THE IMPACT OF ENDOCRINE DISRUPTING CHEMICALS ON A VULNERABLE DEVELOPMENTAL TRANSITION IN THE JUVENILE OVARY

Female reproductive success requires the production of high-quality eggs throughout a woman's reproductive lifespan. The finite ovarian reserve of immature eggs is established around birth. How the ovarian reserve changes over time to shape fertility remains in question. Growing evidence indicates that exposure to endocrine disrupting chemicals (EDCs) adversely affects egg quality. The well-documented decline in egg quality with maternal age is largely attributed to aneuploidy caused by progressive weakening of cohesion between sister-chromatids. Surprisingly, eggs from very young women also have high levels of aneuploidy. Using mouse models, we showed that: (i) this is caused by excessive cohesion impeding chromosome separation; and (ii) cohesion is abruptly weakened during puberty to optimize chromosome segregation in the eggs of sexually mature females. I am investigating the idea that progressive weakening of cohesion defines an oocyte aging clock that shapes female fertility at all ages. Additionally, I am investigating the idea that the abrupt weakening of cohesion at puberty defines a critical developmental transition that is vulnerable to EDCs by exposing juvenile mice to the herbicide Atrazine and the plasticizer Bisphenol-A to exacerbate the maternal-age effect. Meiotic errors are a major cause of the ≥1 million human conceptions that end in miscarriage each year in the USA. Moreover, meiotic chromosome errors are a leading cause of congenital disease. Understanding how environmental factors, such as EDC exposure, influences reproductive success becomes increasingly significant as women delay the birth of their first child.