1 Introduction

Preclinical studies on novel therapies frequently require testing in suitable models, and rodent models are often the first choice for study because of cost. However, reproductive physiology in rodents is strikingly dissimilar from women, and therapeutic interventions in rodents often fail to fully replicate in clinical trials (Pullen et al. 2011). In contrast, macaques share approximately 95% of genetic coding sequence identity with humans (Magness et al. 2005). Moreover, most responses to hormonal therapies in women are fully reproduced in nonhuman primates (NHPs) (Shively and Clarkson 2009). Rhesus and cynomolgus monkeys (*Macaca mulatta* and *M. fascicularis*) have been particularly useful in biomedical studies because of their moderate size. Although strikingly larger, baboons present spontaneous adenomyosis (Barrier et al. 2004), endometriosis (Cornillie et al. 1992), and endometrial hyperplasia (Barrier et al. 2007) similar to women. Moreover, both macaques and baboons can display polycystic ovarian syndrome-like features and are suitable models for interventional therapies relative to ovarian-based infertility (Fraser and Duncan 2009).

Macaques and baboons can be trained to accept a wide variety of manipulations that facilitate drug administration and sample collection. For example, steroid receptor modulators including progestins and progesterone receptor antagonists (PRA) have been administered to macaques transvaginally (Hodgen 1985), orally (Tarantal et al. 1996), systemically by injection (Slayden et al. 1998), and by subcutaneous implant (Brenner et al. 2006). Because the action of these agents on endometrial histology and physiology has been well characterized, the assessment of endometrial histology after administration of novel agents has become a priority in the screening of new therapies before development of clinical trials.

Old World monkeys display menstrual cycles and reproductive tract anatomy similar to women (Brenner and Slayden 1994). Hysterectomized NHPs, like women, continue to undergo normal ovarian cycles indicating that uterine feedback is not required for ovarian function (Metcalf and Livesey 1988; Molskness et al. 2007). The only ovarian factors absolutely required to elicit cyclic responses in the primate endometrium are the ovarian steroids estradiol (E_2) and progesterone (P_4) (Hisaw and Hisaw 1961). The uterine cavity of NHPs is lined by a thick glandular endometrium with four distinct endometrial zones, surrounded by a thick muscular wall or myometrium (Bartelmez 1933, 1951). The upper three of the endometrial zones are frequently referred to as the endometrial functionalis; the zone adjacent to the myometrium is referred to as the basalis zone. The functionalis zone in NHPs is vascularized by unique "spiral" arteries, whereas the basalis zone is vascularized by the basilar arteries. The functionalis zones are typically shed during menstruation and are regenerated each cycle from the basalis zone. The histology and hormone regulation of these zones have been well characterized and provide the basis for use of these animals for studies assessing novel therapies on reproductive tract physiology (Slayden and Keator 2007).

Fallopian tube histology is also similar between NHPs and women. Compared to ovariectomized individuals, estrogen stimulates differentiation of the tubal