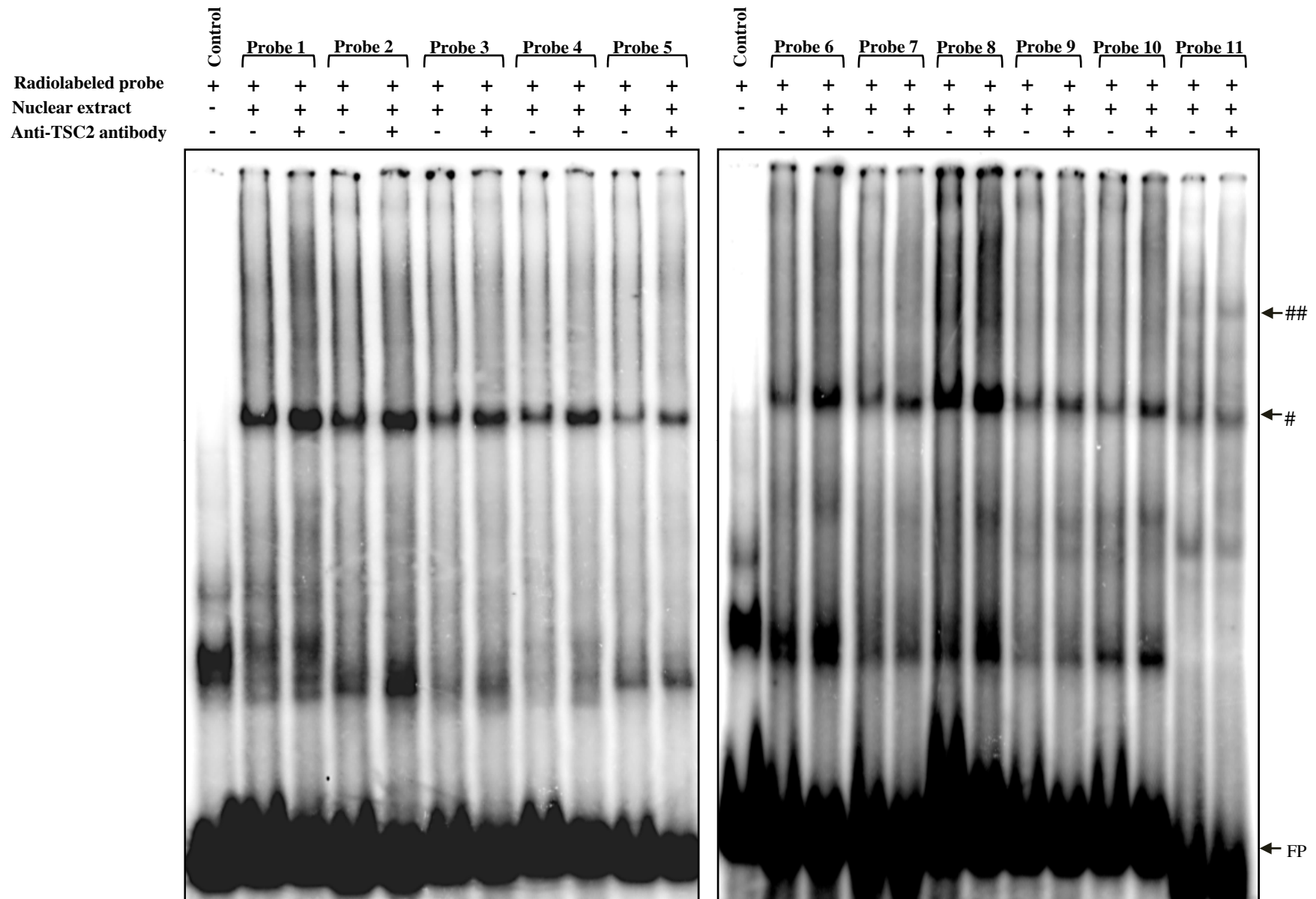


Supplementary Figure S1. Functional annotation of the genes regulated by TSC2. The top 20 functional categories picked up by the IPA software. These functional categories were significantly associated with the microarray data. A $p < 0.05$ was considered to be significant by the IPA software as seen from the threshold marking (red line).



Supplementary Figure S2. Determination of the TSC2 binding region on the *EREG* promoter by EMSA. The end-labeled probes (probes 1-11), together encompassing a region from -857 bp to -303 bp of the *EREG* promoter, were incubated separately with the nuclear lysate from SCC131 cells in the presence or absence of the anti-TSC2 antibody. Note the shift (#) and supershift (##) in the probe 11, showing the binding of TSC2 to the promoter. The control lane represents the end-labeled probe 1 in the absence of the nuclear extract and the anti-TSC2 antibody.

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Probe11 PPP1R14C	GCCT-TGG-----CTAAAAGACT--GATTCAAGT GCCTCTGGGGGCTGGACCGA-GAGGGTCTCGGCGGCTTCTTTAAGGCTGCGGTCCCCGC **** **	26 589
Probe11 PPP1R14C	TATGTC-----CG-----TCACCCTGAGCA CCCCTCGTCCT-CCCCGCCCTCCTCCTCTCGCCGCGGCTCCTCCCGCCTCCAGAGCA . *** ** *.*.*.*.*	46 648
Probe11 PPP1R14C	AC-C----- GC-CGGGCGGCTGGGCGCGCGGCGCAGAGCAGGTGCCGGGAGCCCTTCGC-ATGCGG . * *	49 706
Probe11 SERPI NB13	-----GCCTTGGCT----- TAATGTATGTGTTTCATCAGGCTATACACC-TTTGGTCCAGCGTTGGCTGTACATTGTA ** *****	9 530
Probe11 SERPI NB13	-----AAAA-----GACTGATT----- ATCACCTGCGGTGATAAAAA-TTCTGATGCCTGGTTTCCACTCGAGAGATGCTGACTCAG **** *.*.*.*	21 589
Probe11 SERPI NB13	-----CAAG----- TTGGTCTGGGG-TGGGGCTTGGGCATAGATTTTTTTTAAAGTTCCAAGGAGATTTTAAGG ****	25 648
Probe11 SERPI NB13	----- TG-CACGCAAGGTGGAAAACCACTGCTGAAGCAGATGTGGAGAACTATAAATT-AAGGAT	706
Probe11 SERPI NB13	-----TTATG-----TCCGTCAC----- CCCAGCTACTTAATTGACTTATGCTTCTAGTTCGTTGCCAGCCACCACCGTCTCTCCA ***** :*****:*	38 766
Probe11 SERPI NB13	----CCTGAG-----CAA-----CC----- AAAACCCGAGGTAAGTTCTTATTTTGGCTCCAATTTAAGACCTCTGTATTTTGAAGAA ** *** ** *	49 826
Probe11 MAPK4	-----GCCTTG GA-GCTGGAGCAGCGAGCCGGGCTGTCGGGGCGACCGCGGGAGCTCGCCGTGC-GCCGTG *** **	6 706
Probe11 MAPK4	GCT-----AAAAG----- GCTGGGACCGGCTGGCCGAGCGCGCCGGCGCCGCGGCGCAGACAAAGGGCGGCTCGCG *** .*****	14 766
Probe11 MAPK4	-----ACTGATTC--AAGT----- CCCGGGCCGCCACGCTCTCGGGCTCTGCCTCGGTAAGTGGCTCCCCTCCGCTGGCTTTCT :***. ** *****	26 826
Probe11 MAPK4	-----TATG-----TCCG----- CCTCCCGCCGCTGCGCCTCTCGGAGTTCGGCGGGCTCCGAGAGCGGGGAAGAGATGA *:* *****	34 886
Probe11	----TCACC-----CTG-----AGCAACC-----	49

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MAPK4 GACTTCCCCGCCCCGCACTGCCTCCCCACCTTACCCTAACATAAGCCCCCAGGCCAAGC 946
 **.* ** ** ** **

Probe11 -----GCCTTGGCTAAAAGACTGATT-----CAAG----- 25
 IL18 TTCGACTTCCA-TTGCCTAGGAAAGAGCCTGTTTGAAGCGGGCCCAAGGAGTGCCGAC 648
 *** *.* :**.* **.* **

Probe11 -----TTATGTCC----- 33
 IL18 AG-CAGTCTCCTCCCTCCACCTTCTTCTCATTCTCTCCCAGCTTGCTGAGC-CCTTTG 706
 **.* * **

Probe11 -----GTCACCCTGAGCAA----CC--- 49
 IL18 CTCCCCTGGCGACTGCCTGGACAGTCAGCAAGGAATTGTCTCCAGTGCATTTTGCCCTC 766
 ::*.***: **

Probe11 -----G 1
 ADI P0Q ATACCAGAGGGTAAGAGCAATTCTGTGAAGTTCCAGGCTGGGTGGGGGATGCATGCATAG * 826

Probe11 CCT-TGGCT-----AAAAGACT-----GATTCAAGT- 26
 ADI P0Q CCTCTGGCTGGGATCACCCAGGCTCTCCCGTCCGTAGTAGTGTGGGAGTGGATACAGGTG 886
 *** ***** . . . **.* **

Probe11 -----TATG-----TCCG-T 35
 ADI P0Q GATACTCTGGTCAGAGCAGCACTGGTGGAGGCAGATATGCACTGGGCTTCTTCTCCGTT 946
 ***** ***** *

Probe11 CACCCTGAGCAACC----- 49
 ADI P0Q CTCCCACAGCCCCAAGAGAGAAAAGGTTATTTTCAGACATTCCTTCTAAGATGCA 1000
 *.:***:***. . *

Probe11 -----GCCTTGGCTAAAAGACTGATT-----CAAGTTAT-----GTC--- 32
 MAP1B ACCTCGCCTAGCCTGTGCGACCGCTTCTTGACAGCAAGTTCTACTTGCTGGTGGTCGTC 886
 ****:* **.: . . **.* ** *****.* **

Probe11 -----CGT----- 35
 MAP1B GGCGAGATCGTGACCGAGGAGCACCTGCGGCGTGCCATCGGCAACATCGAGCTCGGTAAG 946

Probe11 -----CACCTGAG-----CAACC----- 49
 MAP1B TGGCCCCGCGCCCCAGAGACGCGCGCTGGGAGACGCGCAAACACGACCCCACC 1000
 *.***:*** *.* **

Probe11 -----GCCTTG 6

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ST6GAL1 AT TTCACCATGTTGGCCAGGATGGTCTCGATCTCCTGACCTCGTGATCCA-CCTGCCTTG 59

Probe11 G---CTAAAAG-ACTG---ATTCAAGT-----TATGT----- 31
 ST6GAL1 GCCTCCCAAAGTGCTGGGAATACAGGCCTGAGCCATCATGC-CTGGACTATGTGTTGGTT 118
* * .***** .*** **.* ** *

Probe11 -----
 ST6GAL1 TCCATGCATGTTTCTGGCGCATAGCCCCATA-GCCCTTGCTACAGTCTTGCTAGAATGC 177

Probe11 -----CCG-----T 35
 ST6GAL1 TGGGCTTTTTAGACTTCAGGGAC-AGGCCCTAAGAAACAGTCTCTCTCCTGCGCTCCTTT 236
*** *

Probe11 CACC-----CTGAG-----CAACC-- 49
 ST6GAL1 CACCTGCCCAAGG-CAAGTTTTTATGTTTTCTGGCCTGACTGTGGCCTTACAACCCT 295
**** **.* *****

Probe11 -----GCCTTGG-----CT 9
 APOC1 AATCCACAAGCAGACAGCCCGCGCCACACCCTGGGCCTGGT-GGTTAAAGATTGACCCCT 118
***** *

Probe11 -----AAAAG-ACTG----- 18
 APOC1 GACCTAATCCGTTAGGTTATCTATAGATTACA-GACATTGTATAGAAAAGCACTGTGAAA 177
***** *****

Probe11 ATCAAGTTATG-----TCCGT-----CACCTG---AGCAA 47
 APOC1 ATCCCTATTCTGTTTTGTTCCGA-TCTAATTACCGGTGCATGCAGCCCCAGTCACGCAT 236
** * .: .**.* **.*: *****: * .*****: * .***:

Probe11 CC----- 49
 APOC1 CCCCTGCTTGTTCA-ATCGATCACGACCCTCTCACGTGCACCCACTTAGAGTTGTGAGCC 295
**

Probe11 -----G-----CCT--TGG-CTAAAA 13
 PCDH9 ACCTATCCTTTGAAAATGTGAGTACCAAGATAAGTGTTCATTACCCTAATGGTCTTCAA 886
* *** **.* **.*: **

Probe11 GACTG-----ATTCAAG-----TTATG----- 30
 PCDH9 AACTATTCTTTAGGGAAATTCATGGAGAAAGTTCATTGACTTTCTGGTCAAGATTCATGC 946
.***. *****: * **.*

Probe11 ----TCCGTCA-----CCCTG---AGCAACC----- 49
 PCDH9 AAATTTTCATCAGTGAAATCCCAAGTCAGAAACTGTGCTGGTAGCACTAGTTAGT 1000
* * .*** **.*: **.*

Probe11 -----GCCTTGGCT----- 9
 ASMT CCAGAGGCTCCGGAAGCCACGGCTGGATTGGAGACAAGATGGGATCCTCAGAGGACCAGG 826

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***: ****
Probe11 -----AAAAGACT-----GATTCAAG-----T 26
ASMT CCTATCGCCTCCTTAATGACTACGCCAACGGCTTCATGGTGTCCAGGTAGGATACGCTC 886
      : ** : ****          * : **** : *

Probe11 TATG-----TCCG----TCACCCT----- 41
ASMT TGTGGGACAAGGGGGAATAGACTTCCGTTTCATCACACTCACGTTCCATTGTTGTGTGTCAGT 946
* . **          ****          **** . **

Probe11 -----GAG-----CAACC----- 49
ASMT CGAGAAAAATGATGAGTCTCCATCATTTTAGGAGGTTTATTTTCCACCGTGAAA 1000
          ***          * . ***

Probe11 -----G-----CCTTGGCTAA-AAGACTG----- 18
FOXF1 CCCGCGTCGTCCGGCCCGTCCAAGGCCAAGAAGACCAACGCCGGCATCCGGCGCCCGGAG 766
      *          ** : : ** * * **** * .

Probe11 -----ATTCA-----AGTTATG----TCCG----TCACCC----- 40
FOXF1 AAGCCGCCCTATTCTACATCGCGCTCATCGTCATGGCCATCCAGAGTTCACCCACCAAG 826
      ****          . ** ** * * *          **** *

Probe11 -----TGAGC-----AACC----- 49
FOXF1 CGCCTGACGCTGAGCGAGATCTACCAGTTCCTGCAGAGCCGCTTCCCCTTCTTCCGGGGC 886

Probe11 -----GCCTT----- 5
HI VEP3 AAGCACCAATAAATGAAATCCTTATCACTGTG-TGCAAGCCTACTGTGCCTTTAGGCATG 177
                                           *****

Probe11 -----GGCT----- 9
HI VEP3 GGACTGGCTTCCTGCGCTGGGAG-TGACAGCTATTCCGAAGTGATAATTGGTGTACTGTG 236
      ****

Probe11 -----AAAAGACTG----- 18
HI VEP3 TCTTTAAAAGGTTA-AACCCCTTTCAAAAAAGGTCTGGACTCCTAGTGAAAAGACAAG 295
          **** . * : **

Probe11 ----- 353
HI VEP3 CGAGG-CATGGGTTGGCTCTGGATTCAGAAAACAGCTGCTGATTAGATTCTGTGTC-TGC

Probe11 -----ATTCAAG----- 25
HI VEP3 AGGCTGAATTTATTCCGTGTTTTTTCAGCAGCACGAATTCAAGAGGGA-TGCTTCTGTTTG 412
          **** *

Probe11 ---TTATGTCCGT-----CA-----CCCT 41
HI VEP3 GGTTCCTGATCGTGATTTATATTTATTAGAGGAATAA-CAGAGGGTGGATCTGTTCCCG 471
      ** . ** : **          **          ***

Probe11 GAGC-----AACC----- 49
HI VEP3 GCGCGAGCATGCTCACAACCAGCCGACTC-TCCATTATCCAGCTGCCTAGTTTGGTGCT 530
* . **          ****

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****. **

Probe11
SLC6A12
-----GCCT--- 4
TTCCGAATGTGCTCCAGGCAGCACCATTT-GCCATCCTGCTTCTAACGCAAACCCCTGAC 530

Probe11
SLC6A12
-----TGG-----CTAAAAGACTGATTCAAG----- 25
TTCATGGATGAGGAACCTGG-AGACCAAAGAGACAAAGGGACTTTTTCAAGTTCACATGG 589
*** *: ** . ***** : *****

Probe11
SLC6A12
-----TTATGTCCGT----- 35
GGACCCCTTC-TTGGGGGCCAGAGATATGACTAAAACCTTATCTCCTTGTGCTCAGGCC 648
***** ** *

Probe11
SLC6A12
-----CACCTG-----AGCAA-----CC----- 49
AG-TGTCTTCCATTAACCCCTGCCTTAGTTAACAAGTGTGTATGGATTGCC-TTCCAT 706
* ***** * ** **

Probe11
SEMA6A
-----GCCT-----TGG---CTAAAAG-- 14
AAGGAGAGAGCGCAGCCCGCGCCCGGAGAGATCCCCTCGATAATGGATTACTAAATGGG 886
*** ** ***** *

Probe11
SEMA6A
--ACTG---ATTCAAGTTA-----TGTCCGTC----- 36
ATACACGCTGTACCAGTTTCGCTCCGAGCCCCGGCCGCCTGTCCGTCGATGCACCGAAAAG 946
** : . *: * ***** *****

Probe11
SEMA6A
----ACCCTGAGCAACC----- 49
GTACGCCCCGGCGCCCGGGCGCGCCCCACCTCCCGGGCAGCTGGACTCCAGCC 1000
. *** * ** . **

Probe11
TNFSF15
-----G-----CCTTGG-----CTA----- 10
AGCTCCTCTGTCTTCATCCTTGG-ATGACCTAGGACAAGTGCCTTCACCTTTTAGAACTT 236
* ***** **

Probe11
TNFSF15
----- 295
TGCTATTCCCATCT-GTACACTGAGAATGAATTTCTATGAGGTTCAAATGACAGAGGGC

Probe11
TNFSF15
-----AAAGA-CTGATTCAA--GTTATGTCCG----- 34
TAGGC-AGCACTTTGCAAAGAGCTGATGCAAATGTGATTTCCGTTTCCCAATCTGC-AAA 353
***** ***** ** ** **

Probe11
TNFSF15
-----TCACC---CTG----- 42
CCACACACCTCTCATCCCTCACTTTCACTTCCAGAAGCACACTCCCC-AGACTGGCACAG 412
** ** **

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Probe11 TNFSF15 -----AGCAACC----- 49
 CTGGTAAGCCTCCAGTGCAGGGAACAGGTATATTTTAA-TTTGCCCCACCCACTGACTTG 471
 ***. : **

Probe11 CDC42EP5 -----GCCTTGG----- 7
 TAGACTCCCACCTGGGCTTCCCA-CCTTCTTCCCCTGAGCTGCATCCTGCCTTGGGACT 236

Probe11 CDC42EP5 -----CTAAAAGACTG----- 18
 CTGCTCTCCCCCTC-CGCTCTCTCTCCCTGCCCGCACCGCCCTGAAGGAATTGCCCTAAC 295
 **. **. **. *

Probe11 CDC42EP5 ATTC-----AGTTATG----- 30
 ACTCA-AACCTCACTCTCTTGTCAATAGACTGGTGCTTAGAATGAGATATG-AGC 353
 * *** ** . *****

Probe11 CDC42EP5 -----TCCG-----TCACC----- 39
 TTTCTATGACGGAGTGGCTCCAGGCAGGGAGGTTTCATCTAGGGGACG-CCGCAGCAAAGC 412
 ***. *** *

Probe11 CDC42EP5 CTGAGCAACC----- 49
 CAGAGCTGCCCTCTCAGACACCCTCCATGCTCTTCAT-CCTCCTGCTGCTTTCCTGCTC 471
 *: *****: **

Probe11 ZFPM1 -----GCCTTGGCT-- 9
 GTGGGGCTCTTGAA-CACACCCCAGAGGGCAACAGTTCTCCATTTCCAGGCCTGAGCTGA 295
 ***** . ***

Probe11 ZFPM1 -AAAA-----GACTGATTCAAGT-----TATG----- 30
 CAGCA-CCGCGCCCAAAACCTCGCTGACCTCTGACTGCTCCGAGAGGGGGCTGTG-GCC 353
 * . * ***** * * . ** : * . **

Probe11 ZFPM1 -----TCCGTC-----ACCCTG----- 42
 CGGGCGCTGTGGGCAACTCCTTCGTGGGTCTCCTGCGGGGCGCCCTG-GAGAGGCTCGGT 412
 *** ** . *****

Probe11 ZFPM1 -----AGCAAC-C----- 49
 GAGGAAAGAGGCCCAAGTGGCAACGCCAGGGCTGCC-GGCTCCCGCGCCCCCTCCTCG 471
 ***** *

Probe11 SOX1 -----G-----CCTTG-----GCTA----- 10
 CAACCGTTGT-GGTGCGGCCACATGTCCTGGAGAGTGTGCAAGACGGGTCGACTTC 648
 * ** ** ** . *

Probe11 -----AAAGACTG-----ATTCAA-----GT----- 26

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SOX1 AC-CAGGACCACGAAAGACAGGGCAGAGTTTCTGTCTTCTTTCACTGTCCCGT-AGAACT 706
 *****.* :***** **

Probe11 --TA---TGTCCGTC-----ACCCTGAGCAA-----C 48
 SOX1 CCTAGCTTGTCCATCGTGCTCCTTGCTTGGGACTCGGGACTGACACTGGGCCAGAAAATC 766
 ** ***** ** ** ** ** ** ** ** *

Probe11 C----- 49
 SOX1 CACCTCTAGATGCCTCAAAGCTCGCTTTCATGCTGGGGGGCGGGCGGGAGCGGGGAAGGG 826
 *

Probe11 -----G----CCTTGG-----CTAAAAGACTG----- 18
 CASKI N1 AATCCCTCGACACCTCCCACGGGAACCCTGGG-CCAGGAACGCCTGACAGCCTGGCGGGC 177
 * *** ** ** ** * . * . * . * . *

Probe11 --ATTCAAG---TTATG----- 30
 CASKI N1 CGGCTCCAGGGGCACTGGCGCCC-GGGTCTCTCGGCGCCCGGTCCCCGCCCGCCCGCTGC 236
 . **.* ** : **

Probe11 -----TCCGTCAC----- 38
 CASKI N1 CTCGGAACCGTCCC-CCGCGGGTCCCGCAGCCTCTGGAAGCCTCTCTGGGCTCAGCCCCG 295
 : ***** *

Probe11 -----CCTGAGCAACC----- 49
 CASKI N1 CGCCG-CCGCCCGCTCGGGGCTCCCAGTGCACCCCCGGCGGCCGCTCCCCAGCCC-GGC 353
 **.* : * ** *

Probe11 -----GCCTTG----- 6
 SOX3 CAACGGGAAGCTTT-GCGGGCTGGCCGGGGGATGGGGCGCCGGTCTGCCTTGACAGGGTT 295

Probe11 GCTAA-----AAG-----ACTG-----ATTCAA-GTT 27
 SOX3 GCAAA-GTTGTTTTCTAAATTCGAAGGCGCCCTCTGCCCTCCCCCAATCTG-CTT 353
 .* ** * : *** * : * : . **

Probe11 ATGT-----CCGTCACC----- 39
 SOX3 GCGTGCCCCCTCCCCCTCCCCCGTCACCTCCTCAGTTTCGTTCT-TTCAAATTTTT 412
 . ** *****

Probe11 -----CTGAG-----CAACC----- 49
 SOX3 GAAACCCTAATTGGTGGCCTCTGAGTGGGCCTCGTGA-CTCCCGCCTCCTAAGTAACTC 471
 ***** * : **

Probe11 -----GCCT----- 4
 KLF16 GGAGTGGGCGCGCCGGGGGGCGGGTTCTCCGGCCGAGCCCCGCC-CCGGCGGCCGCG 412

Probe11 --TGGCTAAAAGACTGATT----- 21
 KLF16 CGCGGCTCGGAGAGTGGTGGAGGGCGCGCCGGGGCGGGG-GGCGTGGCTGCGGCGCCCCGA 471
 ***** ** * *

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Probe11      -----CAAGTTAT-----GTCCGTCA-- 37
KLF16        GGGGGCGTCCTCCGGGCGGGGCGGGCTGT-GGCCGCCCCCGGGGCTCCGGTGCATCAGG 530
                * * * *
                ** * * * *

Probe11      -----
KLF16        ACGCGTCAGGCGGGGCGGGG-CAGGCCGAGCGCGGGCGTCGGCGGGCGGCGCGCCGGGC 589

Probe11      -----CCCT-----GAGCAACC----- 49
KLF16        CTCCTCCTCCT-CCTCCTCCGCTCCCGCACTCGAGCAGCCGCCCGCCGGCCGGACGGACG 648
                ***                * * * * * **
    
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Supplementary Figure S3. Alignment of the probe 11 sequence with promoters sequences of TSC2 regulated genes by the ClustalW2 program. Only the portions of promoter sequences aligning with the probe 11 sequence are shown.