

Gene regulation by gonadal hormone receptors underlies brain sex differences

Gegenhuber B, Wu MV, Bronstein R, Tollkuhn J (2022) Gene regulation by gonadal hormone receptors underlies brain sex differences. *Nature*, 606(7912):153-159.

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While the role of estrogens and their receptors in organizing and activating sexually differentiated brain circuits has been well-described, a complete description of the genomic targets of estrogen receptor alpha (ER- α), a major estrogen-responsive transcription factor, has been elusive. In this paper by Gegenhuber et al., the authors extensively map ER- α genomic binding sites in neurons of the bed nucleus of the stria terminalis (BNST), a sexually dimorphic and steroid-sensitive brain region regulating social behavior. In these tour-de-force experiments, the authors demonstrate two new ER- α expressing and male-biased neuronal subtypes in the BNST, show that these and other ER- α expressing neurons maintain their sex-specific transcriptional identities from early development to adulthood, and identify regions throughout the genome with changes in chromatin accessibility in response to estradiol. Collectively, these experiments provide a rich data set that future research can use to identify gene regulatory pathways underlying hormone-sensitive sexual differentiation of nervous systems and behavior.