

## **Altered abundance of protein involved in chemical biotransformation in inguinal adipose tissue in lean and obese female mice during exposure to dimethylbenz[a]anthracene**

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Lifestyle factors can lead to increased adiposity which can cause reduced female fertility. Obesity, which is associated with reduced oocyte quality, conception, and implantation, affects over 40% of US reproductively aged women. Many environmental toxicants are lipophilic in nature and are sequestered into the adipose tissue. One such toxicant is the polycyclic aromatic hydrocarbon, 7,12-dimethylbenz[a]anthracene (DMBA) which is a known ovotoxicant. DMBA is generated during combustion of organic material present in tobacco products, smoked meats, and diesel exhaust fumes. Chemical biotransformation systemically is necessary to prevent toxicants from impacting the ovary and previous studies support that obese mice suffer increased DNA damage and a reduced ovarian protective response compared to lean counterparts during ovotoxicant exposure. The possibility that this differential ovotoxicity in obese compared to lean mice results from extrahepatic biotransformation in the adipose tissue remains unclear. This study investigated the hypothesis that DMBA exposure will alter adipose tissue proteins associated with chemical biotransformation in lean and obese female mice. Female KK.Cg-a/a (lean; n = 20) and KK.Cg-Ay/J (obese; n = 20) were provided a regular mouse chow diet *ad libitum*. When the obese had ~30% increased body mass compared to lean mice (~10-weeks old), mice received an intraperitoneal injection with corn oil (vehicle control; CT) or DMBA (1 mg/kg) for 7 d. Thus, there were four treatment groups: lean-CT, lean-DMBA, obese-CT, and obese-DMBA (n = 10 each). Euthanasia occurred at day two of diestrus, upon which body, ovary, uterus, spleen, liver, and adipose tissue weights were recorded. Inguinal adipose tissue protein was isolated and western blotting determined that obesity increased ( $P < 0.05$ ) AHR, GSTP1, and CYP1B1 but decreased ( $P < 0.05$ ) CYP19 protein level. In lean mice, DMBA exposure increased ( $P < 0.05$ ) AHR but in contrast in the obese mice, DMBA exposure decreased ( $P < 0.05$ ) AHR protein level. Comparison between lean-DMBA and obese-DMBA mice identified increased ( $P < 0.05$ ) EPHX1 and CYP1B1, and decreased ( $P < 0.05$ ) AHR, CYP1A1 and CYP19 proteins. These findings support the hypothesis that the adipose tissue biotransforms chemicals with a differential response in the adipose tissue from an obese compared to a lean female, potentially affecting female reproductive and general health. Supported by 1R01ES030341-01 and by 1R01ES030341-S2 from NIEHS.

