

FIGURES

Figure 1: Expression of prolactin in eutopic endometrium from patients and healthy controls and in endometriotic lesions

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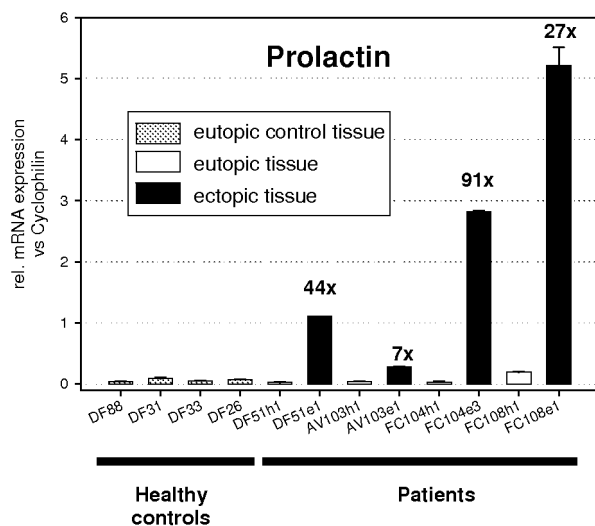


Figure 2: Expression of the prolactin receptor in eutopic endometrium from patients and healthy controls and in endometriotic lesions

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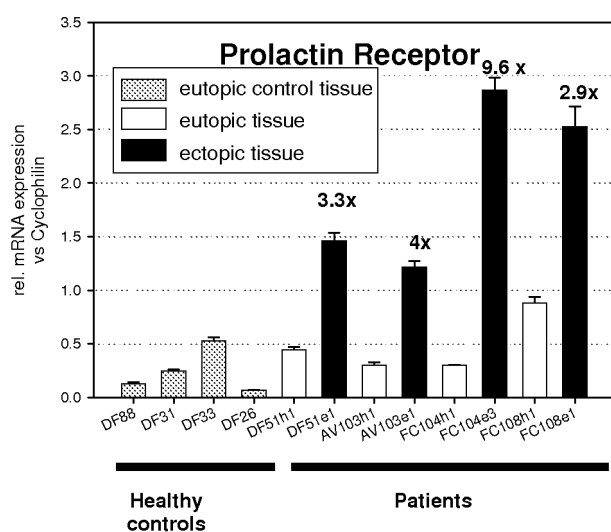


Figure 3: Analysis of prolactin receptor mRNA expression in rat tissues by Northern blot

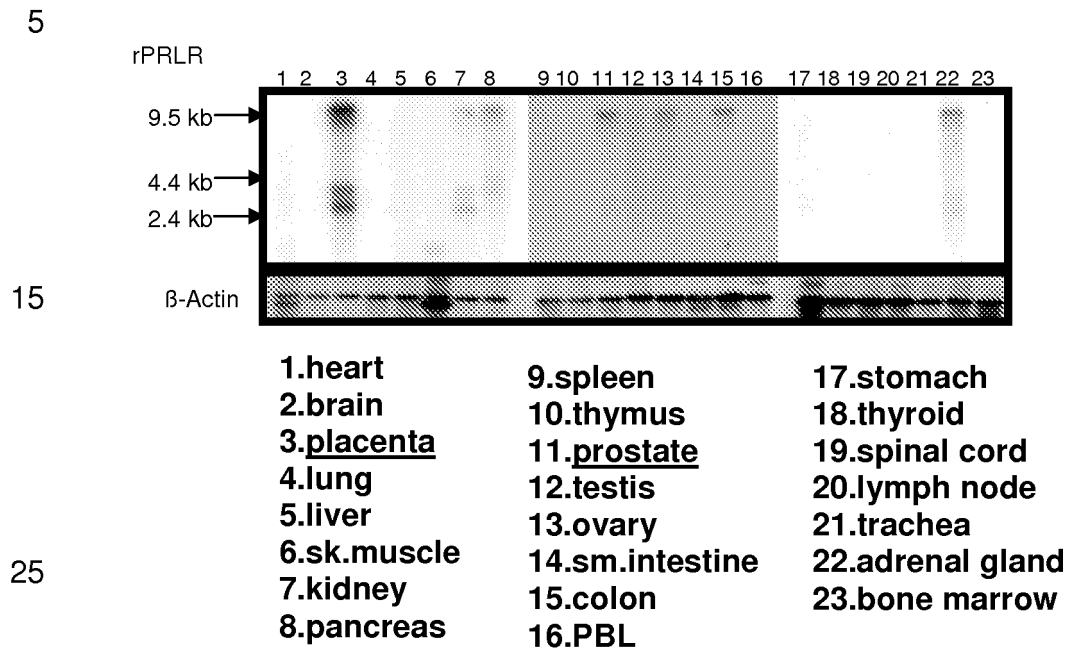


Figure 4: Analysis of prolactin receptor protein expression in rat prostate from castrated animals (gdx) and from intact animals treated with vehicle (intact), dihydrotestosterone (DHT) or estradiol (E2)

Figure 5: Inhibition of Baf cell proliferation (cells stably transfected with hPRLR) by different neutralising PRLR antibodies

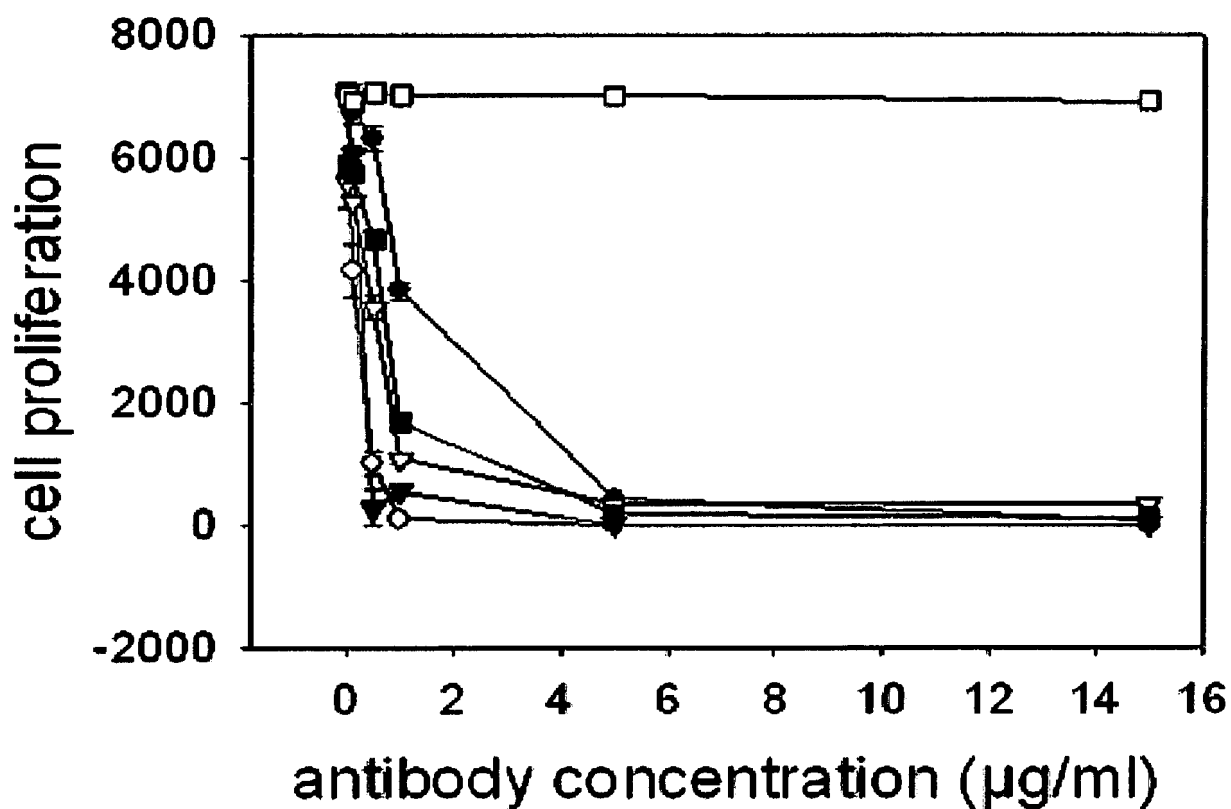


Figure 6: Inhibition of prolactin-induced rat lymphoma cell proliferation (NB2 cells) by neutralising prolactin receptor antibodies

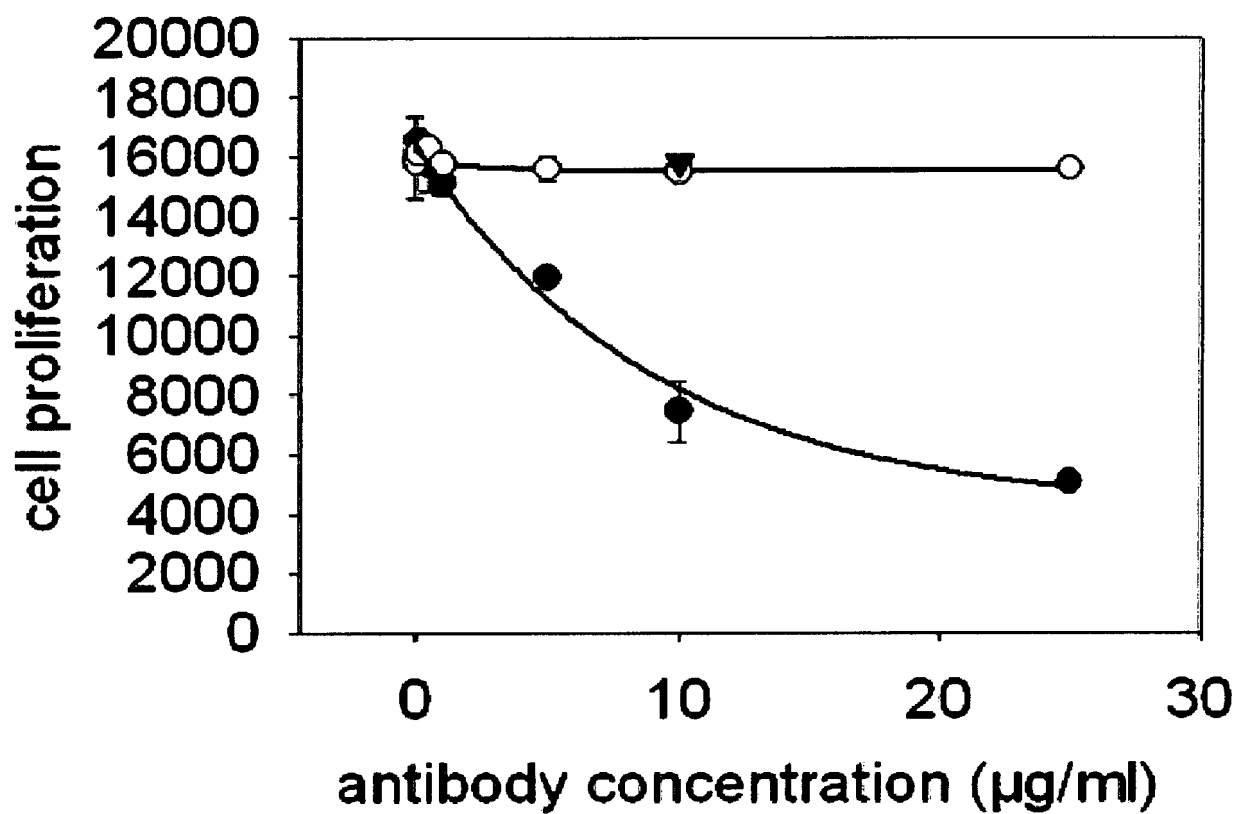


Figure 7: Inhibition of prolactin-induced STAT5 phosphorylation in T47D cells by neutralizing prolactin receptor antibodies and unspecific control antibody

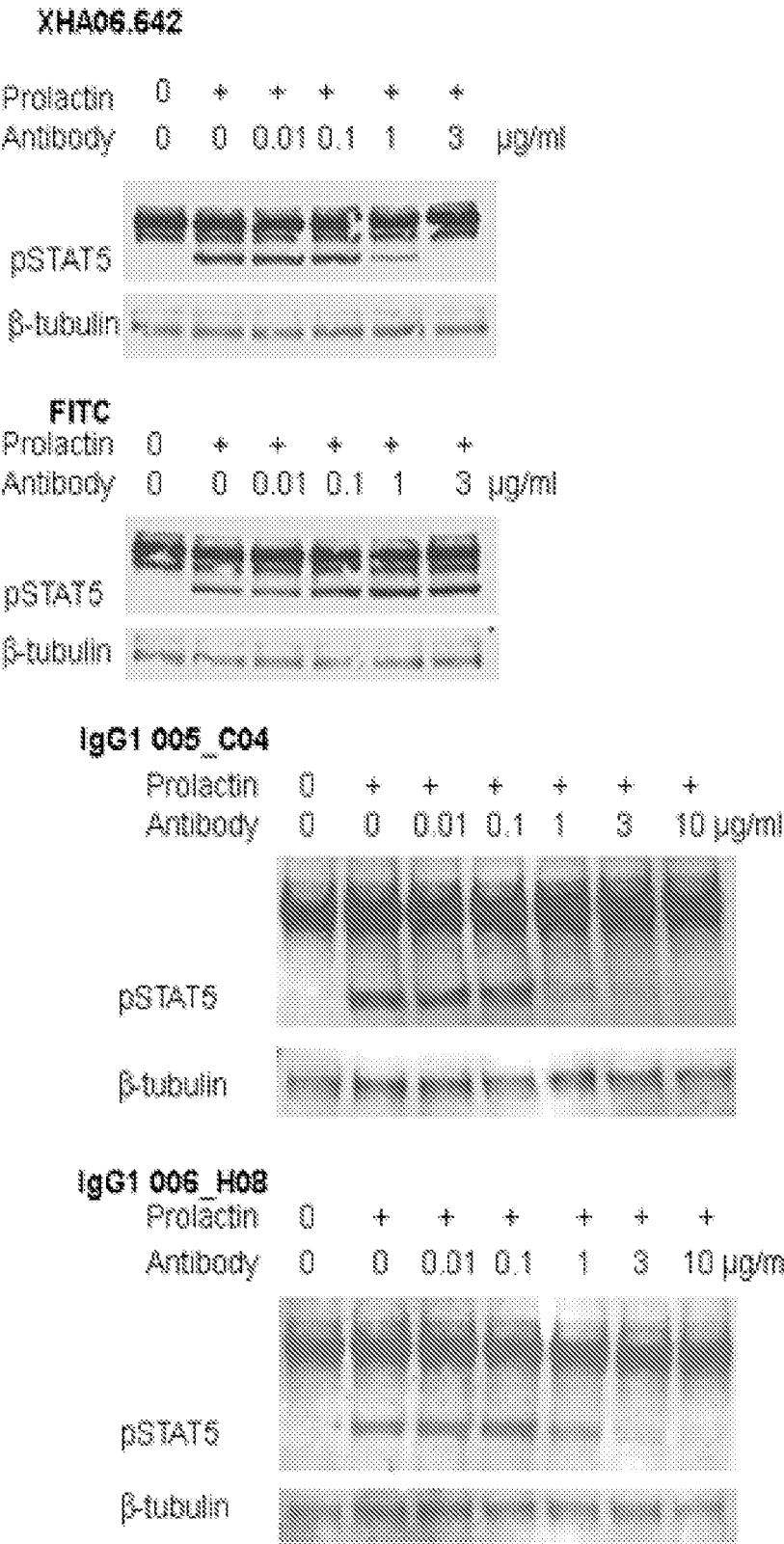


Figure 8: Luciferase assay in HEK293 cells stably transfected with hPRLR and transiently transfected with luciferase under the control of LHRE's. Inhibition of luciferase activity by specific and unspecific antibodies.

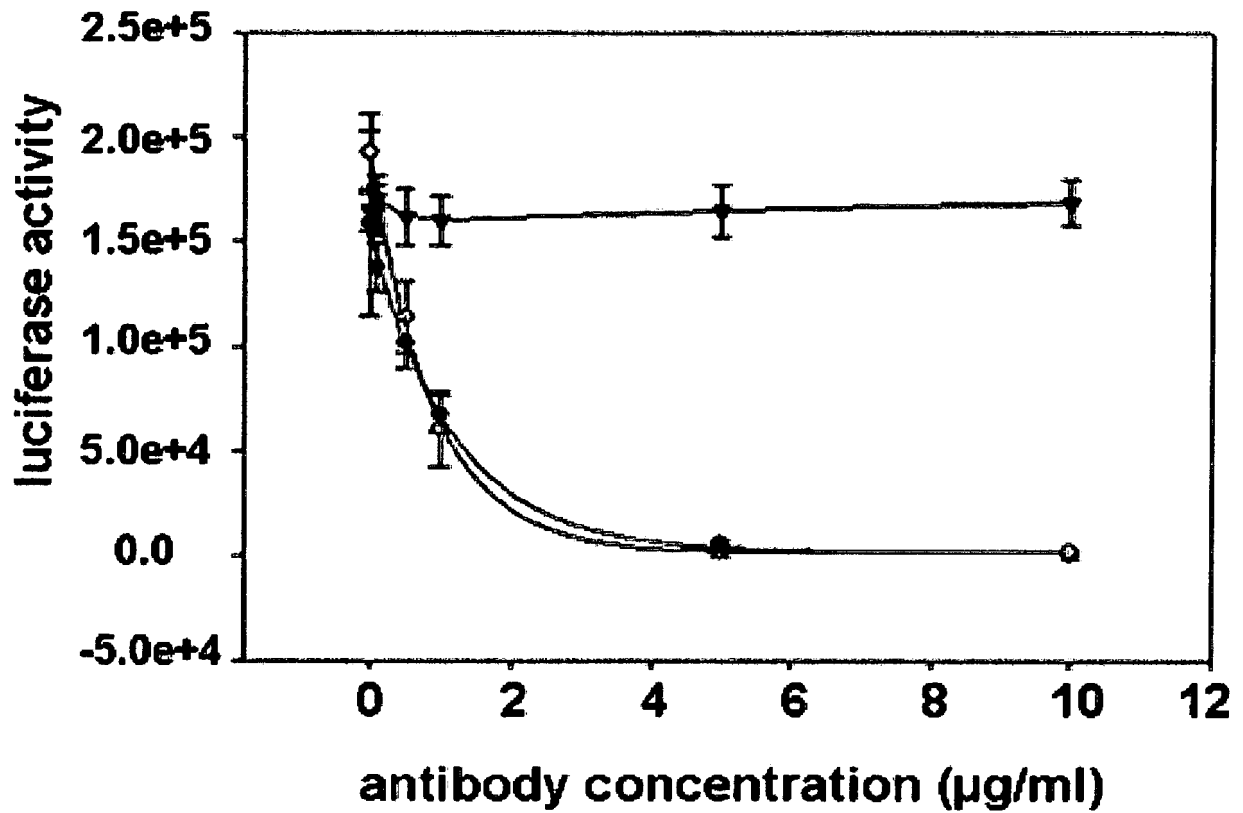


Figure 9: Luciferase assay in Hek293 cells stably transfected with murine PRLR and transiently transfected with luciferase under the control of LHREs – analysis of inhibition of luciferase activity by specific and unspecific antibodies

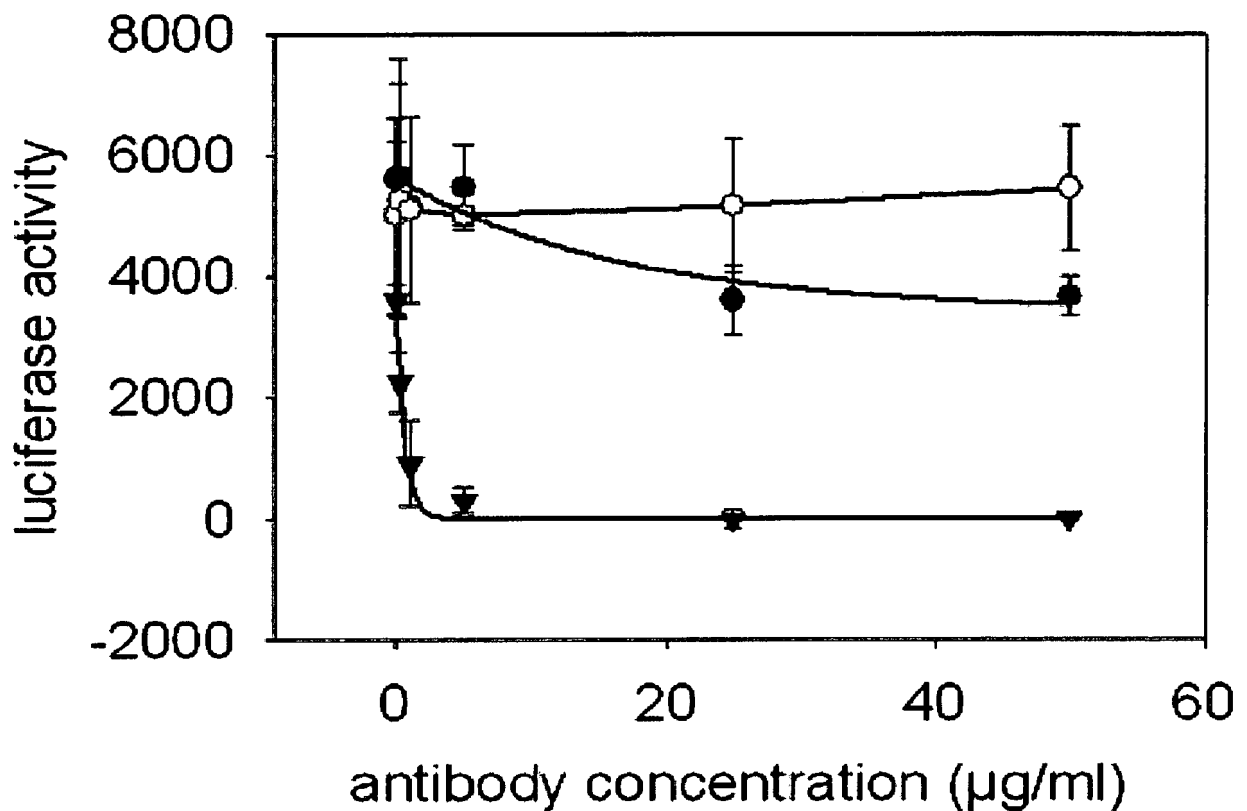


Figure 10: Inhibition of Baf cell proliferation (cells stably transfected with murine PRLR) by different neutralizing PRLR antibodies

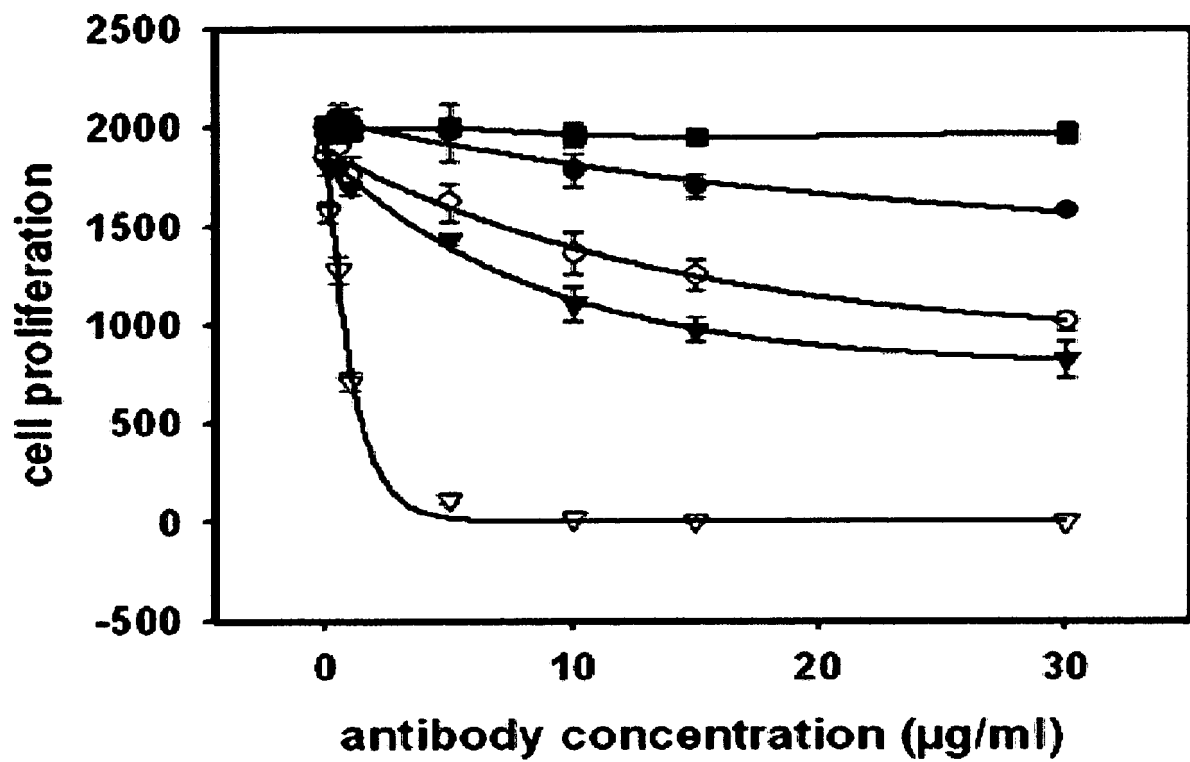


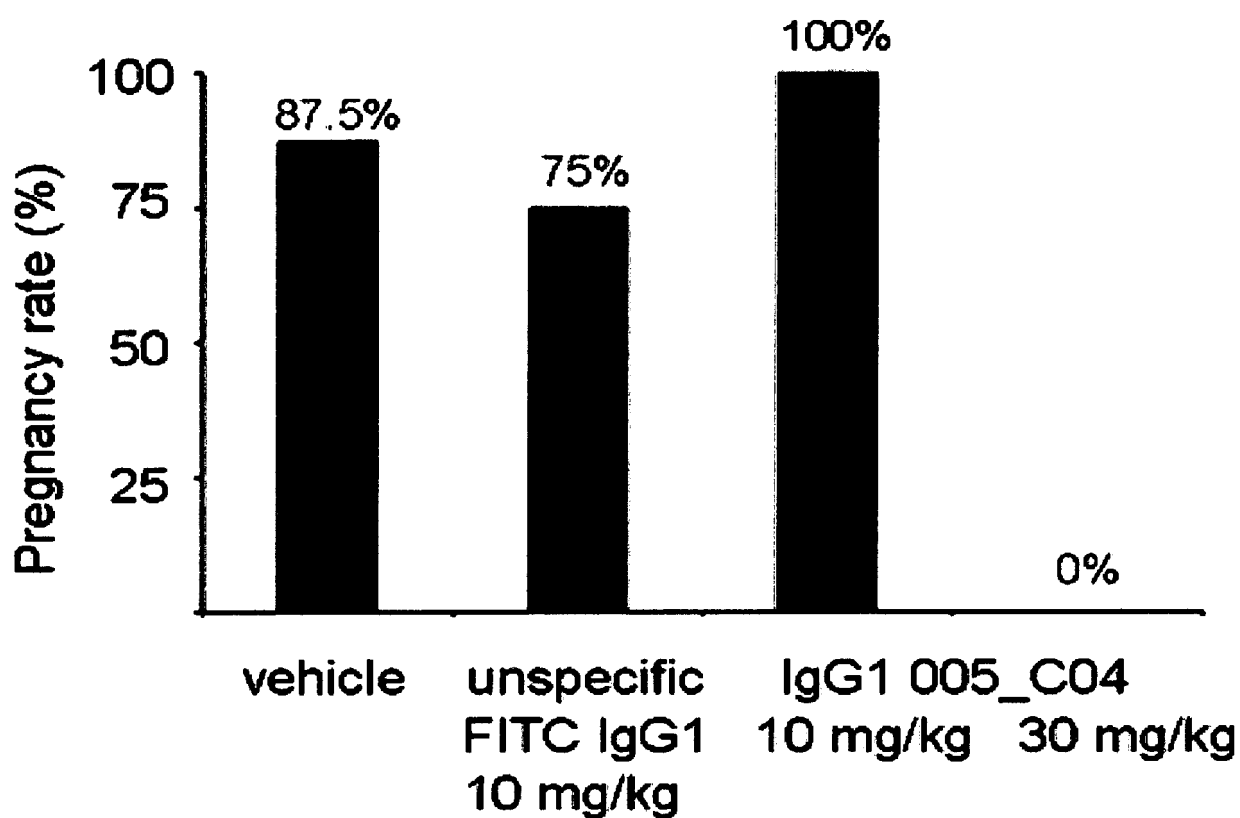
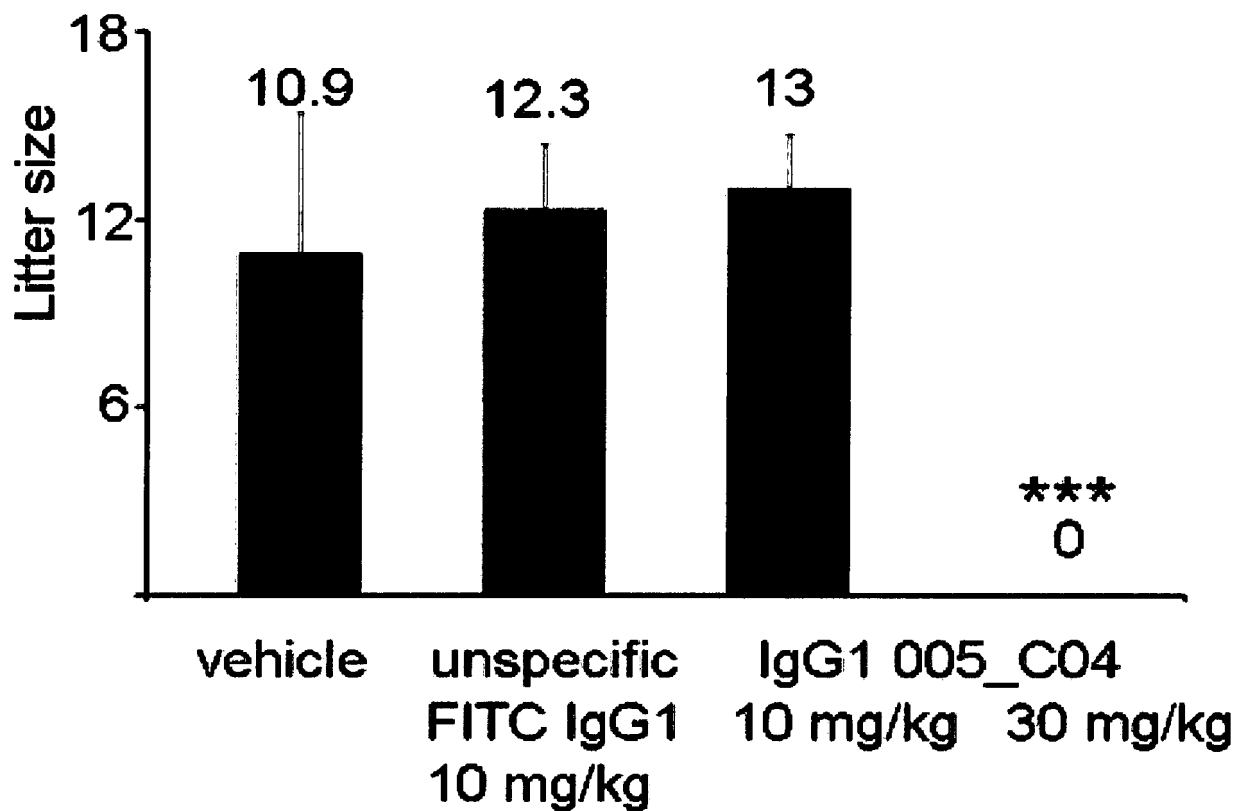
Figure 11: Contraceptive effect of neutralizing PRLR antibodies in mice**A Pregnancy rates**

Figure 11: Contraceptive effect of neutralizing PRLR antibodies in mice**B Litter size**

Kabat HFR1	No.	H1 E/Q	H2 V	H3 Q/E	H4 L	H5 L	H6 E	H7 S	H8 G	H9 G	H10 G	H11 L	H12 V	H13 Q	H14 P	H15 G	H16 G	H17 S	H18 L	H19 R	H20 L	H21 S	H22 C	
Kabat HFR1	No.	H23 A	H24 A	H25 S	H26 G	H27 F	H28 T																	
Kabat HCDR1	No.	H29 - H36 (X)n																						
Kabat HFR2	No.	H37 V	H38 R	H39 Q	H40 A	H41 P	H42 G	H43 K	H44 G	H45 L	H46 E	H47 W												
Kabat HCDR2	No.	H48 - H66 (X)n																						
Kabat HFR3	No.	H67 F	H68 T	H69 I	H70 S	H71 R	H72 D	H73 N	H74 S	H75 K	H76 N	H77 T	H78 L	H79 Y	H80 L	H81 Q	H82 M	H82A N	H82B S	H82C L	H83 R	H84 A	H85 E	
Kabat HFR3	No.	H86 D	H87 T	H88 A	H89 V	H90 Y	H91 Y	H92 C																
Kabat HCDR3	No.	H93 - H102 (X)n																						
Kabat HFR4	No.	H103 W	H104 G	H105 Q	H106 G	H107 T	H108 L	H109 V	H110 T	H111 V	H112 S	H113 S												

Figure 13:

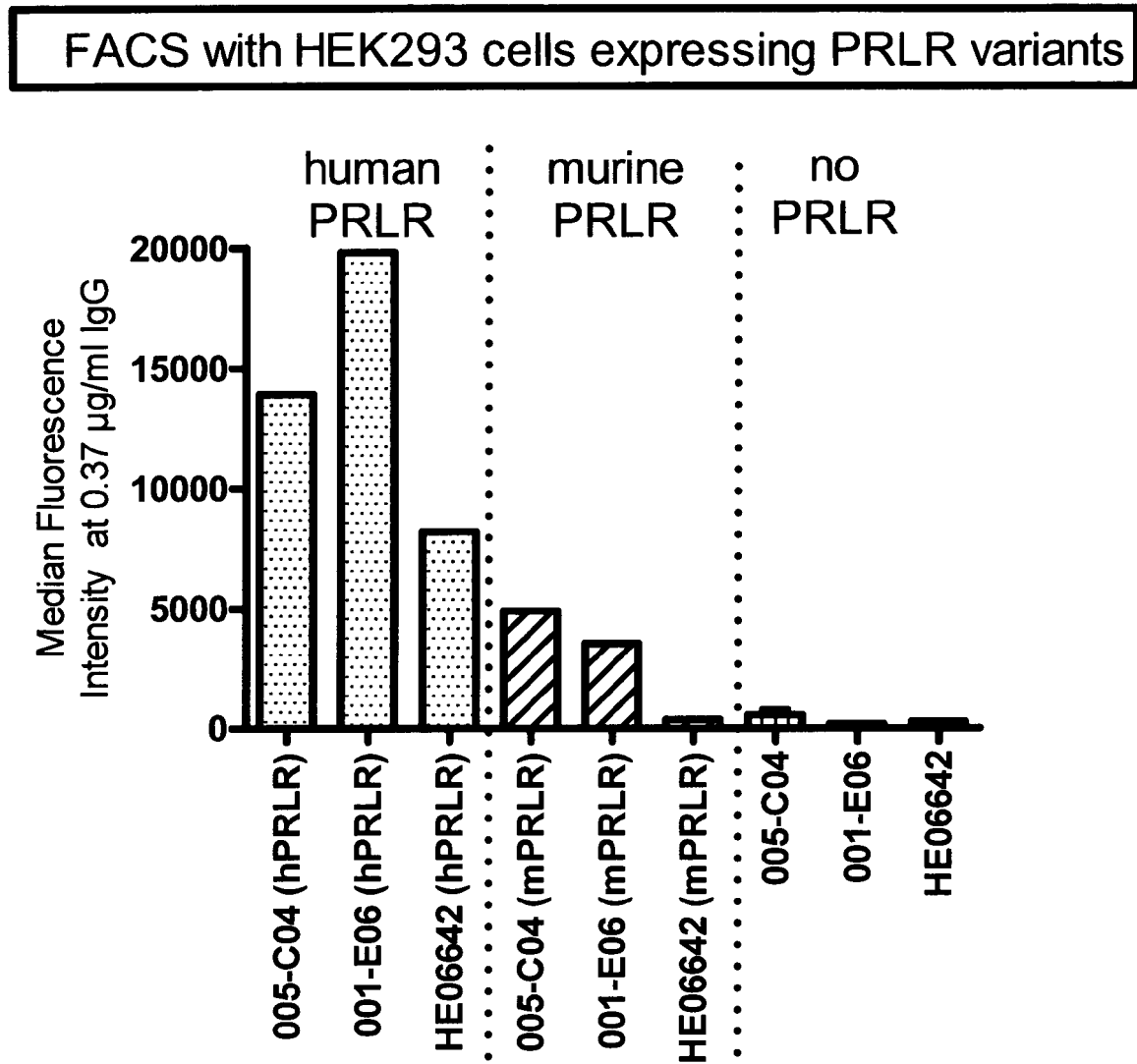


Figure 14: Effect of neutralizing PRLR antibodies on lactation in mice

A Percentage of daily litter weight gain if compared to litter weight on day 1 post partum

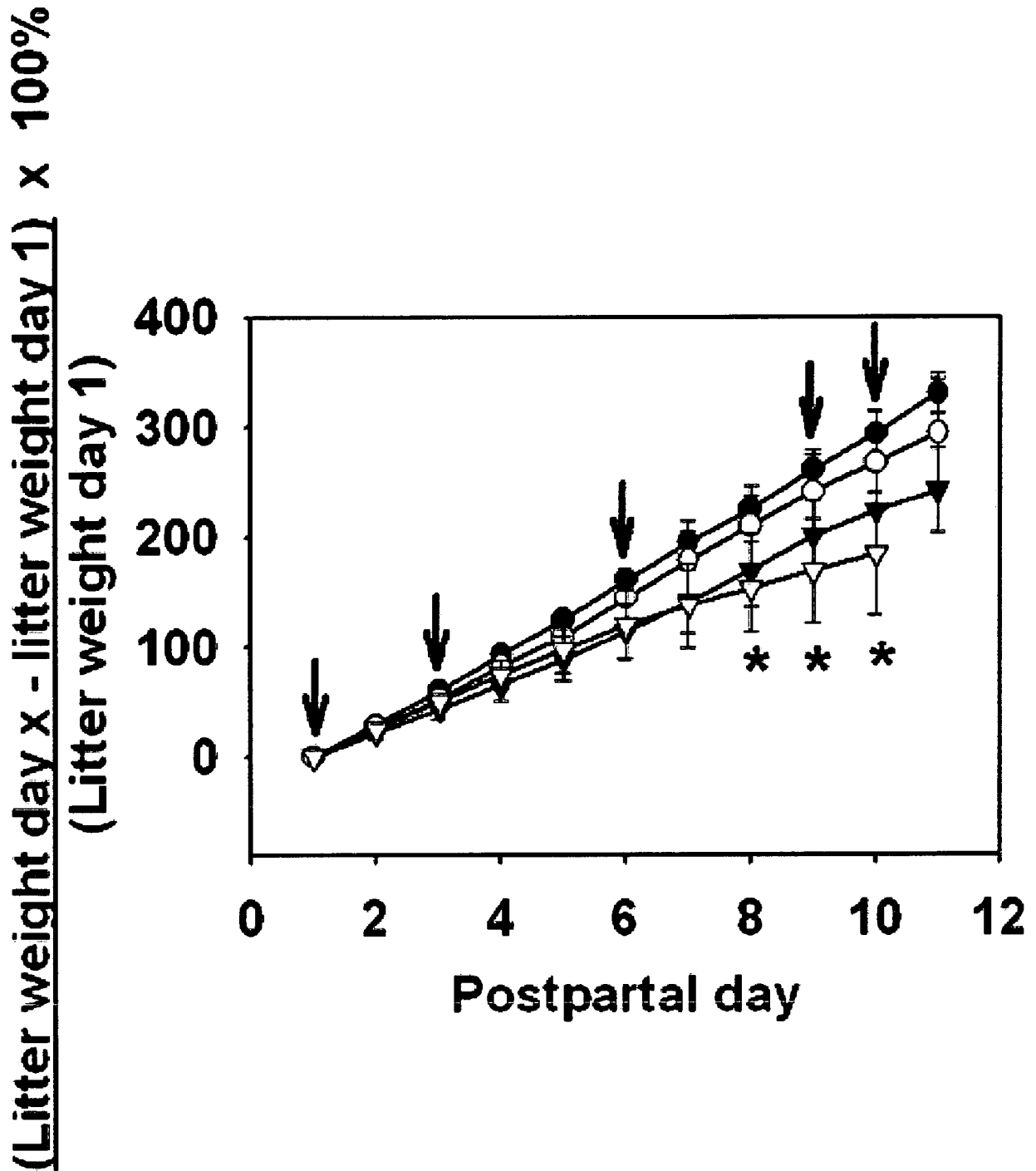


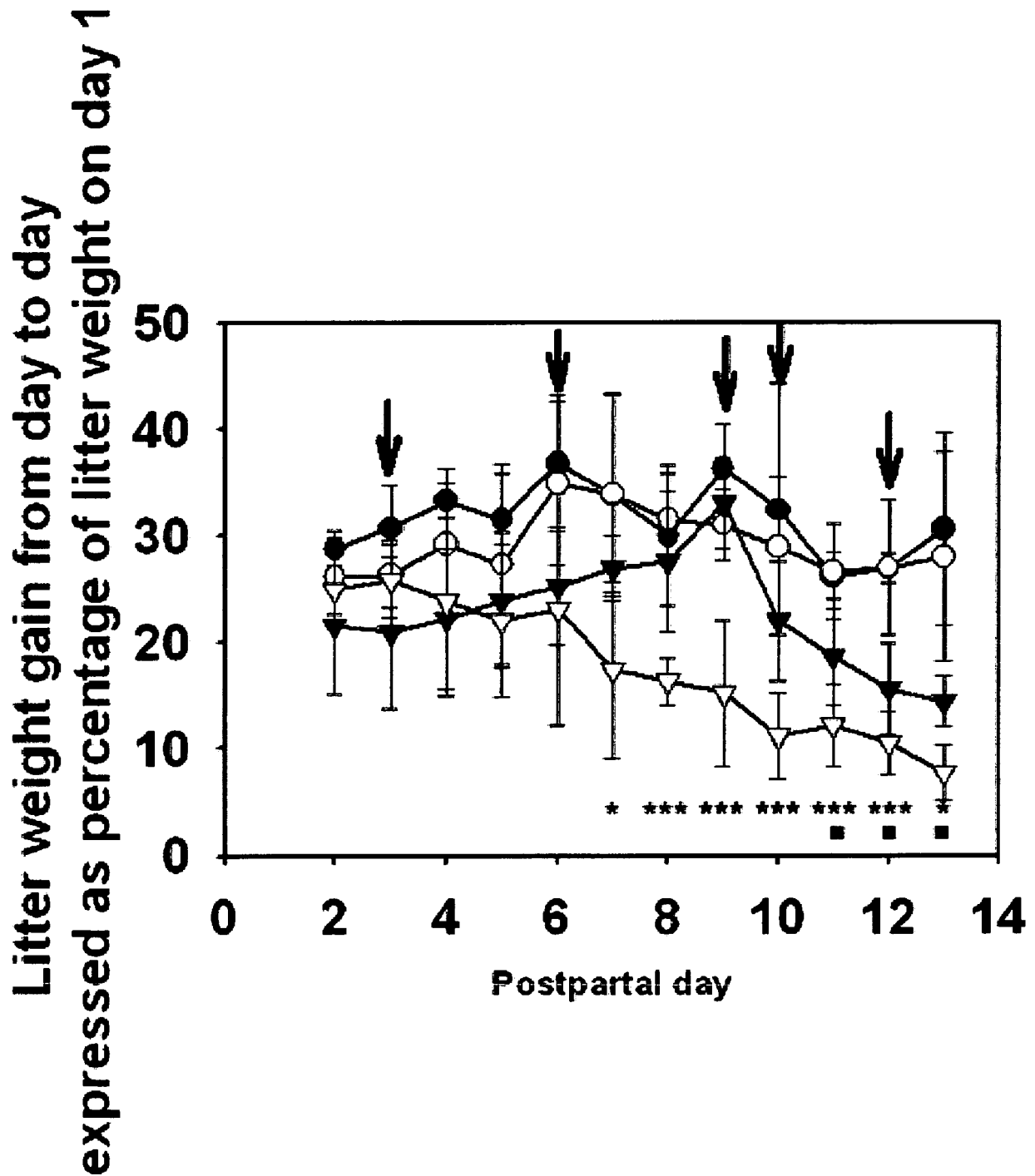
Figure 14: Effect of neutralizing PRLR antibodies on lactation in mice**B** Litter weight gain from day to day expressed as percentage of litter weight on postpartal day 1

Figure 14: Effect of neutralizing PRLR antibodies on lactation in mice

C Involution of mammary glands in lactating mice treated with neutralizing PRLR antibodies

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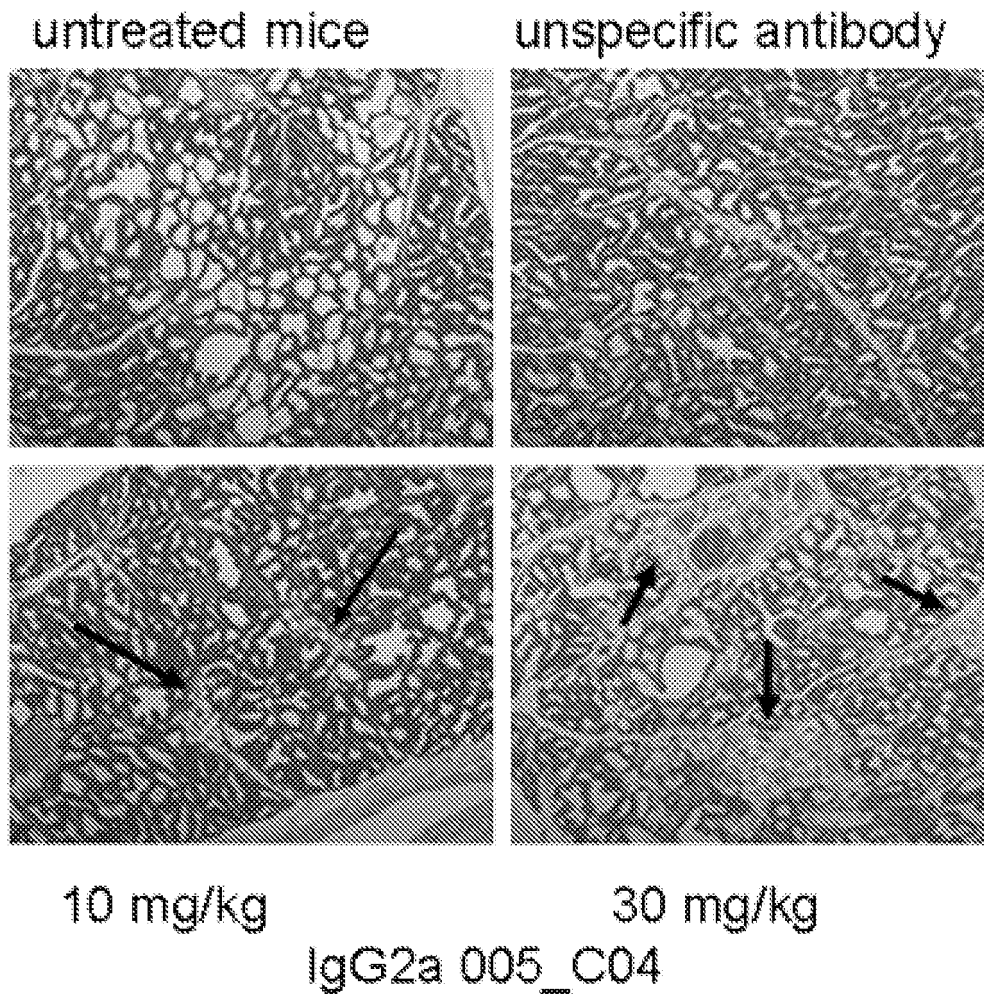
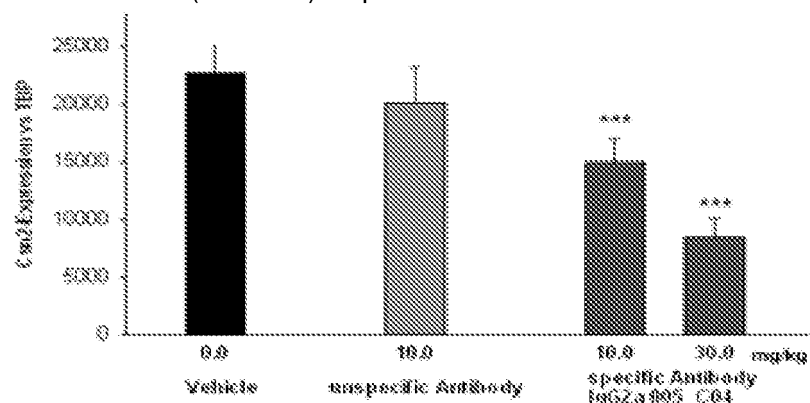


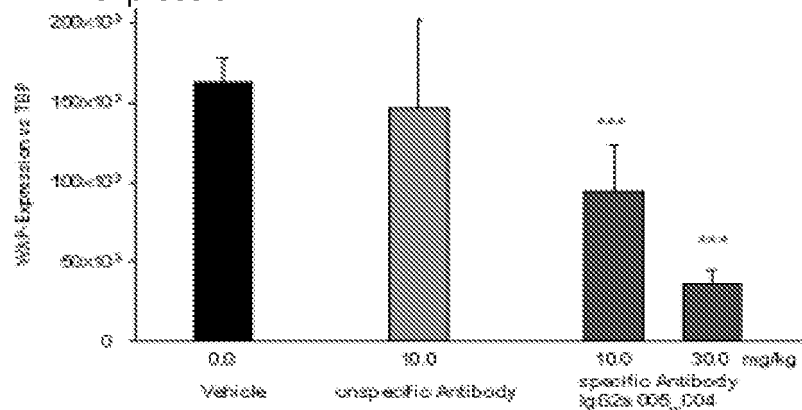
Figure 14: Effect of neutralizing PRLR antibodies on lactation in mice

D Expression of the milk proteins whey acidic protein (WAP), IGF1 and beta-casein (Csn2) is severely reduced in mammary glands from lactating mice treated with neutralizing PRLR antibodies

Beta-casein (snCsn2) expression:



WAP expression



IGF-1 expression

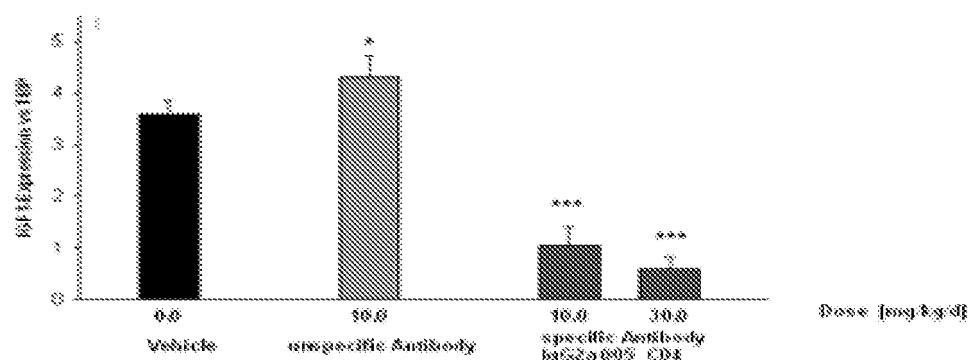
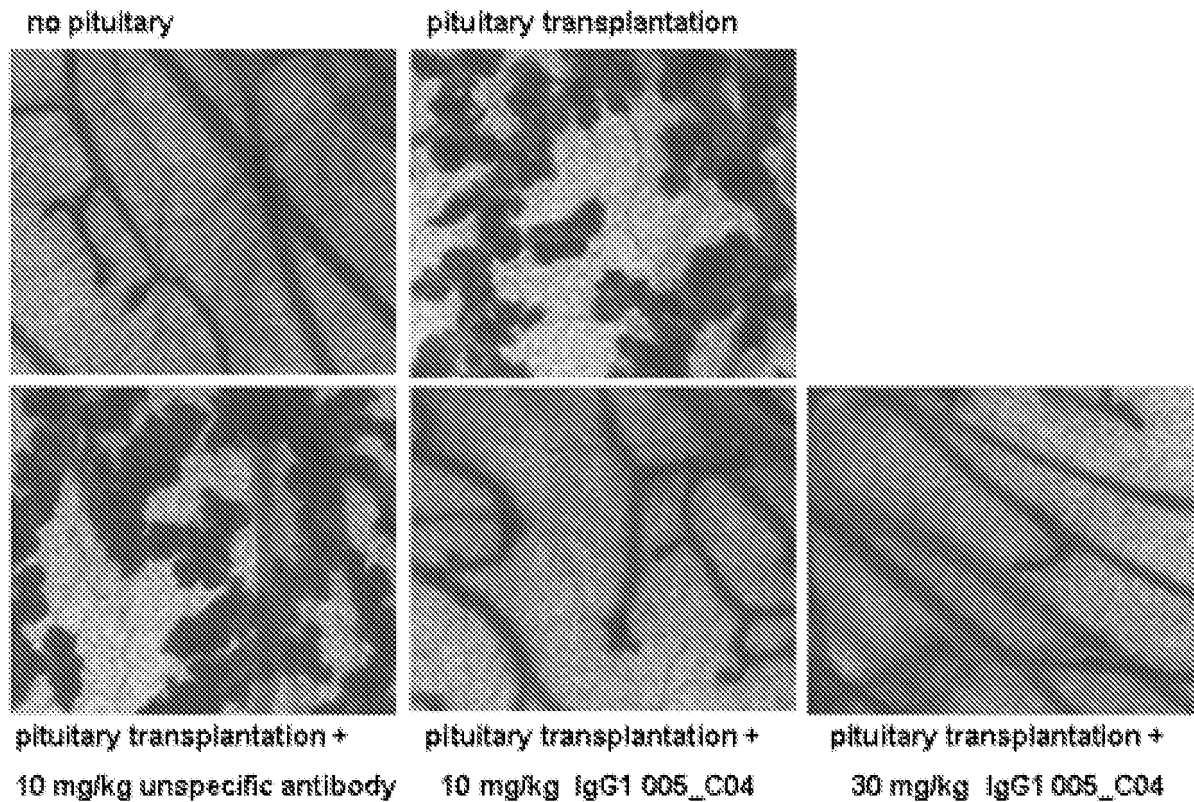


Figure 15: Effect of neutralizing PRLR antibodies on mammary gland epithelial cell proliferation and hyperplasia in a hyperprolactinemic model of benign breast disease

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A Inhibition of side-branching in the mammary gland by neutralizing PRLR antibodies



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Figure 15: Effect of neutralizing PRLR antibodies on mammary gland epithelial cell proliferation and hyperplasia in a hyperprolactinemic model of benign breast disease

B Inhibition of mammary epithelial cell proliferation by using neutralising PRLR antibodies

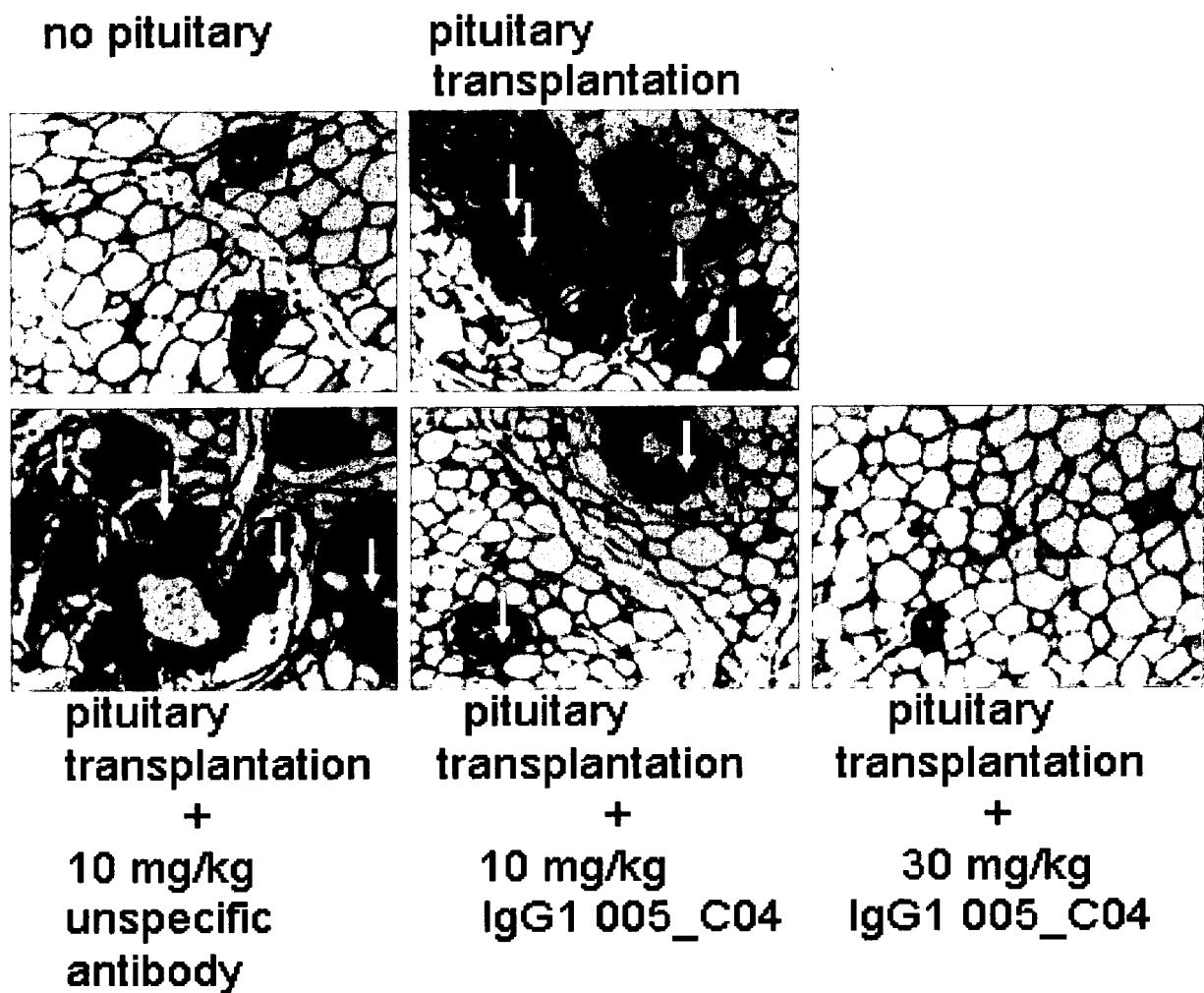


Figure 15: Effect of neutralising PRLR antibodies on mammary gland epithelial cell proliferation and hyperplasia in a hyperprolactinemic model of benign breast disease

C Inhibition of STAT5 phosphorylation in mammary epithelial cells by application of neutralising PRLR antibodies

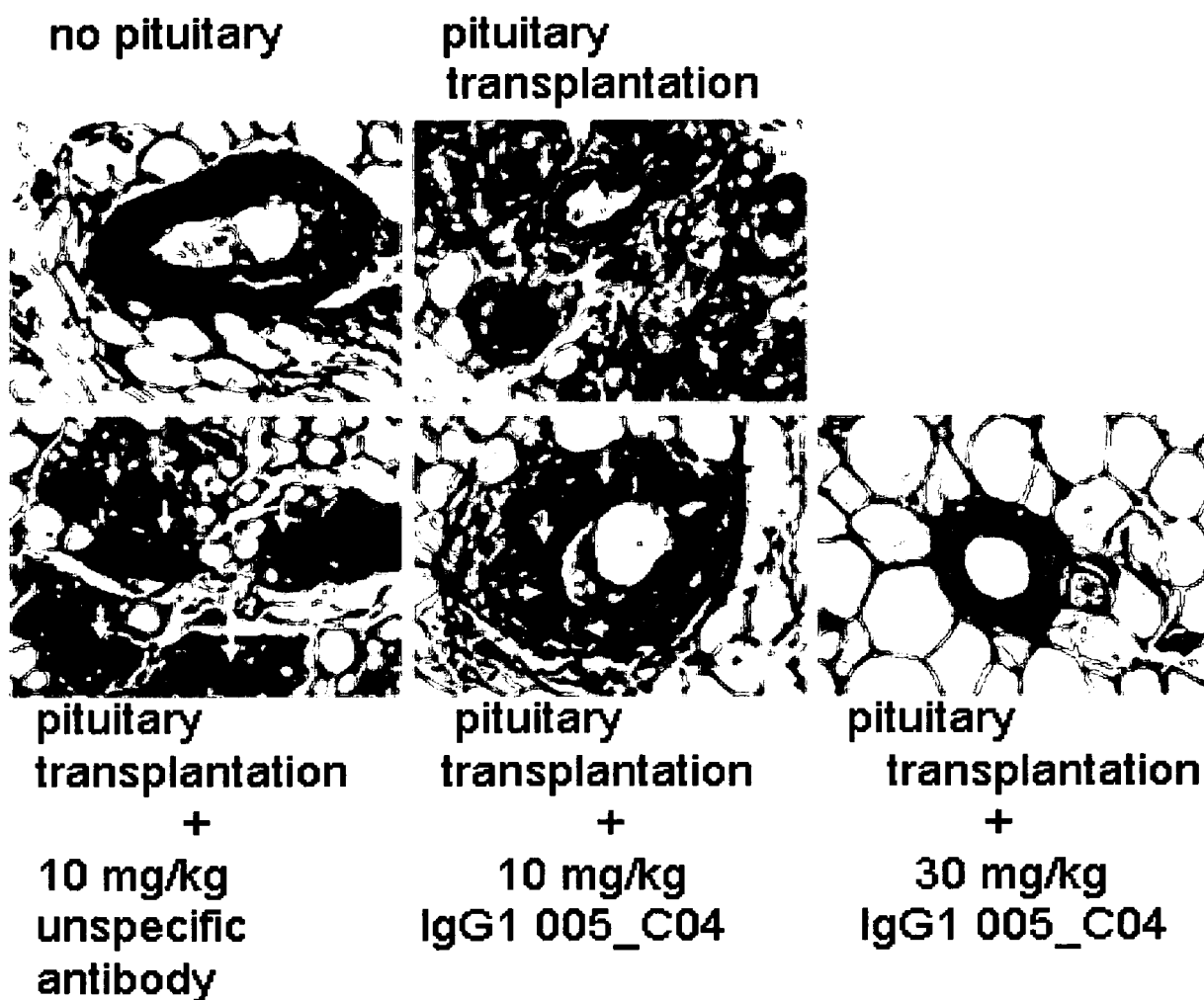


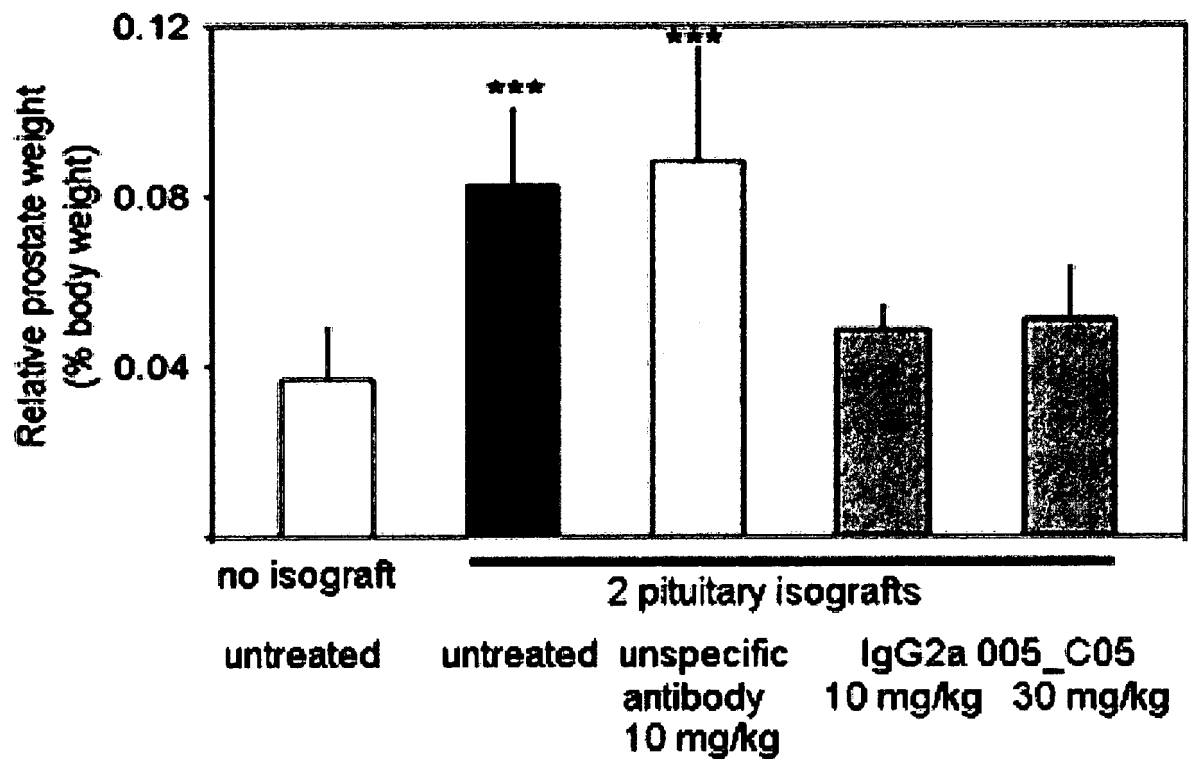
Figure 16: Effect of neutralising PRLR on inhibition of prostate hyperplasia

Figure 17: Effect of neutralizing PRLR antibodies on hair growth in the presence of hyperprolactinemia



No treatment

IgG2a 005_C04

30 mg/kg



Unspecific antibody

IgG2a 005_C04

10 mg/kg

10 mg/kg

Figure 18: Effect of neutralizing PRLR antibodies on hair regrowth in male and female mice under normo- and hyperprolactinemic conditions.

5 A Analysis of female mice

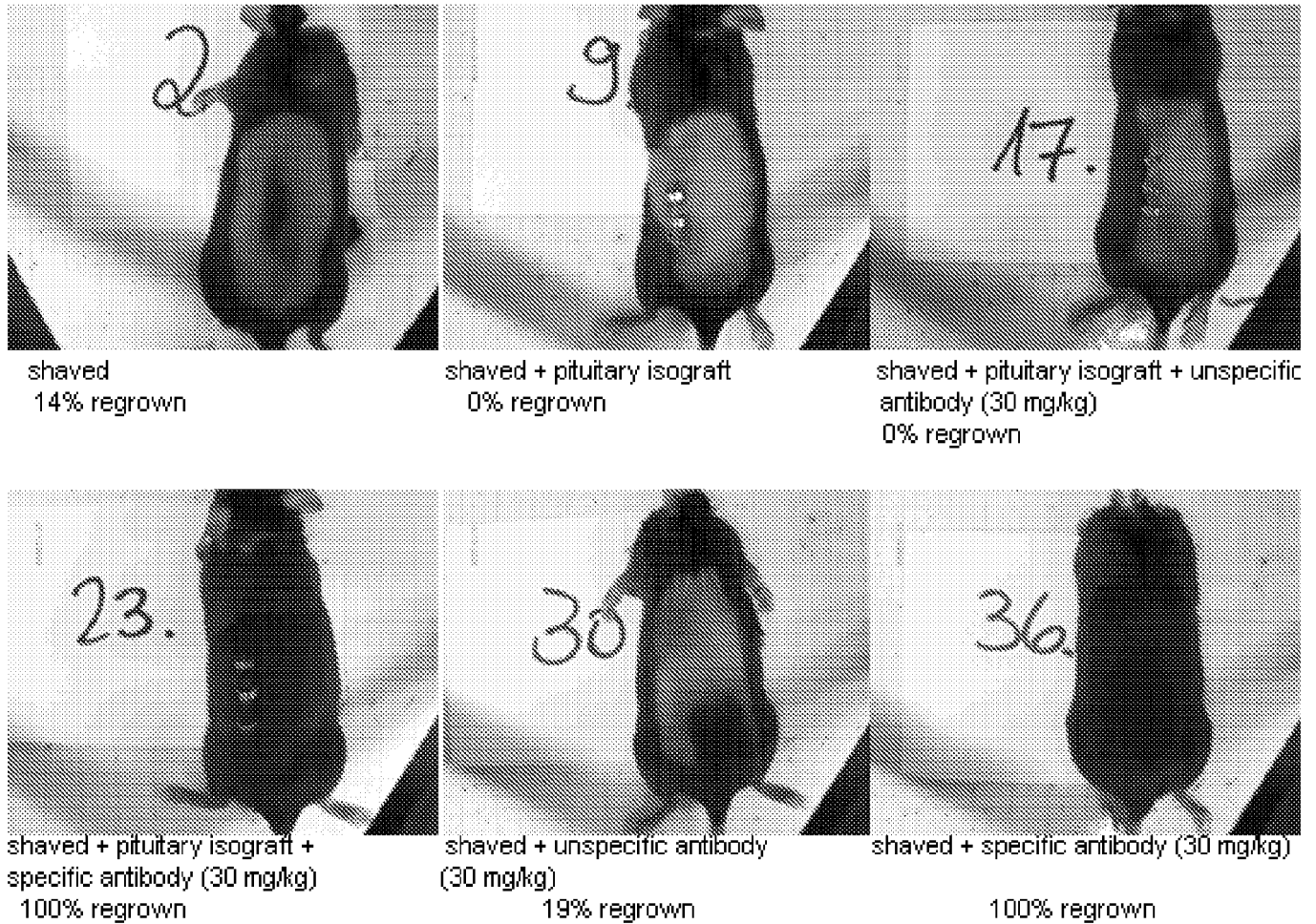


Figure 18: Effect of neutralizing PRLR antibodies stimulation hair regrowth in male and female mice under normo- and hyperprolactinemic conditions.

5 B Analysis of male mice

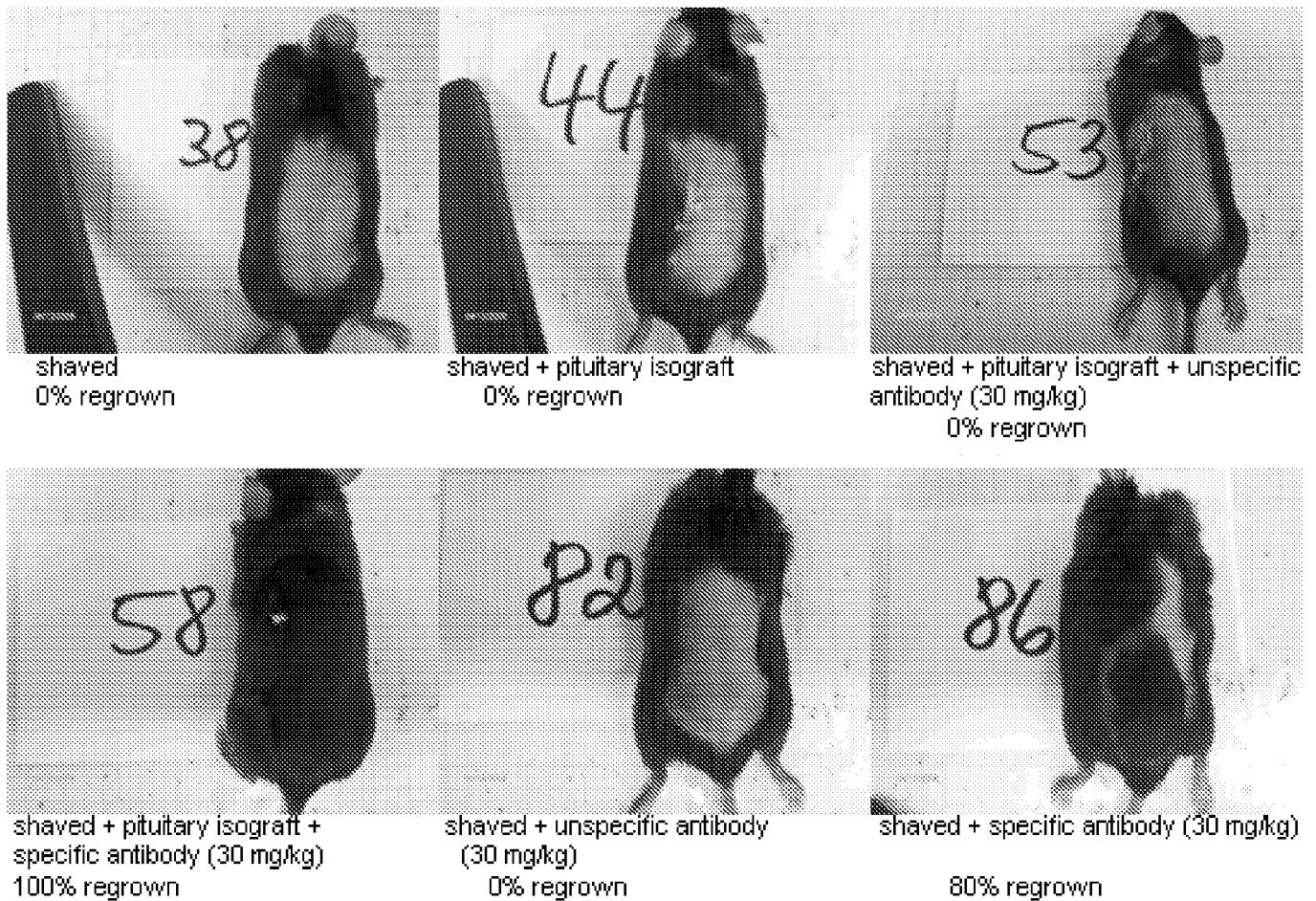
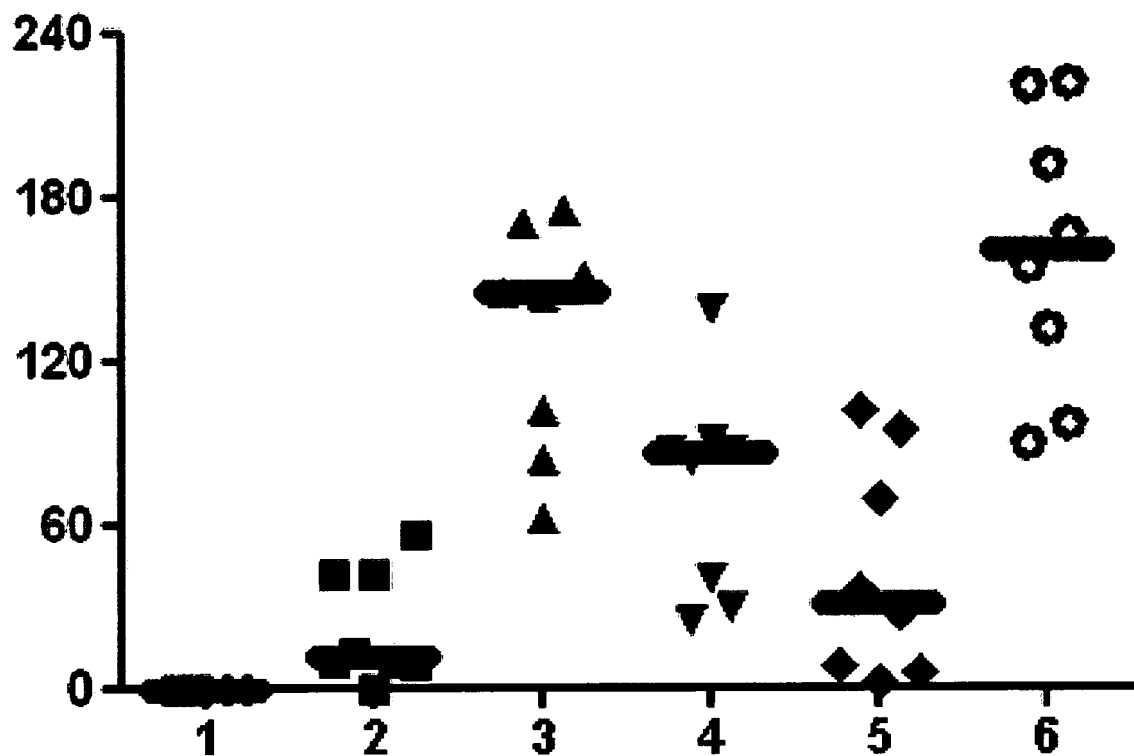


Figure 19: Effect of neutralizing PRLR antibodies on epithelial cell proliferation in the mammary gland under combined estrogen plus progestin hormone therapy



group 1: ovariectomized mice treated with vehicle

group 2: ovariectomized mice treated with 100 ng estradiol

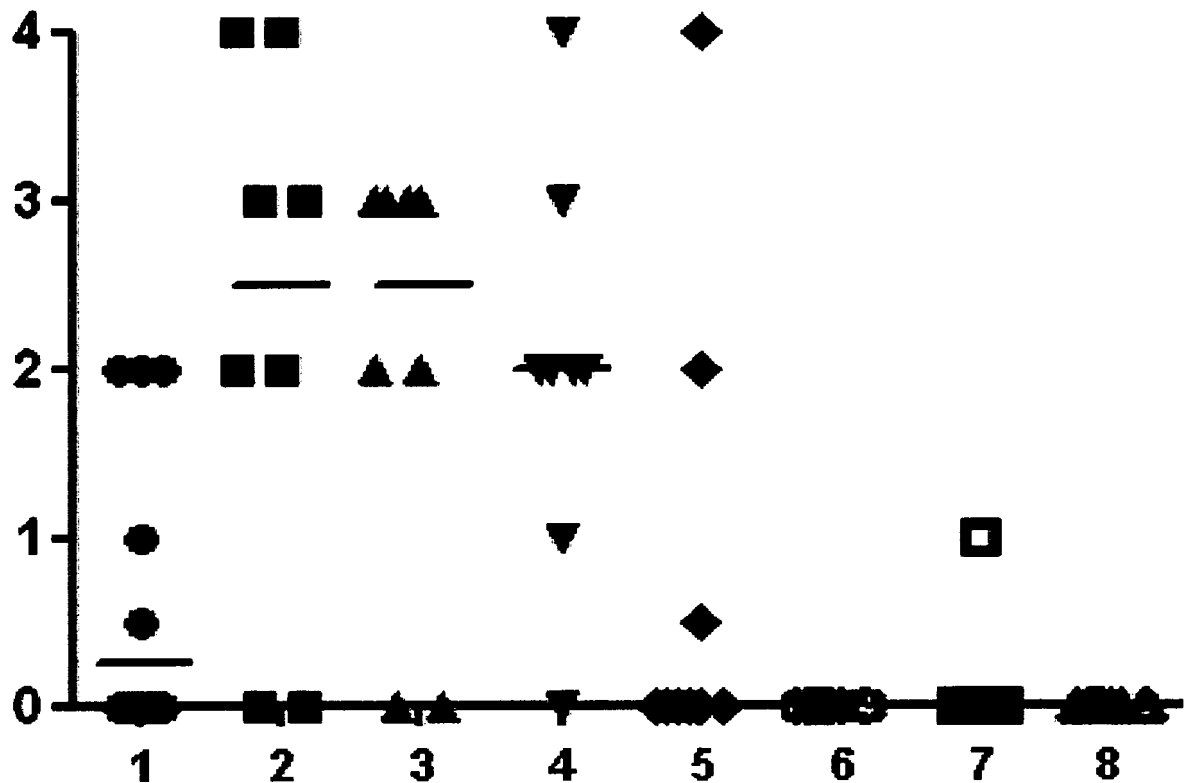
group 3: ovariectomized mice treated with 100 ng estradiol (E) + 100 mg/kg progesterone (P)

group 4: ovariectomized mice treated with E + P and specific antibody 005 C04 at a dose of 10 mg/kg once weekly

group 5: ovariectomized mice treated with E+P and specific antibody
005 C04 at a dose of 30 mg/kg once weekly

group 6: ovariectomized mice treated with E + P and unspecific control antibody at a dose of 30 mg/kg once weekly

Figure 20: Effect of neutralizing PRLR antibodies on endometriosis interna (adenomyosis uteri)



group 1: no pituitary isograft

group 2: pituitary isograft

group 3: pituitary isograft + unspecific antibody 30 mg/kg once weekly

group 4: pituitary isograft + unspecific antibody 30 mg/kg twice weekly

group 5 : pituitary isograft + specific antibody 005_C04 10 mg/kg once weekly

group 6: pituitary isograft + specific antibody 005_C04 10 mg/kg twice weekly

group 7: pituitary isograft + specific antibody 005_C04 30 mg/kg once weekly

group 8 : pituitary isograft + specific antibody 005_C04 30 mg/kg twice weekly

Figure 21. ELISA-based binding tests of matured 005-C04 Fab variants in *E. coli* supernatants with the extracellular domain of the human PRLR.

