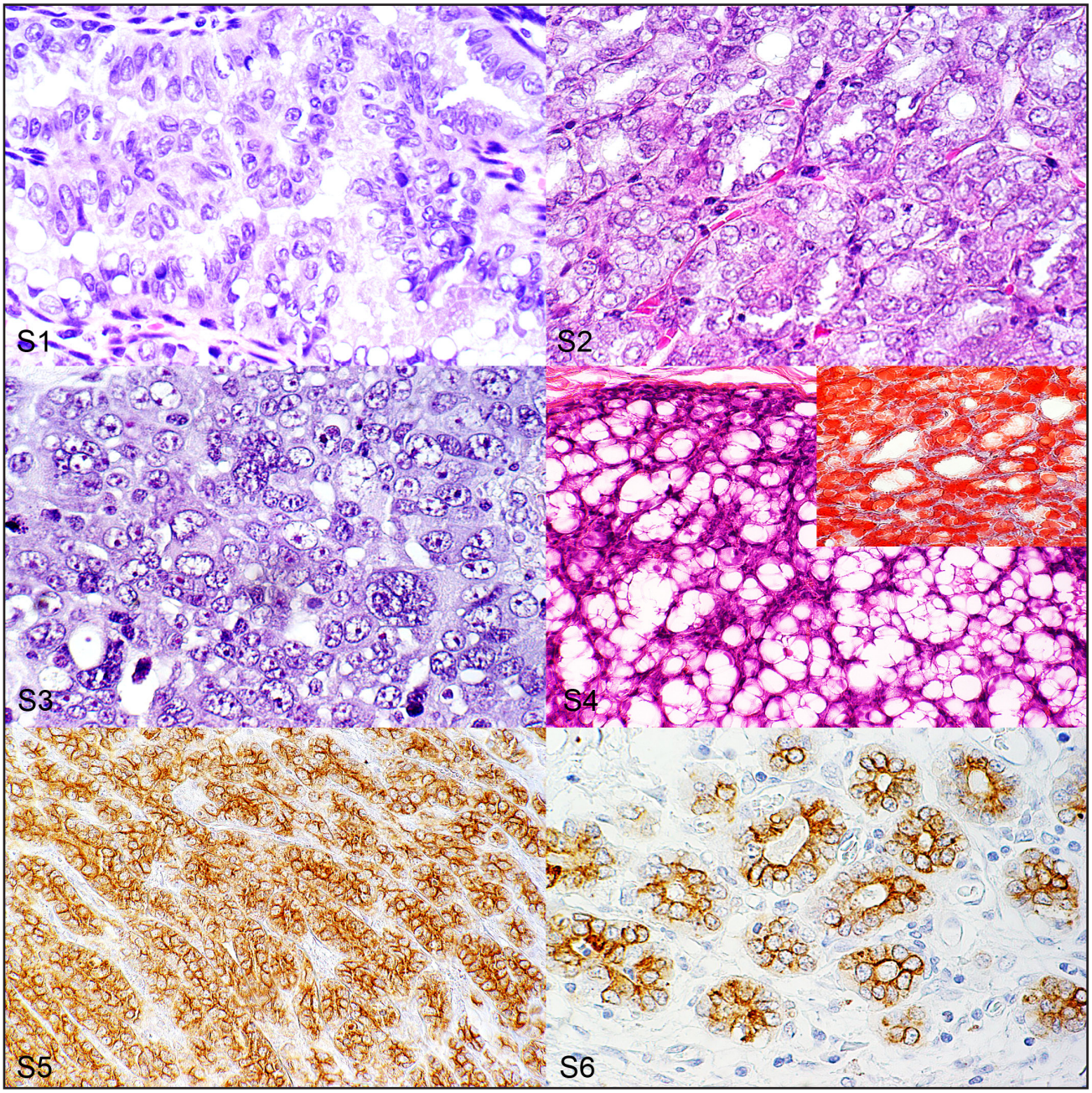
Veterinary Pathology: Supplemental Materials.
Degner et al. Estrogen receptor-α and progesterone receptor expression in mammary proliferative lesions of female pet rabbits.



Supplemental Figures S1-S3. These figures illustrate the nuclear findings in pet rabbit mammary carcinomas with mild (S1: rabbit No. 29), moderate (S2: rabbit No. 15) or marked nuclear pleomorphisms (S3: rabbit No. 8).

Supplemental Figure S4. Carcinoma, mammary gland, rabbit No. 65. The tumor is well differentiated (grade I) with a solid growth pattern. Numerous neoplastic cells contain clear intracytoplasmic vacuoles. Hematoxylin and eosin (HE). Inset: The intracytoplasmic vacuoles are confirmed as lipid droplets. Sudan red stained cryostat section of formalin-fixed tumor tissue.

Supplemental Figures S5-S6. Estrogen receptor-α and progesterone receptor immunonegative carcinoma (S5) and adjacent normal mammary tissue (S6), rabbit No. 52. Tumor cells of the carcinoma (S5) and epithelial cells of the adjacent mammary gland parenchyma (S6) are strongly cytokeratin immunopositive.

Supplemental Table S1. Mitotic counts and expression of estrogen receptor-α and progesterone receptor in proliferative mammary lesions of 124 pet rabbits.

Prolif. lesions (#;%)	MC[a] MV±SD	ERα-/PR- # (%)	ERα-/PR+ # (%)	ERα+/PR- # (%)	ERα+/PR+ # (%)
Carcinoma (119)	**6.3±6.3**	**75/119 (63%)**	**20/119 (17%)**	**2/119 (2%)**	**22/119 (18%)**
T (79/119;66%)	8.0±7.6	56/79 (71%)	12/79 (15%)	1/79 (1%)	10/79 (13%)
C (14/119;12%)	4.0±3.3	3/14 (21%)	3/14 (21%)	0/14 (0%)	8/14 (58%)
S (12/119;10%)	4.0±5.2	8/12 (67%)	3/12 (25%)	0/12 (0%)	1/12 (8%)
P (6/119;5%)	7.0±7.9	2/6 (33%)	0/6 (0%)	1/6 (17%)	3/6 (50%)
T, S (4/119;3%)	6.0±3.1	3/4 (75%)	1/4 (25%)	0/4 (0%)	0/4 (0%)
T, P (2/119;2%)	6.0±1.5	1/2 (50%)	1/2 (50%)	0/2 (0%)	0/2 (0%)
T, C (2/119;2%)	12.0±10.0	2/2 (100%)	0/2 (0%)	0/2(0%)	0/2 (0%)
Gr. I[b] (68/119;57%)	3.0±2.4	40/68 (59%)	12/68 (18%)	1/68 (1%)	15/68 (22%)
Gr. II[c] (49/119;41%)	10.3±7.1	34/49 (70%)	7/49 (14%)	1/49 (2%)	7/49 (14%)
Gr. III[d] (2/119;2%)	13.0±6.0	1/2 (50%)	1/2 (50%)	0/2 (0%)	0/2 (0%)
CIS (2)	**4.0±1.5**	**0/2 (0%)**	**0/2 (0%)**	**0/2 (0%)**	**2/2 (100%)**
Adenoma (3)	**1.4±1.0**	**0/3 (0%)**	**0/3 (0%)**	**2/3 (67%)**	**1/3 (33%)**
L. Hyperpl. (2)	**n/a**	**0/2 (0%)**	**1/2 (50%)**	**1/2 (50%)**	**0/2 (0%)**
Cysts (25)	**n/a**	**8/25 (32%)**	**7/25 (28%)**	**0/25 (0%)**	**10/25 (40%)**
NMG (123)	**n/a**	**31/123 (25%)**	**30/123 (24%)**	**12/123 (10%)**	**50/123 (41%)**

Prolif, proliferative
#, number of cases
%, percentage of cases
[a]MC, Mitotic count, i.e. numbers of mitotic figures in 10 40x high-power fields (diameter of the 400x field of view: 159 μm^2)
MV±SD, Mean value±Standard deviation
ERα-/PR-, estrogen receptor-α negative and progesterone receptor negative
ERα-/PR-, estrogen receptor-α negative and progesterone receptor positive
ERα+/PR-, estrogen receptor-α positive and progesterone receptor negative
ERα+/PR+, estrogen receptor-α positive and progesterone receptor positive
T, tubular. C, cystic. S, solid. P, papillary
T, S, tubular and solid
T, P, tubular and papillary
T, C, tubular and cystic
[b]Gr. I, Grade I: well differentiated (Elston and Ellis, 1991)
[c]Gr. II, Grade II: moderatly differentiated (Elston and Ellis, 1991)
[d]Gr. III, Grade III: poorly differentiated (Elston and Ellis, 1991)
CIS, carcinoma *in situ*
L. Hyperpl., lobular hyperplasia
NMG, normal mammary gland
n/a, not applicable

Supplemental Table S2. Histologic features of carcinomas and carcinomas in *situ* in 121 female pet rabbits.

							Secr Activity[h]		Invasion[i]				
#[a]	D[b]	Growth[c]	T%[d]	MC[e]	NPM[f]	Necr[g]	P Sec	VCs	Str	PT	EM[j]	Sc[k]	Gr[l]
1	C	T,S,C	60	6	2	2	3	3	3	3	1	6	II
2	C	S,C, T	5	2	2	2	4	3	3	3	1	6	II
3	C	T,C	90	2	2	2	4	3	2	3	1	5	I
4	C	T	100	5	2	1	5	4	2	2	1	4	I
5	C	T,C,S	80	0	2	1	3	2	2	2	1	4	I
6	C	T,P,S	77	0	2	3	4	4	2	1	1	4	I
7	C	T,S	60	1	2	4	4	4	3	1	1	5	I
8	C	S,T	20	19	3	4	3	4	3	2	2	8	III
9	C	T,S	90	6	2	1	3	3	3	3	1	5	I
10	C	T,C,S	80	1	2	4	5	4	2	3	2,3	5	I
11	C	S,T	9	6	2	4	3	3	3	3	1	7	II
12	C	T,S	50	4	2	4	3	2	3	3	1	5	I
13	C	T,C,S	80	7	1	1	5	4	2	2	1	4	I
14	C	C,T	15	11	2	2	4	4	2	2	1	7	II
15	C	T,S	65	3	2	3	4	4	2	3	1	5	I
16	C	T,P,S	70	8	2	2	4	4	3	3	1	6	II
17	C	T,S	70	2	2	3	3	3	3	3	1	5	I
18	C	T,S	60	1	2	3	4	4	2	2	1	5	I
19	C	S,T	40	6	2	3	3	3	3	3	1	6	II
20	C	T,S	85	2	2	2	4	5	3	3	1	4	I
21	C	T,S	90	11	2	5	4	3	2	4	1	7	II
22	C	T,S	75	1	2	2	4	3	2	2	2	4	I
23	C	T,C	60	7	2	3	4	3	2	3	1	6	II
24	C	T,C	90	2	2	2	4	4	3	2	1	4	I
25	C	T,C	70	4	2	2	3	3	1	2	1	5	I
26	C	T,C	80	6	2	3	3	2	2	3	1	5	I
27	C	S,T	50	6	2	2	3	3	4	4	1	6	II
28	C	T,C	60	3	2	2	2	2	3	4	1	5	I
29	C	T,C	90	2	1	1	3	3	3	2	1	3	I
30	C	T,C	70	5	2	5	3	2	2	3	1	4	I
31	C	S,T	40	4	2	3	3	3	3	n/a	1	5	I
32	C	T,P,C	70	0	2	3	3	2	4	4	1	5	I

33	C	T,P	70	7	2	3	3	4	3	2	1	6	II
34	C	C,T	20	3	2	1	2	3	2	3	1	4	I
35	C	C,T	40	2	2	3	3	3	2	3	1	5	I
36	C	P,C,T	30	0	2	2	3	3	3	3	1	5	I
37	C	T	100	6	2	2	4	4	3	3	1	5	I
38	C	T,P	80	5	2	1	3	3	3	3	1	4	I
39	C	T,C	65	0	2	2	4	3	3	n/a	1	5	I
40	C	T,S	60	30	2	4	4	4	3	3	1	7	II
41	C	T,C	80	2	2	1	4	3	3	2	1	4	I
42	C	T,C,P	70	0	2	2	4	3	3	2	1	5	I
43	C	T,S,P,C	40	8	2	2	3	3	3	3	1	6	II
44	C	T	100	10	2	1	3	3	3	n/a	1	5	I
45	C	T,S	65	6	3	3	4	4	3	4	2,3	7	II
46	C	T,S	80	6	2	2	3	4	3	2	1	5	I
47	C	C,T	40	9	2	1	3	4	2	2	1	5	I
48	C	T,S,C	70	7	2	1	3	4	2	2	1	6	II
49	C	T,S	70	13	2	2	4	3	2	3	2,3	7	II
50	C	T,C,S	70	15	2	3	4	3	3	3	3	7	II
51	C	T,S	60	1	2	3	3	4	3	2	1	5	I
52	C	T,S	70	2	2	3	4	4	3	3	1	5	I
53	C	T,S	70	14	2	3	4	4	3	3	1	7	II
54	C	T,S	70	5	2	2	4	4	2	1	1	5	I
55	C	P,T	30	7	2	3	4	4	2	3	1	6	II
56	C	T,S	70	0	2	2	3	4	2	2	1	5	I
57	C	T,S	70	19	2	3	3	4	3	4	1	7	II
58	C	T,S	70	6	2	2	3	3	3	2	1	6	II
59	C	T,S	75	10	2	2	4	4	3	2	1	6	II
60	C	T,S	60	3	2	3	4	4	3	3	1	5	I
61	C	T,C,P	65	14	2	2	4	3	4	4	3	7	II
62	C	S,T	40	15	2	2	3	3	3	2	1	7	II
63	C	T,C	60	5	2	3	3	3	2	2	1	5	I
64	C	T,S	60	32	2	1	5	4	2	2	1	7	II
65	C	S,T	50	3	2	1	3	4	2	2	1	5	I
66	C	S,T	40	0	2	2	2	3	2	2	1	5	I
67	C	T,C	70	12	2	1	4	3	2	2	1	7	II

68	C	T,P,S	70	13	2	2	4	3	3	3	1	7	II
69	C	T,P,C	70	12	2	4	5	4	3	3	1	7	II
70	C	T,S,P	70	9	2	2	3	4	2	3	1	6	II
71	C	T,S	80	13	2	2	4	4	3	3	1	6	II
72	C	P,S,T	5	5	2	4	2	4	3	3	1	6	II
73	C	T,S	70	0	2	3	3	5	2	2	1	5	I
74	C	T,P,C	70	1	2	2	5	5	3	2	1	5	I
75	C	T,P,C	60	3	2	2	3	3	3	3	1	5	I
76	C	T,S	70	13	2	2	3	3	3	2	1	7	II
77	C	T,S	70	17	2	4	3	3	2	3	1	7	II
78	C	T,S	80	0	2	2	5	4	3	3	1	4	I
79	C	T,S,P	70	2	2	3	4	4	3	3	1	5	I
80	C	S,T	50	11	2	4	3	4	3	3	1	7	II
81	C	T,S	70	3	2	2	4	4	3	3	1	5	I
82	C	T,P,S	60	3	2	2	3	4	3	2	1	5	I
83	C	T,P,S	50	4	2	2	4	4	2	2	1	5	I
84	C	P,T,S,C	40	24	2	4	3	3	2	2	1	7	II
85	C	C,S,T	5	4	2	2	2	3	3	3	2	6	II
86	C	C,T	50	22	2	2	3	3	2	3	1	7	II
87	C	T,C,S	80	6	2	1	3	3	2	2	1	5	I
88	C	T,C	70	29	2	2	4	4	2	2	1	7	II
89	C	C,P,T	20	0	2	2	3	3	2	2	1	5	I
90	C	C,P,T	10	0	2	1	3	3	2	2	1	5	I
91	C	T,P	80	8	2	2	4	4	2	2	1	5	I
92	C	C,P,T	5	0	2	2	3	3	2	2	1	7	II
93	C	C	0	1	2	2	3	3	2	2	1	6	II
94	C	T,C	50	2	2	3	3	3	3	2	1	5	I
95	C	P,C,T	5	3	2	1	3	3	3	2	1	6	II
96	C	T,C	70	5	2	1	4	4	3	2	1	5	I
97	C	T,C,P	40	9	2	1	3	4	2	2	1	6	II
98	C	C,T,P	30	2	2	1	3	3	2	2	1	5	I
99	C	T,P,C	50	7	2	2	4	4	2	2	1	6	II
100	C	C,T	20	5	2	2	4	3	2	2	1	5	I
101	C	C,T	40	7	2	1	4	3	2	2	1	6	II
102	C	C,P,T	10	5	2	2	5	5	2	1	1	5	I

103	C	T,S	70	2	2	2	4	4	2	2	1	5	I
104	C	S,T	5	6	2	1	3	3	3	3	1	7	II
105	C	T,S	70	4	2	1	4	4	3	n/a	1	5	I
106	C	S,T	45	5	2	3	3	3	3	3	1	5	I
107	C	S,C,T	5	4	2	3	3	3	3	3	1	6	II
108	C	S,T	40	11	2	2	4	3	3	3	2	7	II
109	C	S,C,T	5	7	3	4	3	3	3	4	2	8	III
110	C	P,T	8	3	2	2	3	3	2	3	2	6	II
111	C	T,S	80	2	2	1	4	4	3	2	1	4	I
112	C	T,C	80	0	1	1	3	3	1	2	1	3	I
113	C	T,C	80	5	2	3	3	3	2	2	1	4	I
114	C	T,S	80	4	2	1	4	4	2	2	1	4	I
115	C	T,S	80	6	2	1	4	4	2	1	1	5	I
116	C	T,S	90	0	2	1	3	3	1	2	1	4	I
117	C	T,C	80	6	2	2	4	4	3	4	1	5	I
118	C	T,C	70	14	2	2	4	4	3	3	1	7	II
119	C	C,P,T	9	4	2	2	3	2	3	2	1	6	II
120	CIS	T,P	80	2	2	2	3	3	1	1	1	n/a	n/a
121	CIS	T,P	90	5	1	1	3	2	1	1	1	n/a	n/a

[a]#, Number of the rabbit
[b]D,' Diagnosis: C, Carcinoma; CIS, Carcinoma in situ
[c]Growth, histologic growth pattern(s); T, Tubular; C, Cystic; S, Solid; P, Papillary; the predominant growth pattern is listed first; the least common growth pattern is listed last.
[d]T%, The percentage of the tumor area with tubular growth pattern
[e]MC, Mitotic count, i.e. numbers of mitotic figures in 10 40x high-power fields (diameter of the 400x field of view: 159 μm^2)
[f]NPM, Nuclear Pleomorphism: 1, Mild; 2, Moderate; 3, Marked
[g]Necr, Necrosis: 1, Absent; 2, Minimal (<10% of the tumor area); 3, Mild (10%-39% of the tumor area); 4, Moderate (40%-69% of the tumor area); 5, Marked (≥70% of the tumor area)
[h]Secr Activity; P Sec, Proteinaceous Secretion; VCs, Vacuolated cells: 1, Absent, 2, Minimal (<10% of the tumor area); 3, Mild (10%-39% of the tumor area); 4, Moderate (40%-69% of the tumor area); 5, Marked (≥70% of the tumor area)
[i]Invasion, Tumor Invasion; Str, Stroma; PT, Peritumoral tissue: 1, No invasion; 2, Mild invasion; 3, Moderate invasion; 4, Marked invasion
[j]EM, Tumor cell emboli: 1, No emboli; 2, Intravascular emboli; 3, Intralymphatic emboli
[k]Sc, Total differentiation score according to Elston and Ellis (1991)
[l]Gr, Histological tumor grade according to Elston and Ellis (1991): Grade I, Well differentiated (Total differentiation scores 3-5); Grade II, Moderately differentiated (Total differentiation scores 6-7); Grade III, Poorly differentiated (Total differentiation scores 8-9)
n/a, not applicable

Supplemental Table S3. Expression of estrogen receptor-α in mammary proliferative lesions of 124 pet rabbits.

Proliferative lesions	Cases # (%)	% pos. cells MV±SD	IRS[a] MV±SD	H-score[b] MV±SD
Carcinoma				
Grade I	**68/119 (57%)**	**12.0±24.9**	**0.2±0.4**	**13.6± 29.0**
Tubular	52/68 (76%)	10.1±22.7	0.2±0.4	11.9±27.6
Cystic	8/68 (12%)	25.4±30.1	0.3±0.4	26.7±32.0
Solid	3/68 (4.5%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-solid	2/68 (3%)	0.0±0.0	0.0±0.0	0.0±0.0
Papillary	1/68 (1.5%)	84.2±0.0	1.2±0.0	94.1±0.0
Tubular-papillary	1/68 (1.5%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-cystic	1/68 (1.5%)	0.0±0.0	0.0±0.0	0.0±0.0
Grade II	**49/119 (41%)**	**10.3±22.9**	**0.2±0.5**	**12.5±29.0**
Tubular	27/49 (56%)	1.6±8.2	0.0±0.1	1.6±8.2
Solid	7/49 (14%)	8.0±19.6	0.1±0.3	8.5±20.9
Cystic	6/49 (12%)	45.5±33.3	1.1±0.9	60.5±45.9
Papillary	5/49 (10%)	26.3±25.8	0.4±0.5	29.3±30.4
Tubular-solid	2/49 (4%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-papillary	1/49 (2%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-cystic	1/49 (2%)	0.0±0.0	0.0±0.0	0.0±0.0
Grade III	**2/119 (2%)**	**0.0±0.0**	**0.0±0.0**	**0.0±0.0**
Solid	2/2 (100%)	0.0±0.0	0.0±0.0	0.0±0.0
In situ Carcinoma	2 (100%)	46.7±18.6	0.6±0.4	51.0±22.9
Adenoma	3 (100%)	69.2±24.7	2.6±1.4	115.2±51.1
Lobular Hyperplasia	2 (100%)	21.3±0.0	0.3±0.0	32.5±0.0
Cysts	25 (100%)	24.9±32.9	0.5±0.8	31.9±43.4

#, numbers of cases;
%, percentage of cases
pos. cells, positive cells
MV±SD, Mean value±Standard deviation
[a]IRS, Immunoreactive score: ((weakly positive cells) + (moderately positive cells x 5) + (strongly positive cells x 10)/ 100).
[b]H-score: (weakly positive cells) + (moderately positive cells x 2) + (strongly positive cells x 3).

Supplemental Table S4. Expression of progesterone receptor in mammary proliferative lesions of 124 pet rabbits.

Proliferative lesions	Cases # (%)	% pos. cells MV±SD	IRS[a] MV±SD	H-score[b] MV±SD
Carcinoma				
Grade I	**68/119(57%)**	**18.4±28.7**	**0.7±1.2**	**30.3±49.1**
Tubular	52/68 (76%)	13.6±23.9	0.5±1.0	22.3±41.1
Cystic	8/68 (12%)	56.3±30.6	2.1±1.2	92.1±52.6
Solid	3/68 (4.5%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-solid	2/68 (3%)	5.5±5.5	0.2±0.2	8.1±8.1
Papillary	1/68 (1.5%)	81.6±0.0	3.7±0.0	149.1±0.0
Tubular-papillary	1/68 (1.5%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-cystic	1/68 (1.5%)	0.0±0.0	00.0±0.0	0.0±0.0
Grade II	**49/119(41%)**	**14.8±26.2**	**0.6±1.1**	**24.6±44.7**
Tubular	27/49 (56%)	5.7±16.1	0.2±0.6	9.2±26.4
Solid	7/49 (14%)	19.9±24.6	0.7±1.0	32.4±42.2
Cystic	6/49 (12%)	35.3±30.7	1.4±1.4	60.7±56.5
Papillary	5/49 (10%)	30.9±37.9	1.2±1.5	52.5±65.1
Tubular-solid	2/49 (4%)	0.0±0.0	0.0±0.0	0.0±0.0
Tubular-papillary	1/49 (2%)	65.4±0.0	2.2±0.0	102.7±0.0
Tubular-cystic	1/49 (2%)	0.0±0.0	0.0±0.0	0.0±0.0
Grade III	**2/119 (2%)**	**12.1±12.1**	**0.1±0.1**	**12.1±12.1**
Solid	2/2 (100%)	12.1±12.1	0.1±0.1	12.1±12.1
In situ Carcinoma	2 (100%)	54.0±0.3	2.4±0.2	97.2±3.7
Adenoma	3 (100%)	19.1±27.0	0.8±1.1	33.0±46.7
Lobular Hyperplasia	2 (100%)	31.9±0.00	1.2±0.0	48.4±0.0
Cysts	25 (100%)	32.9±29.02	1.2±1.2	54.2±49.9

#, numbers of cases

%, percentage of cases

Pos. cells, positive cells

MV±SD, Mean value±Standard deviation

[a]IRS, Immunoreactive score: ((weakly positive cells) + (moderately positive cells x 5) + (strongly positive cells x 10)/ 100).

[b]H-score: (weakly positive cells) + (moderately positive cells x 2) + (strongly positive cells x 3).

Supplemental Table S5. Results of the immunostaining for estrogen receptor-α and progesterone receptor in mammary tumors and the adjacent normal mammary tissue of 124 female pet rabbits.

		Estrogen receptor-α							Progesteron receptor						
#/n[a]	D[b]	% pos cells[c]				IRS[d]	H-sc[e]	M[f]	% pos cells[c]				IRS[d]	H-sc[e]	M[f]
		Total	+	++	+++				Total	+	++	+++			
3	C	60.39	50.57	9.82	0.00	1.0	70.21	2	35.41	35.41	0.00	0.00	0.35	35.41	2
5	C	49.62	44.47	5.15	0.00	0.70	54.77	2	56.54	22.38	23.04	11.13	2.49	101.83	2
6	C	0.00	0.00	0.00	0.00	0.00	0.00	1	64.38	64.38	0.00	0.00	0.64	64.38	2
10	C	0.00	0.00	0.00	0.00	0.00	0.00	2	10.27	6.70	2.92	0.65	0.28	14.49	2
11	C	0.00	0.00	0.00	0.00	0.00	0.00	2	18.00	18.00	0.00	0.00	0.18	18.00	2
20	C	0.00	0.00	0.00	0.00	0.00	0.00	2	57.06	22.73	20.13	14.21	2.65	105.60	2
22	C	0.00	0.00	0.00	0.00	0.00	0.00	2	22.71	22.71	0.00	0.00	0.23	22.71	2
32	C	63.68	48.85	14.83	0.00	1.23	78.52	2	60.50	16.67	24.83	19.00	3.31	123.33	2
34	C	0.00	0.00	0.00	0.00	0.00	0.00	1	31.52	13.91	13.04	4.57	1.25	53.70	2
36	C	84.23	74.40	9.83	0.00	1.24	94.06	2	81.58	28.64	38.39	14.55	3.66	149.07	2
38	C	26.13	26.13	0.00	0.00	0.65	26.13	2	15.93	15.93	0.00	0.00	0.16	15.93	2
40	C	0.00	0.00	0.00	0.00	0.00	0.00	1	15.90	12.47	2.67	0.76	0.33	20.10	2
41	C	40.65	40.65	0.00	0.00	1.41	40.65	2	50.96	18.60	22.29	10.06	2.31	93.38	2
42	C	0.00	0.00	0.00	0.00	0.00	0.00	1	6.71	4.12	2.59	0.00	0.17	9.30	2
45	C	0.00	0.00	0.00	0.00	0.00	0.00	1	22.01	9.68	9.68	2.64	0.85	36.97	2
47	C	14.87	14.87	0.00	0.00	0.15	14.87	2	36.68	17.83	13.42	5.43	1.39	60.96	2
49	C	43.47	43.47	0.00	0.00	0.43	43.47	2	73.74	31.50	40.28	1.95	2.52	117.92	2
56	C	12.19	5.83	6.36	0.00	0.38	18.55	2	0.00	0.00	0.00	0.00	0.00	0.00	1
62	C	0.00	0.00	0.00	0.00	0.00	0.00	2	7.55	1.95	3.50	2.10	0.40	15.26	2
65	C	0.00	0.00	0.00	0.00	0.00	0.00	2	10.96	7.58	1.57	1.81	0.34	16.14	2
72	C	18.66	18.66	0.00	0.00	0.19	18.66	2	0.00	0.00	0.00	0.00	0.00	0.00	1
74	C	54.62	54.62	0.00	0.00	0.55	54.62	2	60.75	19.17	27.33	14.25	2.98	116.58	2
75	C	0.00	0.00	0.00	0.00	0.00	0.00	1	14.16	8.53	5.32	0.30	0.38	20.08	2
79	C	0.00	0.00	0.00	0.00	0.00	0.00	2	18.68	6.99	9.00	2.68	0.79	33.05	2
85	C	77.93	56.91	18.62	2.40	1.74	101.35	2	26.20	7.88	15.24	3.08	1.15	47.60	2
89	C	64.86	56.76	8.09	0.00	0.97	72.95	2	85.07	35.74	37.28	12.04	3.43	146.44	2
90	C	47.65	46.66	1.00	0.00	0.52	48.65	2	74.30	28.77	40.15	5.37	2.83	125.19	2
92	C	52.37	49.10	3.27	0.00	0.65	55.65	2	64.67	21.29	26.34	17.03	3.23	125.08	2
93	C	65.40	34.43	27.68	3.29	2.06	99.67	2	38.47	31.34	7.13	0.00	0.67	45.61	2
95	C	49.96	49.96	0.00	0.00	0.50	49.96	n/a	74.62	37.44	33.98	3.19	2.39	115.00	n/a
96	C	61.71	59.78	1.93	0.00	0.69	63.64	2	70.45	23.67	38.38	8.40	3.00	125.63	2
97	C	0.00	0.00	0.00	0.00	0.00	0.00	1	40.84	13.55	22.33	4.96	1.75	73.09	2
98	C	0.00	0.00	0.00	0.00	0.00	0.00	1	80.66	34.79	44.70	1.17	2.70	127.70	2
99	C	0.00	0.00	0.00	0.00	0.00	0.00	1	65.38	28.05	37.34	0.00	2.15	102.72	2
100	C	0.00	0.00	0.00	0.00	0.00	0.00	2	47.25	33.39	13.86	0.00	1.03	61.10	2
102	C	75.74	74.16	1.58	0.00	0.82	77.31	2	94.94	40.39	41.82	12.73	3.77	162.23	2
107	C	0.00	0.00	0.00	0.00	0.00	0.00	1	47.87	20.26	21.73	5.87	1.88	81.35	2
108	C	56.04	52.35	3.69	0.00	0.71	59.73	2	65.98	33.43	18.64	13.91	2.66	112.43	2
110	C	62.66	47.42	15.24	0.00	1.24	77.90	2	79.89	29.75	32.64	17.49	3.68	147.52	2

112	C	91.42	62.18	25.29	3.94	2.28	124.59	2	88.10	48.45	32.24	7.41	2.48	135.17	2
116	C	0.00	0.00	0.00	0.00	0.00	0.00	2	18.17	8.06	6.32	3.79	0.78	32.07	2
117	C	66.47	47.11	17.92	1.45	1.51	87.28	2	55.04	15.22	26.70	13.11	2.80	107.96	2
119	C	77.29	48.47	28.82	0.00	1.93	106.11	2	82.33	30.24	40.62	11.48	3.48	145.90	2
n=30	C	0.00	0.00	0.00	0.00	0.00	0.00	1	0.00	0.00	0.00	0.00	0.00	0.00	1
n=19	C	0.00	0.00	0.00	0.00	0.00	0.00	2	0.00	0.00	0.00	0.00	0.00	0.00	2
n=19	C	0.00	0.00	0.00	0.00	0.00	0.00	1	0.00	0.00	0.00	0.00	0.00	0.00	2
n=8	C	0.00	0.00	0.00	0.00	0.00	0.00	2	0.00	0.00	0.00	0.00	0.00	0.00	1
120	CIS	28.11	28.11	0.00	0.00	0.28	28.11	1	54.29	19.76	22.38	12.14	2.53	100.95	2
121	CIS	65.34	56.80	8.54	0.00	1.00	73.89	2	53.63	20.37	26.65	6.61	2.20	93.50	2
122	A	91.29	44.52	28.79	17.98	3.68	156.04	2	0.00	0.00	0.00	0.00	0.00	0.00	1
123	A	81.57	30.84	36.61	14.13	3.55	146.44	2	0.00	0.00	0.00	0.00	0.00	0.00	1
124	A	34.65	26.07	8.58	0.00	2.67	102.64	2	57.35	20.59	31.76	5.00	2.29	99.12	2

[a]#, Case number of the rabbit with this immunoreaction; n, Total number and case numbers of rabbits with this type of immunoreaction
n=30; 30 rabbits with this type of immunoreaction, i.e. rabbits 1, 9, 12, 18, 21, 23, 24, 25, 30, 33, 35, 37, 39, 44, 50, 51, 52, 58, 63, 64, 66, 67, 69, 80, 88, 91, 94, 101, 111, 114
n=19, 19 rabbits with this type of immunoreactions, i.e. rabbits 2, 4, 7, 8, 19, 26, 28, 31, 53, 55, 60, 61, 68, 73, 77, 81, 83, 86, 104
n=19, 19 rabbits with this type of immunoreactions, i.e. rabbits 13, 14, 16, 17, 27, 29, 43, 57, 59, 70, 71, 76, 78, 103, 105, 106, 109, 113, 118;
n=8, 8 rabbits with this type of immunoreactions, i.e. rabbits 15, 46, 48, 54, 82, 84, 87, 115
[b]D, Diagnosis; C, Carcinoma; CIS, Carcinoma in situ
[c]% pos cells, Percentage of immunopositive tumor cells; Total, percentage of all immunopositive tumor cells; +, percentage of tumor cells with a mild immunoreaction; ++, percentage of tumor cells with a moderate immunoreaction; +++, percentage of tumor cells with a strong immunoreaction
[d]IRS, Immunoreactive score: ((weakly positive cells) + (moderately positive cells x 5) + (strongly positive cells x 10)/ 100).
[e]H-sc, H-score: (weakly positive cells) + (moderately positive cells x 2) + (strongly positive cells x 3).
[f]M, adjacent normal mammary tissue: 1, no immunoreaction; 2, positive immunoreaction; n/a, not applicable, since no adjacent normal mammary tissue was available for investigation

Supplemental Table S6. Correlation between the degree of immunostaining for estrogen receptor-α and progesterone receptor and different histological parameters in 119 mammary carcinomas of pet rabbits.

Variables	Score (3-9)[a]	Grade (I, II, III)[b]	%T growth[c]	Mitotic count[d]
ERα IRS[e]	NS[g] (Lme, A)	NS[g] (Lme, A)	p<0.001 (Lme)	p<0.001(Src, ρ: -0.36)
ERα H-score[f]	NS[g] (Lme, A)	NS[g] (Lme, A)	p<0.001 (Lme)	p<0.001(Src, ρ: -0.37)
PR IRS[e]	NS[g] (Lme, A)	NS[g] (Lme, A)	p<0.001(Lme)	p<0.001(Src, ρ: -0.33)
PR H-score[f]	NS[g] (Lme, A)	NS[g] (Lme, A)	p<0.001 (Lme)	p<0.001(Src, ρ: -0.34)

[a]Score, Total differentiation score according to Elston and Ellis (1991)
[b]Grade I: well differentiated; Grade II: moderately differentiated;
Grade III: poorly differentiated (Elston and Ellis, 1991)
[c]% T growth, the percentage of the area with a tubular growth pattern
[d]Mitotic count, i.e. numbers of mitotic figures in 10 40x high-power fields (diameter of the 400x field of view: 159 μm^2)
ERα, estrogen receptor-α
[e]IRS, Immunoreactive score: ((weakly positive cells) + (moderately positive cells x 5) + (strongly positive cells x 10)/ 100).
[f]H-score: (weakly positive cells) + (moderately positive cells x 2) + (strongly positive cells x 3).
PR, progesterone receptor
[g]NS, not statistically significant; results with $p > 0.05$ were considered as statistically not significant.
Lme, linear mixed effects model
A, Analysis of variance
Src, Spearman's rank correlation (ρ: Spearman's Rho)

Supplemental Table S7. Statistical difference of the mitotic count in estrogen receptor-α and/or progesterone receptor immunopositive and immunonegative pet rabbit mammary carcinomas.

#[a]	Category 1 Immunonegative	Category 2 Immunopositive	Difference in the MC[b] (Test)
A.	ERα IRS[c] =0 (n=95)	ERα IRS[c] >0 (n=24)	p<0.001 (MWW)
B.	ERα H-score[d] =0 (n=95)	ERα H-score[d] >0 (n=24)	p<0.001 (MWW)
C.	PR IRS[c] =0 (n=77)	PR IRS[c] >0 (n=42)	p<0.001 (MWW)
D.	PR H-score[d] =0 (n=77)	PR H-score[d] >0 (n=42)	p<0.001 (MWW)
E.	Lack ERα and PR (n=75)	ERα and PR (n=22)	p<0.001 (MWW)

Immunonegative tumors (category 1) contained a significantly higher mitotic count than immunopositive tumors (category 2). Comparisons were performed separately for estrogen receptor-α (ERα) and progesterone receptor (PR) by using their immunoreactive scores (IRS) and H-scores, respectively (A-D). In addition, double immunonegative and double immunopositive tumors (E) were compared.

[a]#, Performed comparison A-E

[b]MC, Mitotic count, i.e. numbers of mitotic figures in 10 40x high-power fields (diameter of the 400x field of view: 159 μm^2).

[c]IRS, Immunoreactive score: ((weakly positive cells) + (moderately positive cells x 5) + (strongly positive cells x 10)/ 100).

[d]H-score: (weakly positive cells) + (moderately positive cells x 2) + (strongly positive cells x 3).

[e]MWW, Mann-Whitney-Wilcoxon test