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A short anogenital distance (AGD) in males is a marker for incomplete masculinization and a predictor of adverse effects on male reproductive health. For this reason, AGD is used to assess the endocrine disrupting potential of chemicals for risk assessment purposes. The molecular mechanisms underpinning this chemically induced shortening of the AGD, however, remains unclear. Although it is clear that AR-mediated signaling is essential, evidence also suggest the involvement of other signaling pathways. This study presents the first global transcriptional profile of the anogenital tissue in male rat fetuses with chemically induced short AGD, also including comparison to normal male and female control animals. The anti-androgenic drug finasteride (10mg/kg bw/day) was used to induce short AGD by exposing time-mated Sprague Dawley rats at gestation days (GD) 7-21. The AGD was 37% shorter in exposed male fetuses compared to control males at GD21. Transcriptomics analysis on anogenital tissues revealed a sexually dimorphic transcriptional profile. More than 350 genes were found to be differentially expressed between the three groups. The expression pattern of four genes of particular interest (Esr1, Padi2, Wnt2 and Sfrp4) was also tested by RT-qPCR analyses, indicating that estrogen and Wnt2 signaling play a role in the sexually dimorphic development of the anogenital region. Our transcriptomics profiles provide a stepping-stone for future studies aimed at characterizing the molecular events governing development of the anogenital tissues, as well as describing the detailed Adverse Outcome Pathways for short AGD; an accepted biomarker of endocrine effects for chemical risk assessment.

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