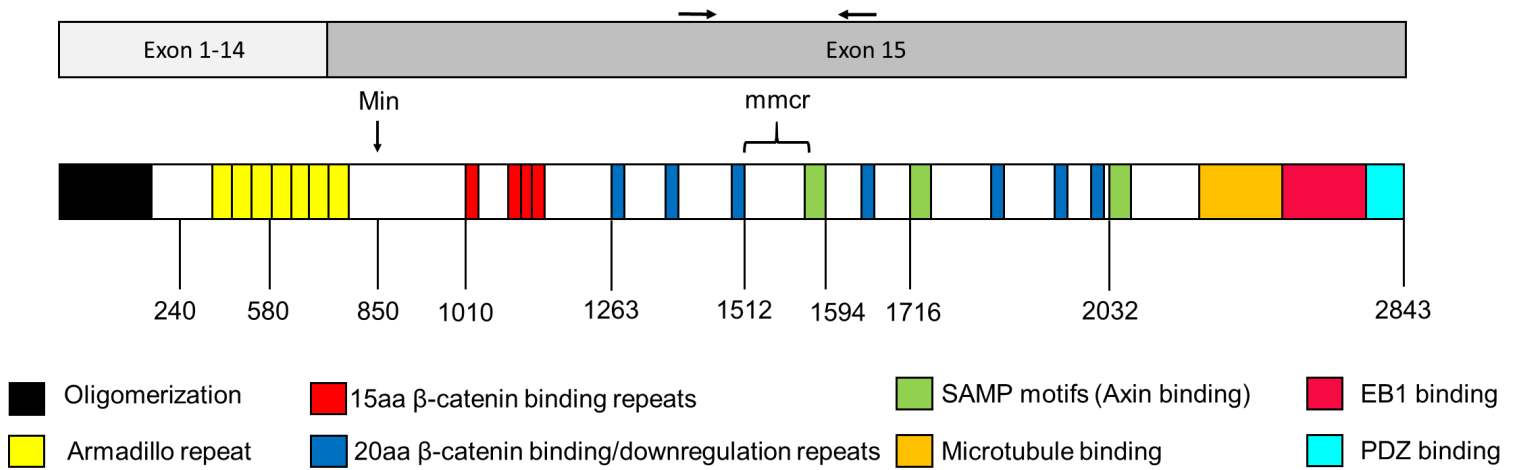


**Supplementary Figure 1.** Schematic depiction of the *Apc* gene transcript (upper) and the corresponding Apc protein (lower) with the codon number corresponding to functional domains. Location of germline *Apc*<sup>min</sup> and somatic *Apc*<sup>mmcr</sup> mutations are shown. Arrows represent primers used to amplify the *Apc*<sup>mmcr</sup> region from genomic DNA templates for DNA sequencing.



**Supplementary Table 1. Distribution of *Apc*<sup>mmcr</sup> mutations across individual mice.** Each “x” represents an independent tumor with the indicated mutation. M1, M2...M14 indicate individual mice. M1-M8 were exposed to DMBA. M9-14 were exposed to ENU.

<b>DMBA</b>	M1	M2	M3	M4	M5	M6	M7	M8
1512 G>T		x	x				x	
1517 A>T	xxx					x		x
1520 G>T					x			
1522 A>T		x		x	xx	xxx	x	
1529 G>T						x		
1535 G>T					x		x	
1540 C>T								x
1542 G>T	xx		xx		xx		x	
1543 G>T			x	x				
1550 A>T	xxx			x	x	xx	xxx	
1554 A>T						x		
1558 G>T						x		
1559 A>T							x	
1517 Δ		x						
1530 +T							xx	x
1547 +T								x
1554 +T			x					
1559+T					x			
1560 +G				x				
Wt		xx	x	x	xx		xx	

<b>ENU</b>	M9	M10	M11	M12	M13	M14
1516 C>T	xx		x	x	x	
1521 T>G					x	
1528 C>T				x		x
1529 G>T	x	x	x			
1535 G>T					x	
1538 C>A		x				
1540 C>T	x	xx				
1544 C>A	x					
1548 C>T		xx	xx	xx		
1561 T>A		xx				
1562 T>A		xx				
1562 T>G			x			xx
1571 G>T		xxx				
1573 T>A						x
1575 G>T			x			
1576 T>A	x	x	x	xx	x	xx
1560 Δ						x
Wt		x	x	xxx	xxxx xxx	

**Supplementary Table 2. Strand-biased mutations are pervasive across a range of sequence contexts.** No one context was a hallmark of a single strand for either adenines or thymines, arguing against sequence-context dependent adduct formation.

\*Corresponds only to the NPBP. The bases 5' or 3' do not necessarily overlap with the indicated codon.

### DMBA Exposure

<u>Sense Strand Adenines</u>						<u>Antisense Strand Adenines</u>					
<u>Codon*</u>	<u>5'</u>	<u>NPBP</u>	<u>3'</u>	<u>mutation</u>	<u># mutants</u>	<u>Codon*</u>	<u>5'</u>	<u>NPBP</u>	<u>3'</u>	<u># mutants</u>	
1517	G	A	A	A>T	5	1576	T	A	C	0	
1522	A	A	G	A>T	8	1573	T	A	A	0	
1550	T	A	A	A>T	10	1562	T	A	A	0	
1554	A	A	A	A>T	1	1561	T	A	A	0	
1559	A	A	A	A>T	1	1521	T	A	A	0	

### ENU Exposure

<u>Sense Strand Thymines</u>						<u>Antisense Strand Thymines</u>					
<u>Codon*</u>	<u>5'</u>	<u>NPBP</u>	<u>3'</u>	<u>mutation</u>	<u># mutants</u>	<u>Codon*</u>	<u>5'</u>	<u>NPBP</u>	<u>3'</u>	<u># mutants</u>	
1521	T	T	A	T>G	1	1559	T	T	T	0	
1561	T	T	A	T>A	2	1554	T	T	T	0	
1562	T	T	A	T>A	2	1550	T	T	A	0	
				T>G	3	1522	C	T	T	0	
1573	T	T	A	T>A	1	1517	T	T	C	0	
1576	G	T	A	T>A	8						