

## Vaginal thread formation in the healthy offspring of untreated Long-Evans rats

M. LaRue<sup>1</sup>, D. Hill<sup>2</sup>, N. Chernoff<sup>2</sup>

<sup>1</sup>Oak Ridge Institute for Science and Education Internship/Research Participation Program at the U.S. Environmental Protection Agency, NHEERL, Research Triangle Park, NC 27711, USA

<sup>2</sup>U.S. Environmental Protection Agency, NHEERL, Research Triangle Park, NC 27711, USA

Vaginal threads are characterized as cords of mesenchymal tissue that cross the vaginal opening. They are sometimes apparent in rats after weaning, and typically disappear within 1-2 days as the female reaches puberty. If persistent, they can increase uncertainty in assessing reproductive system maturity and vaginal opening, and may also interfere with parturition. The occurrence of vaginal threads has been associated with prenatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), but there is evidence that other pesticides such as vinclozolin, androgens such as testosterone and trenbolone, and anti-androgenic compounds including polychlorinated biphenyls (PCBs) can cause thread formation from *in-utero* exposures. During a multigenerational study investigating the influence of undernutrition on postnatal development, we observed vaginal threads in two generations of Long-Evans rats. The generation treatments were as follows: F0 – control or restricted diet throughout pregnancy; F1 – control or restricted diet pre-weaning, control diet during pregnancy; F2 – control diet. Persistent threads were observed at nearly equal frequency (≈30%) in control and food restricted F0 offspring (F1), and noted in 67% of control and 80% of restricted diet F1 offspring (F2). The discovery of these threads was surprising since the mothers of both affected generations were not exposed to xenobiotics, and their appearance and viability was normal. These findings highlight the uncertainty of vaginal thread determinants, and emphasize the need for further research and enhanced reporting of vaginal thread occurrence, as called for by the Environmental Protection Agency's Endocrine Disruptor Screening Program (EDSP). Due to the importance of *in-vivo* rodent assays in assessing the maturation of the reproductive system, causal factors involved in vaginal thread formation need to be identified, and controlled if possible, to ensure proper interpretation of studies evaluating potential adverse effects of chemicals on reproductive system maturation.