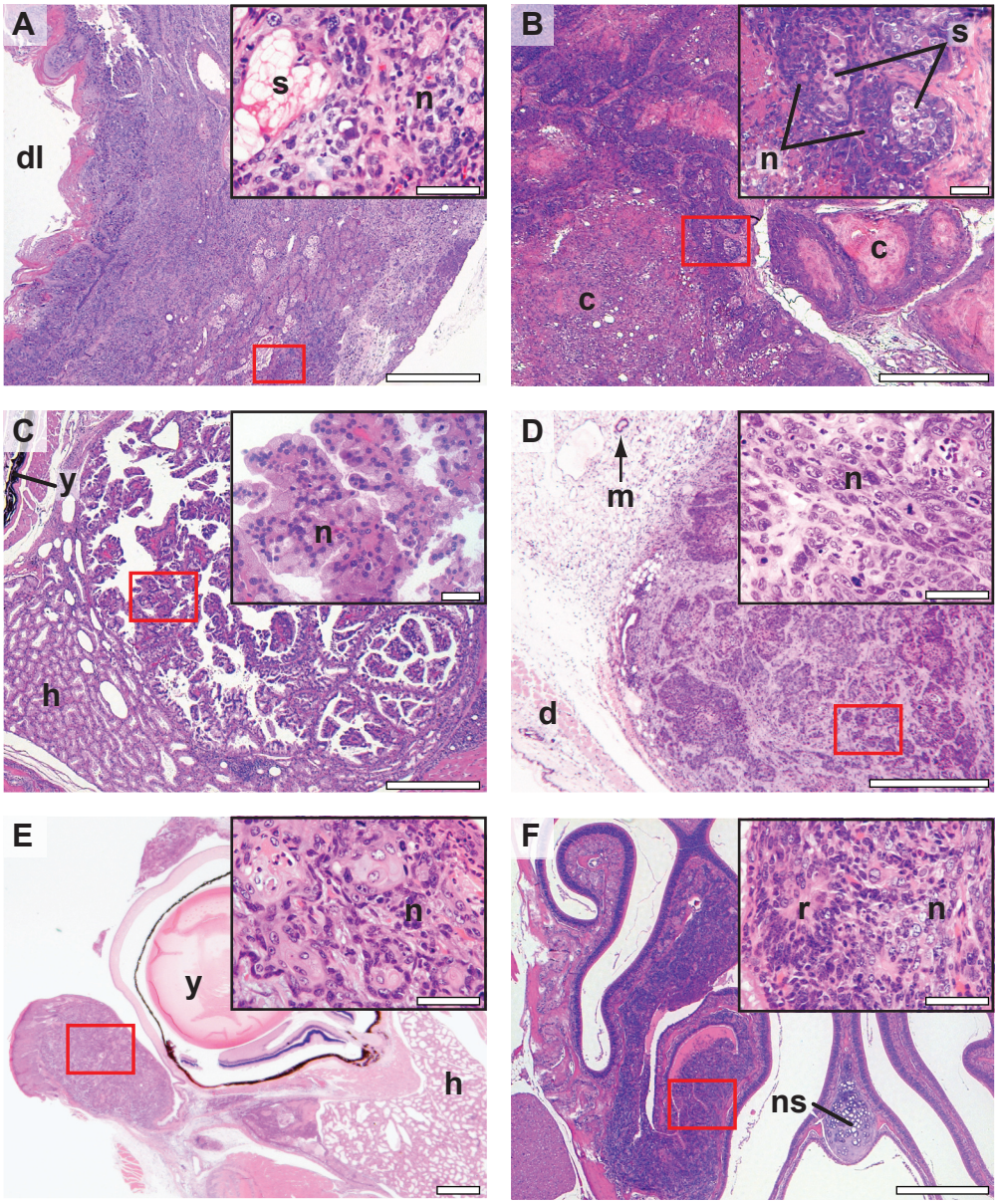
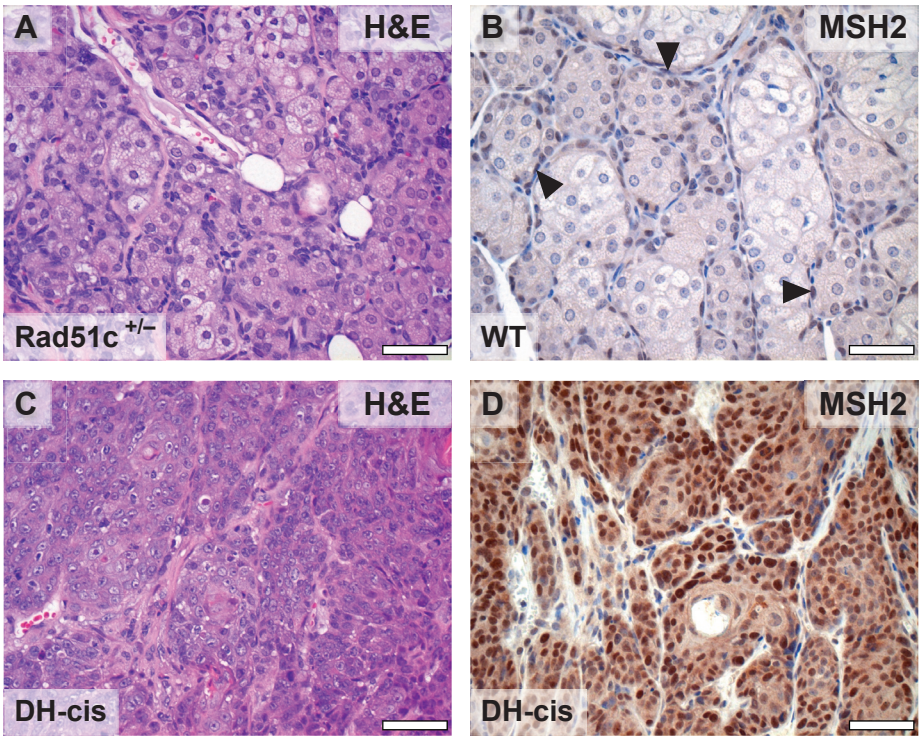
Supplementary Figure 1



Supplementary Figure 1. Histology of tumors characteristic for *Rad51c* mutants. (**A**) Preputial gland carcinoma in a *DH-cis* male. (**B**) Zymbal's gland carcinoma in a *DH-cis* male; (**C**) Harderian gland adenoma in a *Rad51c*$^{ko/+}$ male. (**D**) Mammary gland carcinoma in a *DH-cis* female. (**E**) Basal cell carcinoma, skin/subcutis, possibly Meibomian gland, in a *DH-cis* female; (**F**) Neuroepithelial carcinoma in a *DH-cis* male; Bowman's gland area, nasal section. Area shown in insets is marked with a red frame in each respective figure. s, normal sebaceous cells; n, neoplastic epithelial cells; dl, duct lumen; c, sebaceous cyst lumen; y, eye; h, Harderian gland; ns, nasal septum; r, neural rosettes. Scale bar corresponds to 500 µm in the main figures and to 50 µm in the insets.

Supplementary Figure 2



Supplementary Figure 2. Msh2 is not downregulated in preputial gland carcinomas in *DH-cis* mice. (**A** and **B**) normal control preputial gland stained with hematoxylin and eosin (H&E) and with antibodies against Msh2 (MSH2), respectively. Arrowheads indicate Msh2-positive basal cells. (**C** and **D**) Preputial gland carcinoma from a *DH-cis* male stained the same way as the controls. Note the number of cells staining strongly positive for Msh2 in (D). Genotype is indicated in the lower left corner for each image. Scale bar corresponds to 50 μm.

Supplementary Table 1. *Rad51c* is essential for embryo viability.

Developmental stage	Number of litters dissected	Total number of embryos	Portion of Phenotypically abnormal embryos		Portion of Phenotypically normal embryos		Empty decidua, lost, or genotype not determined	Deviation from expected mendelian distribution[†], *P*-value (χ2-test)
			ko/ko	ko/+	ko/+	+/+		
E5.5	2	22	5 (23%)		17 (77%)		0	0.805
E6.5	5	57	12 (21%)		44 (79%)		1	0.531
E7.5*	12	132	38 (29%)		94 (71%)		1	0.236
	3	31	5 (18%)	0 (0%)	21 (68%)	5 (16%)	1	0.272
E8.5*	12	126	49 (39%)		77 (61%)		0	**0.0004**
	5	50	16 (32%)	2 (13%)	18 (36%)	14 (28%)	6	0.540
E10.5*	5	51	14 (27%)[§]		37 (73%)		0	0.686
	2	22	5 (23%)[§]	0 (0%)	8 (36%)	9 (39%)	1	0.213
Newborn	59	395	0 (0%)	0 (0%)	239 (61%)	256 (39%)	0	**2.723E-30 (0.009)**[‡]

*Shaded fields indicate litters, from which embryos have been genotyped.
[†]Deviation from the Mendelian 1:2:1 genotype and 1:3 phenotype ratio was tested. Statistically significant differences are highlighted in bold.
[‡]The number of *Rad51c*$^{ko/+}$ and wild-type progeny was tested against 2:1 ratio.
[§]Embryos were almost resorbed.

Supplementary Table 2. Complete list of observed neoplasms grouped by target organ, gender, and genotype.

Target organ and tumor type	Females					Males				
	WT	Rad51c$^{ko/+}$	Trp53$^{ko/+}$	DH-trans	DH-cis	WT	Rad51c$^{ko/+}$	Trp53$^{ko/+}$	DH-trans	DH-cis
Adrenal										
Pheochromocytoma	-	-	-	-	-	-	-	-	1	-
Bone										
Osteosarcoma	-	2	5	11	7	-	-	-	1	-
Cecum										
Adenoma	-	-	-	-	-	-	1	-	-	-
Epididimis										
Hemangioma	-	-	-	-	-	-	-	-	-	1
Fat pads, gonadal										
Hemangiosarcoma	-	-	-	-	-	-	-	-	-	1
Hematopoietic neoplasm										
Lymphoma, small cell	-	-	-	1	2	-	-	1	-	-
Lymphoma, follicular center cell (B-cell)	-	1	1	4	1	-	-	1	-	2
Lymphoma, diffuse large cell (B-cell)	-	-	-	-	-	-	-	-	1	-
Lymphoma, splenic marginal zone	-	-	-	1	-	-	-	-	-	-
Lymphoma, NOS	-	-	1	1	-	-	-	1	1	1
Histiocytic sarcoma	-	-	-	2	-	-	-	2	1	-
Mast cell sarcoma	-	-	-	1	-	-	-	-	-	2
Liver										
Adenoma, hepatocellular	-	-	-	-	-	-	-	-	1	-
Cholangiocarcinoma	-	-	-	-	-	-	-	-	1	-
Lung										
Adenoma, alveolar Type II cell		2	-	2	-	-	2	3	1	1
Carcinoma, alveolar Type II cells	-	2	-		-	1	1	3	-	-
Mammary gland										
Adenocarcinoma	-	2	3	1	7	-	-	-	-	-
Muscle										
Rhabdomyosarcoma	-	-	-	-	2	-	-	5	5	1
Sarcoma, NOS	-	-	-	-	-	-	1	6	8	5
Hemangiosarcoma	-	-	1	-	-	-	-	-	-	-
Mediastinum										
Myxosarcoma	-	-	-	1	-	-	-	-	-	-
Mesentery										
Hemangiosarcoma	-	-	-	-	-	-	-	-	-	1
Ovary										
Cystadenoma	-	-	-	-	-	-	-	-	-	-
Granulosa cell tumor	-	-	-	-	-	-	-	-	-	-
Hemangiosarcoma	-		-	1	2	-	-	-	-	-
Pituitary										
Adenoma, pars distalis	2	2	-	-	1	-	-	-	-	-
Salivary gland										
Myoepithelioma	-	-	-	-	1	-	-	-	-	-
Sebaceous glands										
Preputial gland carcinoma	-	-	-	-	-	-	-	-	1	10
Zymbal's gland adenocarcinoma	-	-	-	2	-	-	-	1	-	5
Spinal cord										
Neurofibrosarcoma	-	-	-	-	-	-	-	-	-	1
Spleen										
Hemangiosarcoma	-	-	-	-	1	-	-	-	-	-
Skin										
Hemangiosarcoma	-	-	1	-	1	-	-	-	-	-
Myxosarcoma / myxoma	-	-	-	-	-	-	-	-	1	-
Squamous cell papilloma	-	-	-	-	2	-	-	-	-	-
Squamous cell carcinoma	-	-	-	-	1	-	-	-	1	2
Sarcoma, NOS	-	-	-	-	-	-	-	-	1	-
Mast cell tumor	-	-	-	-	-	1	-	-	-	-
Trichoepithelioma	-	-	-	-	-	-	-	-	-	-
Testis										
Neoplasm, NOS	-	-	-	-	-	1	-	-	-	-
Thyroid										
Adenoma, follicular cells	-	-	-	-	1	-	-	-	-	-
Urinary bladder										
Submucosal mesenchymal tumor	-	-	1	-	-	-	-	-	-	-
Uterus										
Polyp, endometrial	-	-	-	-	2	-	-	-	-	-
Leiomioma	-	-	-	1	-	-	-	-	-	-
Hemangiosarcoma	-	-	-	-	-	-	-	-	-	-
Muzzle area										
Harderian gland adenoma / carcinoma	1	1	-	-	-	-	2	1	1	1
Bowman's gland neuroepithelial carcinoma	-	-	-	-	-	-	-	1	-	1
Olfactory neuroblastoma	-	-	-	1	1	-	-	-	-	1
Meibomian gland, squamous cell carcinoma	-	-	-	-	1	-	-	-	-	1
Vomeronasal neuroepithelial carcinoma	-	-	-	-	1	-	-	-	-	-
Squamous cell carcinoma	-	-	-	-	1	-	-	-	-	1
Carcinoma, NOS	-	-	-	-		-	-	-	1	-
Total number of animals	17	38	11	26	23	21	32	20	24	24
Number of animals that died by 600 days	2	12	10	25	23	3	9	16	23	23
Total number of animals with neoplasms	2	7	8	21	22	2	6	16	22	22
Total number of primary neoplasms	3	12	13	30	35	2	7	25	27	38

Supplementary Table 3. Quantification of Rad51 and γH2AX foci in *Rad51c*-deficient and control MEFs.

Genotype	Treatment	Total number of cells counted	Average number of Rad51 foci per cell	Average number of γH2AX foci per cell	P-value*
wt	none	62	2.3	4.5	n.a.
***Rad51c*$^{ko/+}$**	none	64	2.0	3.4	0.380
***Trp53*$^{ko/ko}$**	none	55	1.9	3.1	0.350
***Rad51c*$^{ko/ko}$*; Trp53*$^{ko/ko}$**	none	50	0	10.6	**0.001**
wt	IR	55	16.2	48.3	n.a.
***Rad51c*$^{ko/+}$**	IR	52	18.7	49.0	0.507
***Trp53*$^{ko/ko}$**	IR	50	29.1	67.3	**0.007**
***Rad51c*$^{ko/ko}$*; Trp53*$^{ko/ko}$**	IR	51	0	37.5	**<0.001**

*Statistically significant differences from wild-type cells are highlighted in bold (Wilcoxon text).