

treatment also elevates endometrial AR. Because androgens are known to inhibit some estrogen-dependent endometrial growth, elevations in AR induced by PRA could allow endogenous androgens to suppress proliferation.

PRAs can induce striking changes of the spiral arteries (Slayden et al. 1998, 2001a), which initially appears hypertrophied and then degrade with chronic administration. Endometrial abnormalities are also reported for women after PRA therapy. These changes in women do not fully replicate those seen in NHPs, but both are associated with non-mitotic glandular dilation and arterial abnormalities (Baird et al. 2003; Williams et al. 2007). These vessels, which are unique to the primate endometrium, are primary targets for PRA action even though the endothelium and smooth muscle of the arteries lack PR. Only the perivascular stromal cells express PR and AR, and these may be the cells most affected by PRAs. The damage to the spiral arteries, which includes narrowed lumens and hyalinized walls, probably leads to reduced vascular perfusion which could play an important role in the endometrial antiproliferative effect (Chwalisz et al. 2000a).

5 Induction of Endometriosis

Endometriosis is a gynecological disorder defined by the presence of endometrium-like tissues at “ectopic” sites outside the uterus (Burney and Giudice 2012). The predominant theory, the Sampson Hypothesis (Bricou et al. 2008; Sampson 1940), proposes that endometriosis arises from retrograde menstruation of endometrial fragments through the fallopian tubes. While this theory has not been unequivocally proven, there is substantial evidence that endometriosis-like lesions can be created in NHP models through endometrial transplantation. The limitations on clinical studies, and those using naturally occurring endometriosis in NHPs, have resulted in the development of strategies to create endometriosis-like lesions in non-primate animal models (Grummer 2006). Spontaneous endometriosis is rare in most primate colonies (Story and Kennedy 2004), and there are no reliable noninvasive screening technologies to identify animals with the disease (D’Hooghe et al. 2009). Induction of endometriosis in the baboon was initially described by D’Hooghe (D’Hooghe et al. 1994; D’Hooghe et al. 2009), and although the efficiency of the baboon model was recently challenged (Dehoux et al. 2011), it has been utilized extensively by Fazleabas and coworkers over the last decade at the University of Illinois at Chicago and Michigan State University (Fazleabas 2006; Fazleabas 2010; Harirchian et al. 2012).

6 Conclusions

Old World NHPs, especially macaques and baboons, continue to provide a unique and valuable animal model for experimentally testing the role of novel receptor ligands. The close physiological and anatomical responses of these species to