

Effects of the GnRH agonist, deslorelin, on prolactin cells

Jennifer Smith and Donal Skinner
Neuroscience and Zoology and Physiology

Introduction

Gonadotropin-releasing hormone (GnRH) agonists have been used extensively to treat gonadal steroid-dependent disorders in humans—such as prostate cancer, endometriosis, uterine fibroids and central precocious puberty (see **Figure 1**). Several studies have also shown the contraceptive ability of GnRH agonists in animals. Despite their widespread use, little remains known about cytoarchitectural changes taking place in the primary target of GnRH agonists, the pituitary.

We have already shown that GnRH agonists reduce gonadotropes synthesizing follicle-stimulating hormone (FSH) in the pituitary, but we are unaware of their effects on lactotropes—cells which produce prolactin, a multifunctional hormone. Evidence suggests that GnRH agonists may affect lactotropes through an intimate relationship these cells share with gonadotropes. Lactotropes are anatomically associated with gonadotropes, and several peptides in gonadotropes have been shown to stimulate lactotrope function. Further, peripheral injections of GnRH increase the plasma concentrations of prolactin in adult rats and humans, and blocking endogenous GnRH causes hyperprolactinemia in female rats.

The effect of GnRH on prolactin release is complex, but gonadotropes do appear to be necessary for normal lactotrope activity. We hypothesized that long-term administration of GnRH agonists, which significantly affects gonadotropes, would modulate the number of lactotropes present in the pituitary of adult male rats.

Methods

Approximately 135-day old Sprague-Dawley rats were used. Animals received 1 of 2 treatments for 6 weeks (see **Figure 1**): a 1.1mg deslorelin implant alone (DESL; $n=6$) or a sham implant insertion (control; $n=6$). After treatment, animals were anesthetized with ketamine and xylazine, injected iv with heparin, sampled for blood via cardiac puncture and then transcardially perfused with Zamboni's fixative, and 20% sucrose. The pituitaries were collected and stored in 20% sucrose at 4°C. Pituitaries were sectioned (20 μ m) on a cryostat and placed on Silane-coated slides. Pituitary sections were washed, incubated in a cocktail containing the primary guinea pig antiserum against prolactin (1:10K; NIDDK), washed, incubated in PBS with a Texas red-conjugated secondary antiserum (1:250; Jackson ImmunoResearch) and then given a final wash and coverslipped with Vectashield® mounting medium with DAPI. Five photos (220 \times 295 μ m) under 400X magnification were randomly taken from each of two mid-sagittal sections from each rat, and the number of cells immunoreactive for prolactin and the total number of cells were counted using Image-J. Data was then analyzed by an unpaired t-test. $P < 0.05$ was considered statistically significant.

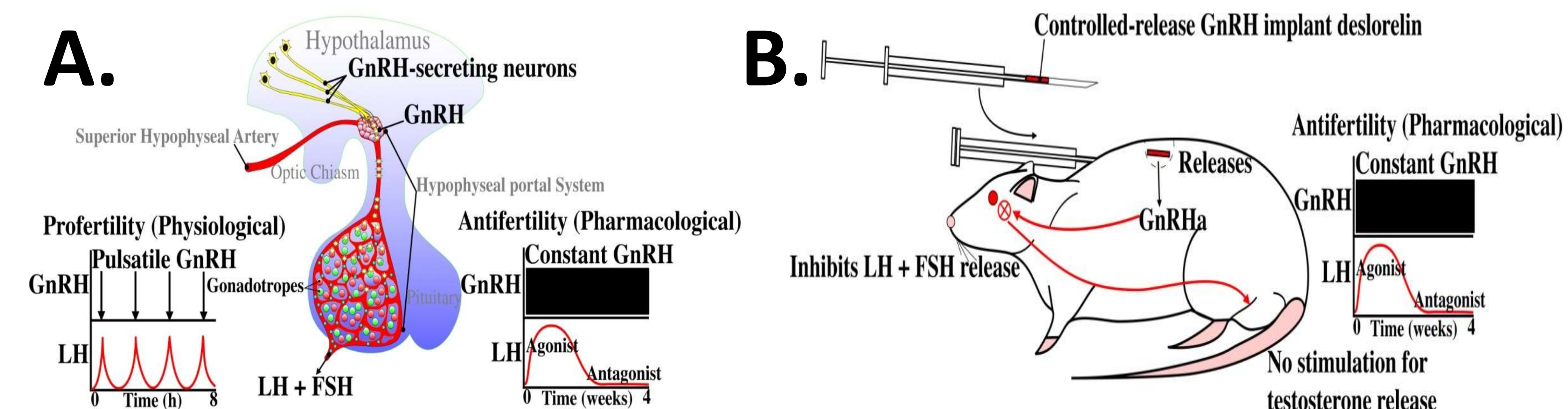


Figure 1. A) Schematic representing the effect of GnRH on pituitary function. B) Representation of procedure for and effect of inserting GnRH agonist implant in the rat.

Results

Both the percentage of prolactin cells (see **Figure 2 and 3**) and the total number of cells (not shown) failed to differ between treatment groups.

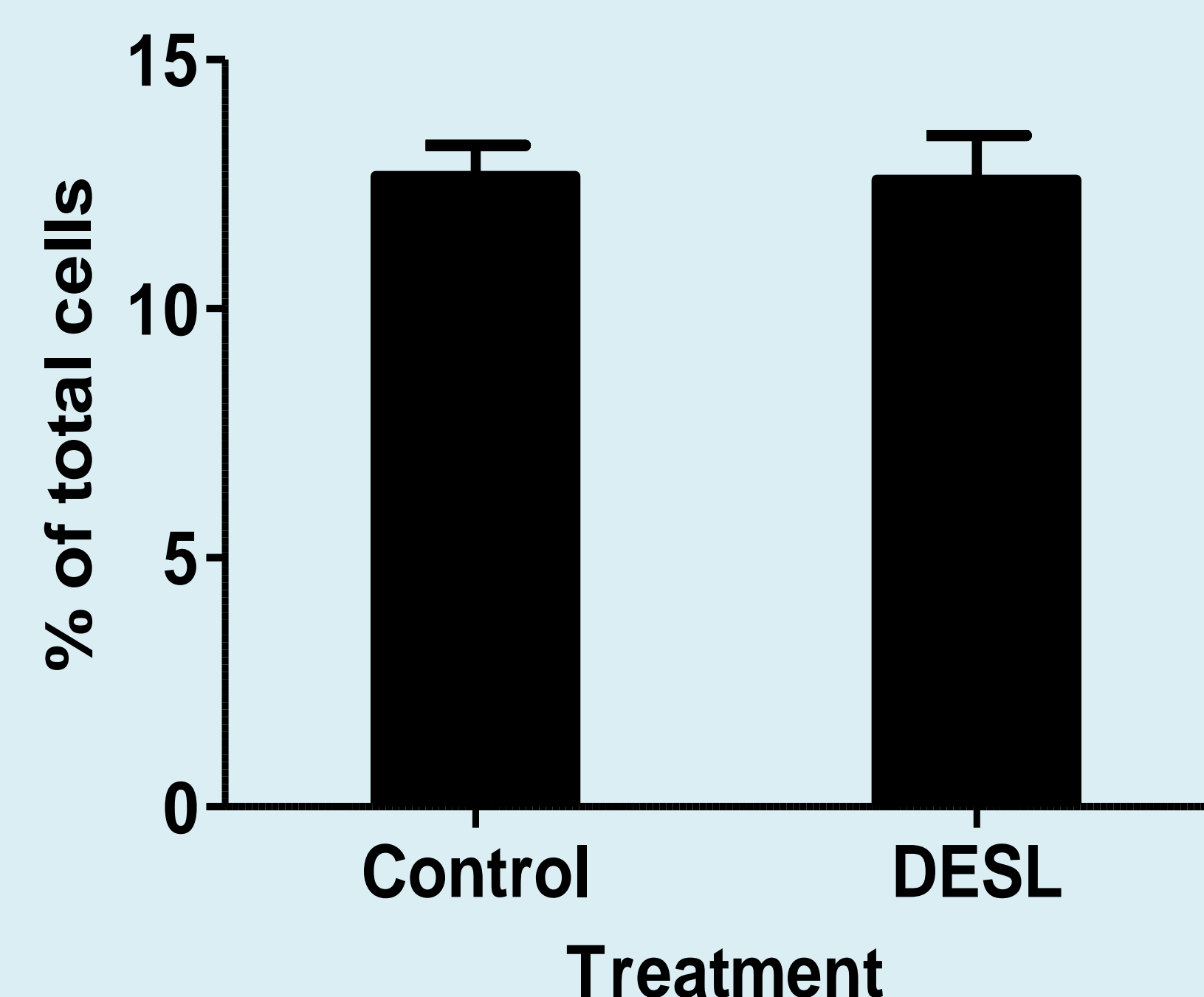


Figure 2. Percentage of pituitary cells synthesizing prolactin in control and deslorelin (DESL)-treated animals. Data are presented as mean \pm SEM.

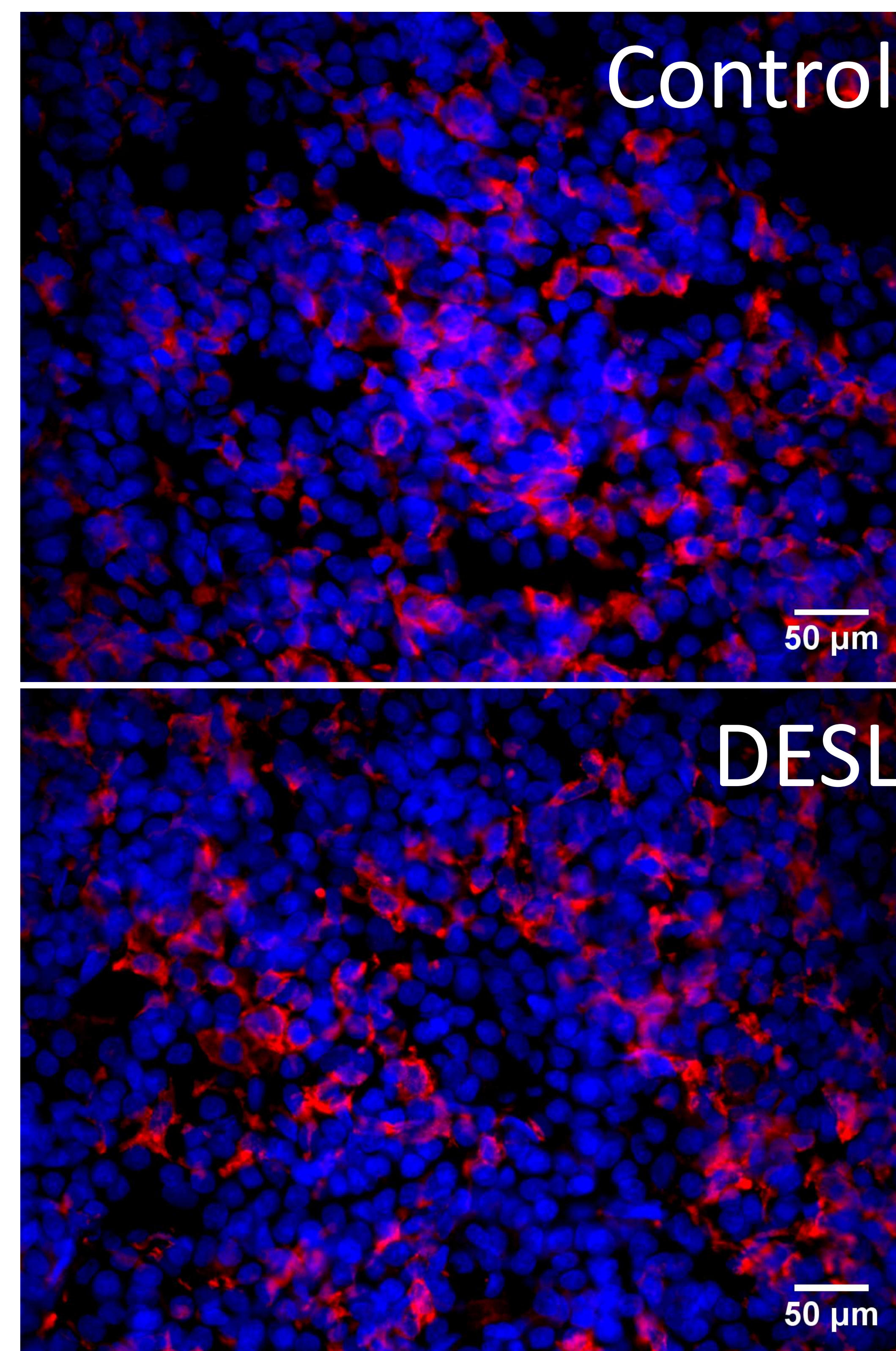


Figure 3. Representative photographs of lactotropes in control and deslorelin (DESL)-treated animals.

Discussion

The results differ from our hypothesis that the known reduction in FSH-synthesizing cells during treatment would affect the lactotrope population. It is possible, however, that lactotropes depend on LH rather than FSH cells. Further research into the relationship between lactotropes and gonadotropes during treatment with GnRH agonists is required.

Acknowledgements

Funding by NIH
INBRE program
Donal Skinner
Arik Smith