Supplementary data:

Table S1. Effects of TGF-β1 on chromosomal instability in cells expressing HPV16 E6/E7+hTERT

Cell line	Chr. in non-clonal structural aberrations/ 100 cells*	Anaphase bridges (%)	Chr. in clonal structural aberrations/ 100 cells*
NC104-E6E7hTERT			
PD14	13	3	0
PD40	15	2	1
PD70	14	3	2
NC105-E6E7hTERT			
PD14	15	3	0
PD40	18	4	2
PD70	16	2	3
NC104-E6E7hTERT(TGF-β1)			
PD14	12	3	0
PD40	17	3	0
PD70	18	4	2
NC105-E6E7hTERT(TGF-β1)			
PD14	13	5	0
PD40	17	4	2
PD70	19	3	2

*Chr.: Chromosomes.

Table S2. Relative telomere signal intensity in CIN cells with respect to stromal cells in 20 patients

Specimen	Average ratio of telomere signal intensity in CIN to that in stromal cells		*P* value
	Strong TGF-β1 expression*	Weak TGF-β1 expression*	
CIN I	0.35 ± 0.05 (n=3)	- (n=0)	-
CIN II-III	0.31 ± 0.07 (n=14)	0.54 ± 0.08 (n=3)	0.024
Combined	0.32 ± 0.08 (n=17)	0.54 ± 0.08 (n=3)	0.028

*TGF-β1 expression was recorded as strong or weak according to intensity of immunostaining (exemplified in Fig. S5A and C, respectively), and supported by ≥ 50% or < 30% of cells with positive nuclear phosphor-Smad2/3 staining, respectively.

Legends for supplementary figures:

Fig. S1. Growth curves and SKY karyotypes. (*A*-*C*) Growth curves of immortalized cervical epithelial cells derived from three independent donors. (*D*) SKY karyotypes for NC104-E6E7 and NC105-E6E7 cells at a late PD. The red arrows indicate chromosomes with structural aberrations. Karyotype description for (*D, top*): 46,XX,der(20)dup(20)(q?)t(3;20)(q25;q?). Karyotype description for (*D, bottom*): 57,XX,+1,+5,+5,+6,+7,del(7)(q11),+9,+13,+18,+20,+20,+21.

Fig. S2. SKY karyotype for post-crisis NC104-E6E7 (TGF-β1-treated) cells. Karyotype description:
79,XXX,+X,+1,i(3)(q10),+5,+6,+7,+8,der(8;10)(p10;q10),+9,dic(12;14)(qt;pt),+14, der(14;22)(q10;q10),-15,+20,+20,+21,der(21;22)(q10;q10),+22,i(22)(q10)del(q12).

Fig. S3. Western blot analysis for Rad51 expression in NC105-E6E7 and NC104-E6E7 cells treated with 0.3 ng/ml and 0.5 ng/ml TGF-β1, respectively. Actin served as the protein loading control.

Fig. S4. SKY karyotypes for typical clones of NC106-E6E7(SB-431542) at PD40. The arrow indicates the chromosome rearrangement. Karyotype description for clone 1 (*A*): 48,XX,+5,-17,+20,+20,der(20)t(17;20)(p/q?;qt). Karyotype description for clone 2 (*B*): 47,XX,+20.

Fig. S5. Representative images of immunohistochemical and telomere FISH analyses of serial sections of two cases of CIN III with differential expression of TGF-β1. (*A*) Strong

TGF-β1 (mainly in cytoplasm), nuclear phosphor-Smad2/3 expression, and cytoplasmic c-Myc staining in the serial sections of CIN III from the same patient. (*B*) shows telomere FISH signals in the area indicated by a square in (*A*), demonstrating dramatically reduced telomere signal intensities in the CIN region as compared with stromal cells. (*C*) Weak TGF-β1 and phospho-Smad2/3 expression, but strong nuclear c-Myc staining, in another CIN III patient. (*D*) Image of telomere signals in the demarcated area in (*C*), demonstrating marginally reduced telomere signal intensities in the CIN cells as compared with stromal cells.