EXTENDING THE INTERVAL OF ACTION AND EFFECTIVENESS OF THE EMERGENCY CONTRACEPTIVE ULIPRISTAL ACETATE

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Highly effective emergency contraception provides women the means to avoid pregnancy following an act of unprotected intercourse. Levonorgestrel (LNG; Plan B™) and UPA are two EC options. LNG is available without a prescription, but is not as effective as UPA since UPA prevents pregnancies for up to 72 hours after intercourse, whereas LNG only works for 48 hours after unprotected intercourse. Thus, UPA has recently emerged as the most effective hormonal EC option. At present, however, it is unclear why the effectiveness of UPA drops dramatically when administered around the time that the pituitary initiates ovulatory events through the release of LH.

In theory, progesterone receptor antagonists should prevent post-ovulatory fertilization and implantation, but in actuality the ability of UPA to prevent pregnancy is greatly diminished when taken during the periovulatory interval. The mechanism for the post-LH reduction in UPA effectiveness is unknown, but a greater understanding could lead to strategies that enhance efficacy. In this regard, the data from the studies supported through this SFP Research Fund grant revealed a novel cytochrome P450 family member (CYP3A5), belonging to the class of enzymes responsible for drug metabolism, is highly expressed in the primate follicle following an ovulatory stimulus and in the corpus luteum. Moreover, the CYP3A5 enzyme was shown to directly metabolize UPA to a compound that lacks any biological activity. Thus, these results support our hypothesis that the presence of CYP3A5 in the primate ovary after the midcycle LH surge serves to limit the ability of UPA to block progesterone actions that are critical for fertility, including the release of the oocyte as well as the formation and function of the corpus luteum.