Supplemental material

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Gut

Supplementary Table 1. Details on experimental conditions during multiplex qIHC staining

Antibody	Antigen Retrieval	Primary Antibody	Secondary Antibody)/ dilution	Hoechst 33342	TSA/ dilution
Anti-MCM2	Steaming at pH.6.0, 20 mins	1:1000	Anti-Rabbit, 1:1000	1:100	Opal 520, 1:100
Anti-γH2AX	Microwaving at pH 9.0, 16 mins	1:1000	Anti-Mouse, 1:1000	1:100	Opal 690, 1:100
Anti-EpCAM, Anti-pan-Cytokeratin	Steaming at pH.6.0, 20 mins and microwaving at pH 6.0, 16 mins	1:250 (EpCAM), 1:1000 (pan-Cytokeratin)	Anti-Mouse, 1:1000	1:100	Opal 570, 1:100
Anti-CD44v9	Steaming at pH 9.0, 20 mins	1:100	Anti-Rat (Alexa Fluor 488), 1:200	1:100	NA

Supplementary Table 2. Scoring of Ki67 and MCM2 staining in human gastric samples.

Sample	Ki67/MCM2-Tissue (A)	Ki67/MCM2-Tissue (B)	Ki67/MCM2-Tissue (C)
Normal	<10%/<10%	<10%,/<10%	<1%/<1%
Gastritis	40%/40%	50%/50%	30%/20%
IM	30%/70%	40%/60%	15%/5%

Supplementary Table 3. Patient details for TMA used for MCM2 staining

Clinicopathological features	Normal	Inflammation	Intestinal Metaplasia
	N=6	**N=6**	**N=6**
Age (Mean)	40.5	57.7	55.5
Age range	16-56	53-69	40-74
Sex			
Male	5	3	5
Female	1	3	1

Supplementary Table 4. Patient details for TMA with IM and IGC cores

Clinicopathological features	Intestinal Metaplasia	Adenocarcinoma
	N=26	**N=14**
Age (Mean)	58.9	58.1
Age range	32-74	43-68
Sex		
Male	23	11
Female	3	3

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Supplementary Table 5. Patient details for TMA used γH2AX staining

Clinicopathological features	Normal	Inflammation	Intestinal Metaplasia
	N=7	N=8	N=6
Age (Mean)	37.4	58.6	55.5
Age range	16-50	52-71	40-74
Sex			
Male	6	4	5
Female	1	4	1

Supplementary Table 6. Patient details for GCEP samples used for γH2AX staining

Clinicopathological features	Normal	Gastritis	Intestinal Metaplasia
	N=6	N=7	N=6
Acute Inflammation			
Negative	6	3	3
Mild/Moderate	-	3	3
Marked	-	1	-
Chronic Inflammation			
Negative	6	-	-
Moderate	-	-	3
Marked	-	7	3
H. pylori status			
Negative	6	2	5
Mild/Moderate	-	3	1
Marked	-	2	
Atrophy			
Negative	6	7	-
Mild/Moderate	-	-	3
Marked	-	-	1
Unknown	-	-	2
Smoking			
Y	-	1	3
N	6	6	3
Alchohol			
Y	-	1	1
N	6	6	5

Supplementary Table 7. Patient details for MCM2 and γH2AX staining of gastric tissues with different extents of inflammation

Clinicopathological features	
	N=9
Inflammation Score	
Negative	3
Mild/Moderate	6
Marked	-
***H. pylori* status**	
Negative	9
Positive	-

Supplementary Table 8. Patient details for MCM2 and γH2AX staining of IM samples from GCEP with different extents of genomic instability

Clinicopathological features	Genome stable	Genome unstable
	N=8	**N=7**
Chronic Inflammation		
Negative	1	-
Mild/Moderate	7	7
Marked	-	-
Acute Inflammation		
Negative	7	6
Mild/Moderate	1	1
Marked	-	-
Atrophy		
Negative	2	1
Mild/Moderate	3	2
Marked	-	-
Unknown	3	4
***H. pylori* status**		
Negative	7	7
Positive (mild)	1	-
IM status		
Mild/Moderate	-	1
Marked	8	6

Supplementary Table 9. Correlation analysis between CD44v9 and γH2AX in IM samples

	Sample ID*	Category	*r*	p-value
1	**#1**	Genome-stable	-0.629	< 0.00001
2	**#3**	Genome-stable	-0.476	< 0.00001
3	**#6**	Genome-stable	-0.576	< 0.00001
4	**#7**	Genome-stable	-0.7	< 0.00001
5	**#8**	Genome-stable	-0.658	< 0.00001
6	**#9**	Genome-unstable	-0.628	< 0.00001
7	**#12**	Genome-unstable	-0.547	< 0.00001
8	**#13**	Genome-unstable	-0.653	< 0.00001
9	**#14**	Genome-unstable	-0.416	< 0.00001
10	**#15**	Genome-unstable	-0.401	< 0.00001

Supplementary Table 10. An integrated view of alterations observed in the genome-unstable IM lesions subjected to genomic and IHC analysis.

	Sample ID*	% CD44V9+	Mutation No.	Mutation	CNA segments	Methylation cluster	Hypermethylation
				Mutation in DNA repair genes			Hypermethylation of DNA repair genes
1	**#9**	10.79	25	No	1	High	Yes
2	**#10**	NA**	28	*ATM*	0	High	Yes
3	**#11**	NA**	51	*FANCA, HLTF, REV3L, POLE*	0	Intermediate	No
4	**#12**	13.9	14	No	3	High	Yes
5	**#13**	1.31	28	No	0	NA**	NA**
6	**#14**	34.17	38	No	1	High	Yes
7	**#15**	6.33	23	No	1	NA**	NA**