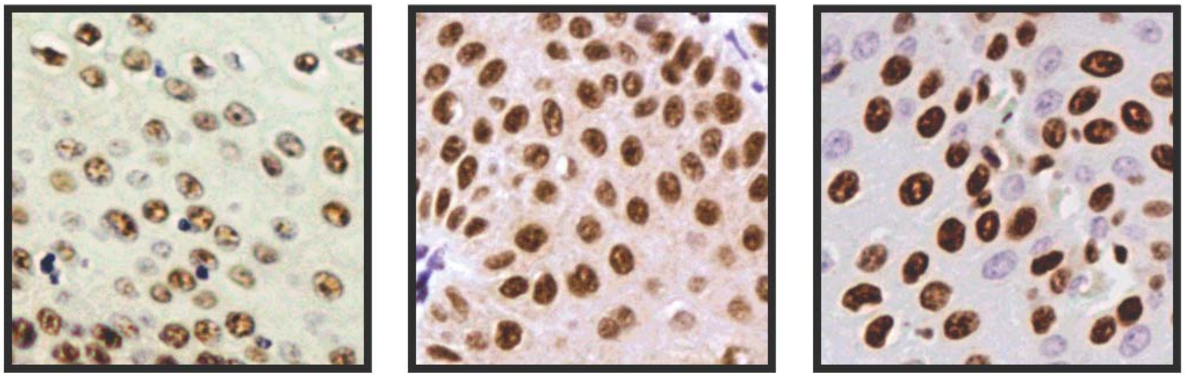
Supplementary Figure 1



ATR DNA-PKcs Ku80

Supplementary Figure 1. Sample photomicrographs of representative tumor sections stained with three DSB repair biomarkers, showing the patterns of nuclear localization expected for each.

Supplementary Table 1

Biomarker	Pathway	Antibody	Dilution
ATM	HR	AbCam: ab32420	1:100
ATR	HR	Cell Signaling: 2790S	1:100
Mre11	HR	Cell Signaling: 4847	1:500
Nbs1	HR	Novus: NBP1-06609	1:100
Rad50	HR	AbCam: ab89	1:400
FANCC	HR	Novus: NBP1-03280	1:500
FANCD2	HR	Novus: NBP1-18976SS	1:200
TP53BP1	HR	Cell Signaling: 4937	1:100
TP53BP2	HR	Novus: NB110-40638	1:100
BRCA1	HR	Novus: NB100-77325	1:100
BRCA2	HR	Novus: NB100-65084	1:50
Rad51	HR	Novus: H00005888-B01	1:100
TOPBP1	HR	AbCam: ab2402	1:100
ATRIP	HR	Cell Signaling: 2737S	1:100
ATRX	HR	Novus: NB100-60685	1:100
Ku80	NHEJ	Cell Signaling: 2180S	1:800
DNA-PKcs	NHEJ	AbCam: ab32566	1:25
Artemis	NHEJ	AbCam: ab35649	1:100
p16	CC	CINtec: 9517	1:3
p21	CC	Novocastra: WAF-1	1:25
p53	CC	Dako: M7001	1:100
Rb	CC	Calbiochem: OP66	1:30
Src	CC	Cell Signaling: 2109	1:800
β catenin	EMT	BD: 610154	1:500
E-cadherin	EMT	Zymed: 13-1700	1:100
Notch1	EMT	Cell Signaling: 3608S	1:100
Shh	EMT	AbCam: ab53281	1:100
Vimentin	EMT	Dako: M0725	1:900
Twist	EMT	AbCam: ab50581	1:500
Osteopontin	Hypoxia	AbCam: ab8448	1:500
PDGFB	Hypoxia	Santa Cruz: SC-7878	1:10
VEGF	Hypoxia	Santa Cruz: SC-152	1:50
EGFR	CSR	Invitrogen: 31G7	1:50
IGFR-1β	CSR	Cell Signaling: 3027	1:150
PTEN	Survival	Dako: M03627	1:100
Survivin	Survival	Cell Signaling: 2808	1:400
ERCC1	NER	AbCam: ab2356	1:100
HPV (ISH)	-	Ventana: 800-4295	-

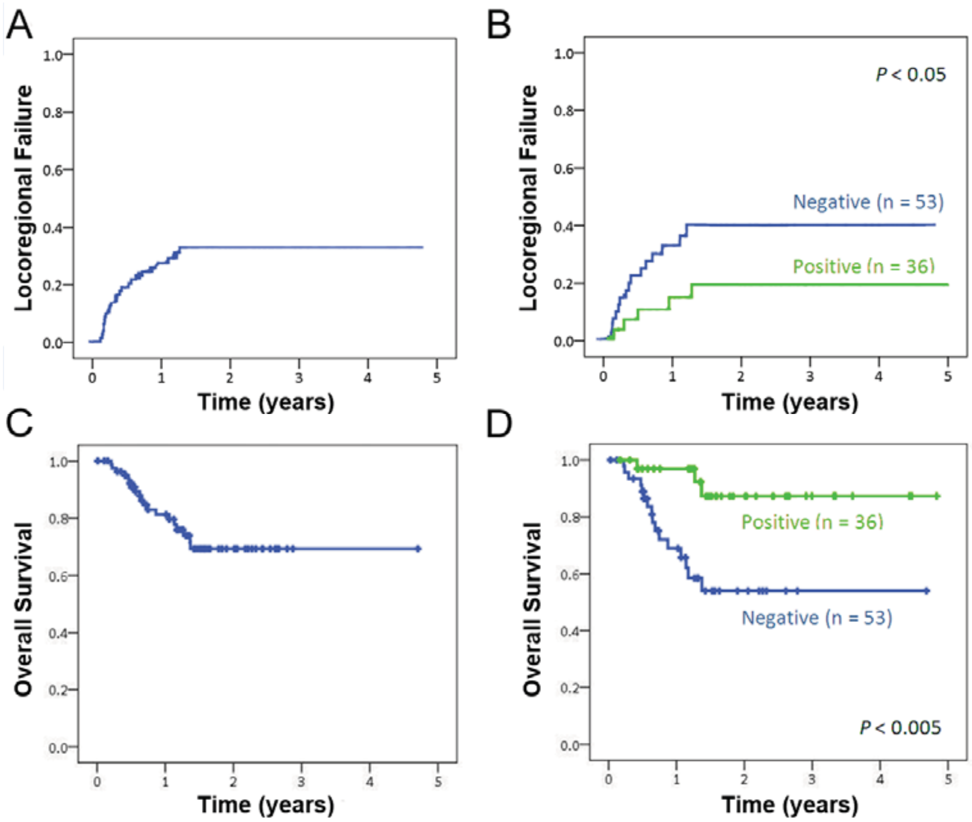
Supplementary Table 1. Antibodies used for biomarker profiling. Vendors and catalog numbers are provided, along with the antibody dilutions used for staining and the canonical pathways represented by each marker. Pathways: CC – cell cycle, CSR – cell surface receptor, EMT epithelial-mesenchymal transition, HR – homologous recombination, NER – nucleotide excision repair, NHEJ – non-homologous end joining.

Supplementary Table 2

Score	Intensity	Percent Positive
Low	0, 1+	0-100%
	2+	5-50%
Medium	2+	55-70%
	3+	5-50%
High	2+	75-100%
	3+	55-100%

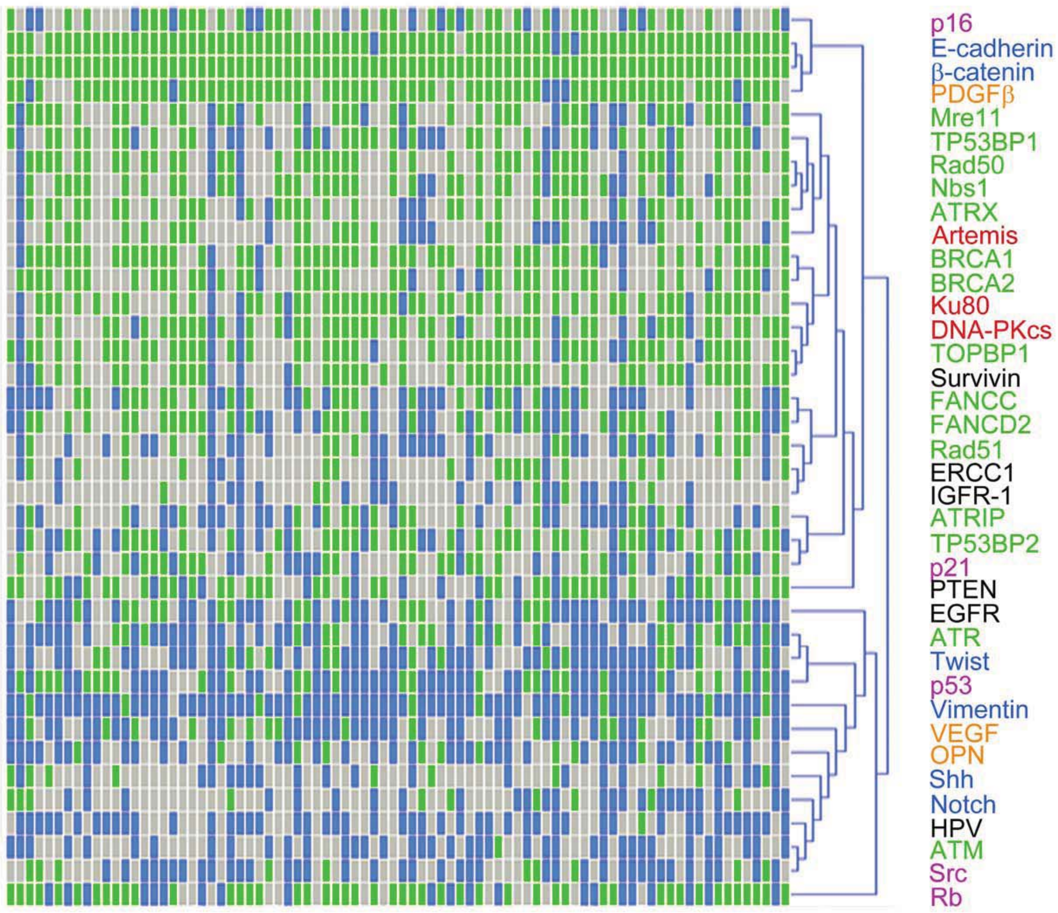
Supplementary Table 2. A summary of the algorithm used to convert IHC staining parameters into an overall expression score for each biomarker studied. Of note, HPV typing by in situ was not scored this way; it was scored as negative vs. positive, per clinical guidelines.

Supplementary Figure 2



Supplementary Figure 2. Cumulative locoregional failure (A and B) and overall survival (C and D) rates for the entire cohort (A and C) as well as the patient subsets stratified by tumor HPV status (B and D).

Supplementary Figure 3



Supplementary Figure 3. A heatmap is shown representing an unsupervised hierarchical clustering of the biomarker set. Biomarker names are colored according to their functional classification: non-homologous end joining (red), homologous recombination (green), cell cycle (purple), epithelial/mesenchymal transition (blue), and hypoxia (orange).

Supplementary Table 3

Endpoint	Biomarker	Spearman's rho Coefficient	Univariate *P* value	Multivariate *P* value
LRC	**Ku80**	0.497	<0.005	**0.05**
	DNA-PKcs	0.395	0.008	NS
OS	**Ku80**	0.503	<0.005	**0.02**
	Shh	0.368	0.01	NS
	BRCA1	0.36	0.02	NS
	DNA-PKcs	0.357	0.02	NS

Supplementary Table 3. Linear univariate and multivariate modeling of locoregional control (LRC) and overall survival (OS) probabilities as a function of clinical and biomarker covariates for the HPV-negative subset of the testing cohort. Positive correlations imply a larger risk of failure for increasing expression values. NS = not significant ($P > 0.05$).

Supplementary Table 4

Endpoint	Biomarker	Spearman's rho Coefficient	Univariate *P* value	Multivariate *P* value
LRC	Ku80	0.450	0.007	NS
	ATM	0.432	0.01	**0.03**
	p53	0.376	0.03	NS
	ATR	0.370	0.01	**0.03**
	E-cadherin	- 0.342	0.02	**0.04**
OS	**VEGF**	0.373	0.02	**0.04**
	Ku80	0.361	0.04	NS

Supplementary Table 4. Linear univariate and multivariate modeling of locoregional control (LRC) and overall survival (OS) probabilities as a function of clinical and biomarker covariates for the HPV-positive subset of the testing cohort. Positive correlations imply a larger risk of failure for increasing expression values. NS = not significant ($P > 0.05$).