SSR 54TH ANNUAL MEETING

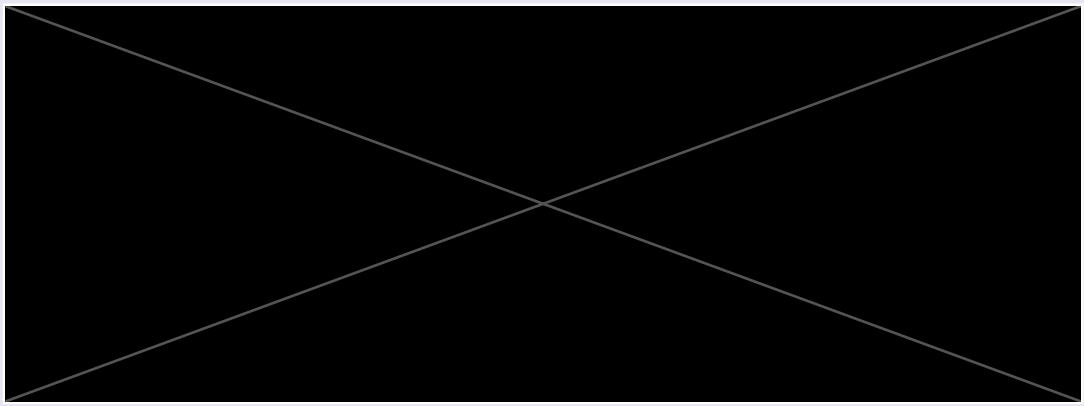
Reproductive Biology:
Solutions for Adult Disease

Dec. 15–18, 2021

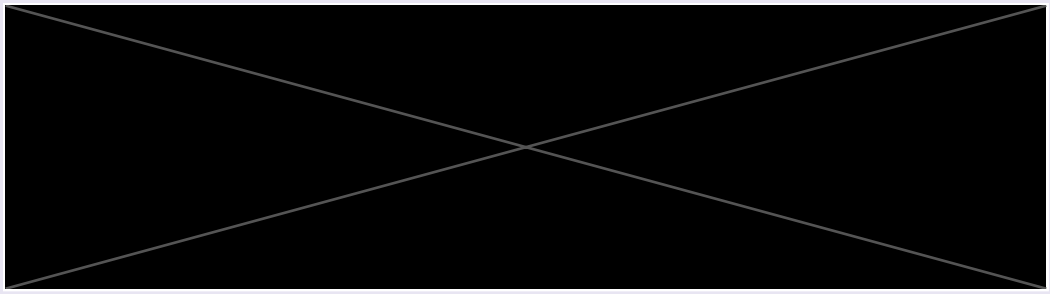
St. Louis Union Station Hotel
St. Louis, MO

SSR
Society for the Study of Reproduction

Reproduction… Where the Future is Conceived

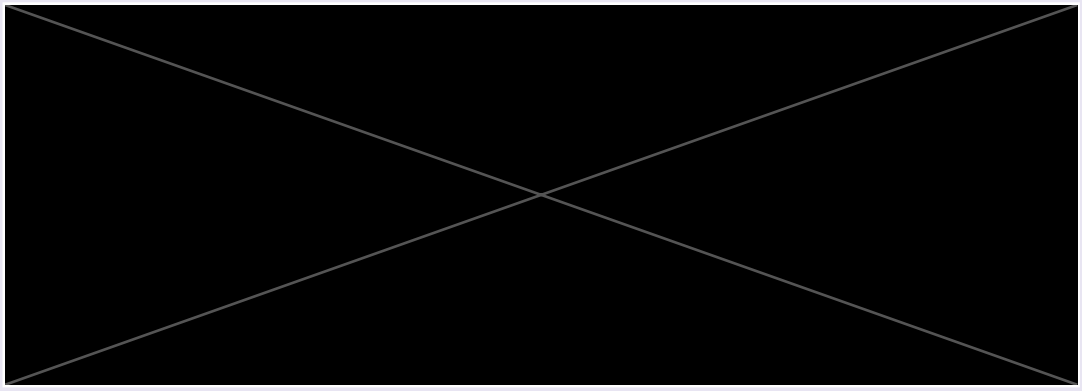


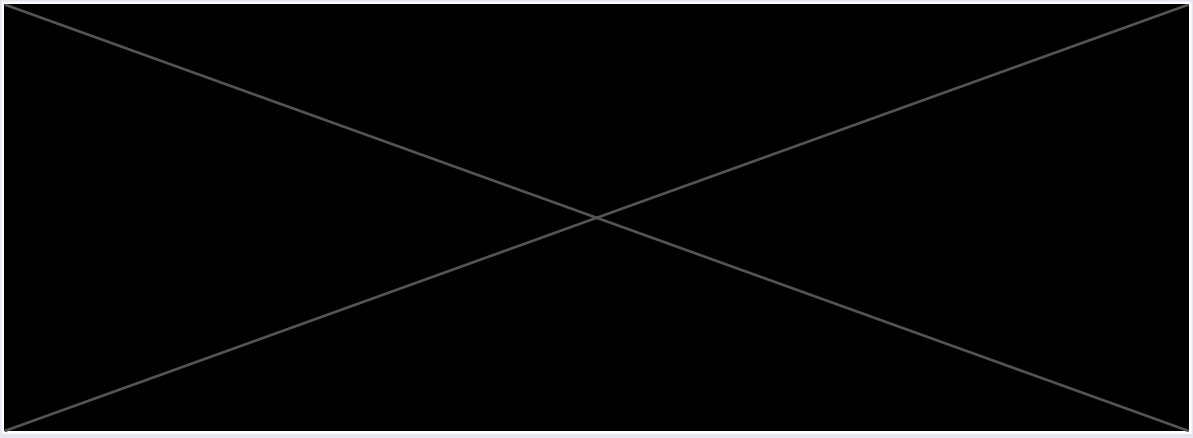
2021 SSR Trainee Research Award Post-Doctoral Poster Competition Finalist

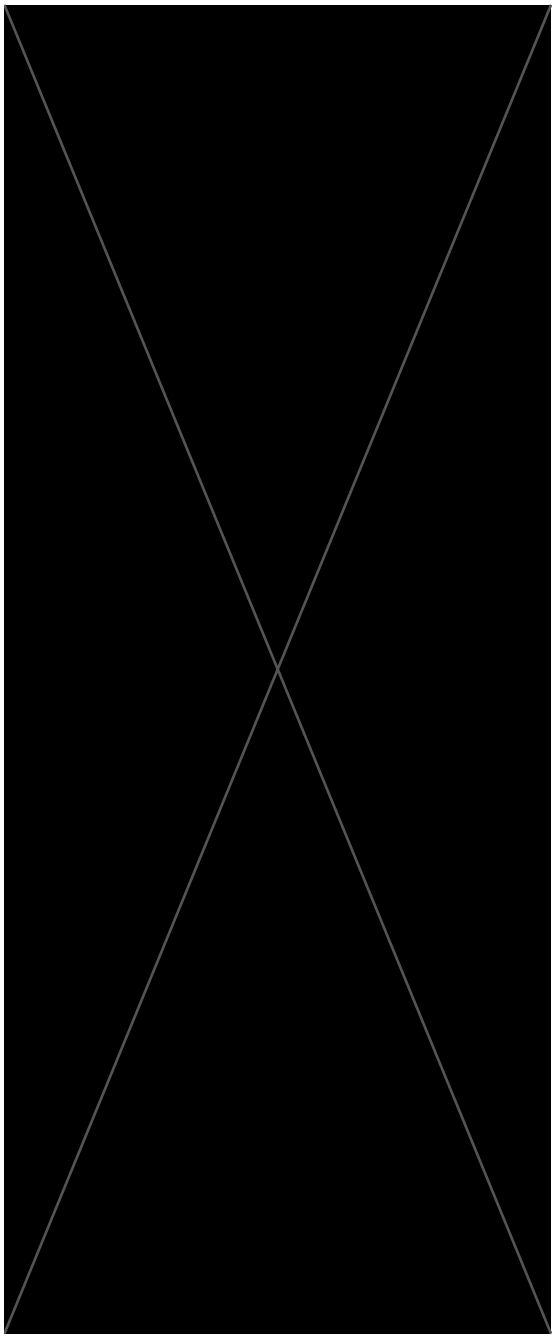


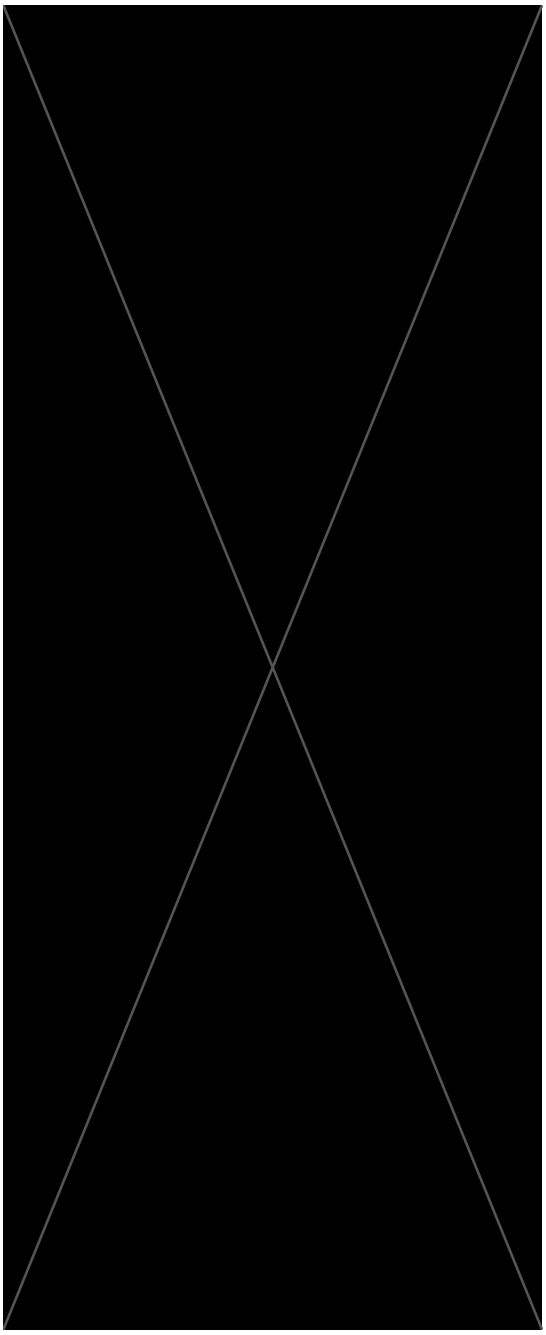
A Mouse Model to Investigate the Reproductive Consequences of Testosterone Administration After Suppressing Puberty in Transgender Boys

Cynthia Dela Cruz, University of Michigan, USA



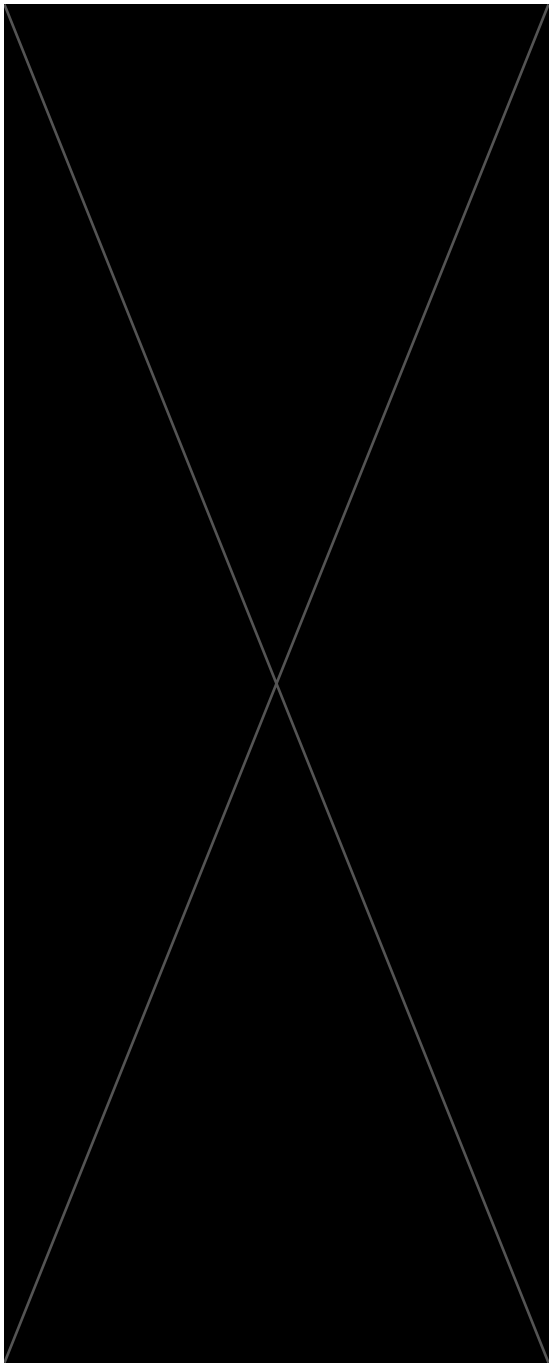


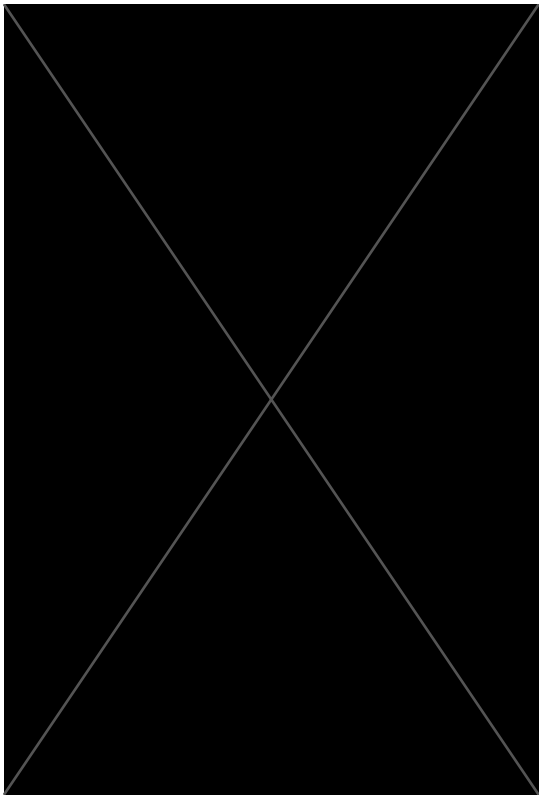




FT22: A Mouse Model to Investigate the Reproductive Consequences of Testosterone Administration After Suppressing Puberty in Transgender Boys

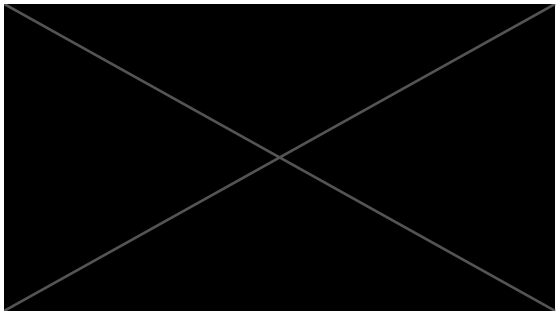
Cynthia Dela Cruz, University of Michigan, USA





P251 A Mouse Model to Investigate the Reproductive Consequences of Testosterone Administration After Suppressing Puberty in Transgender Boys

Cynthia Dela Cruz, Hadrian M. Kinnear, Prianka H. Hashim, Faith L. Chang, Likitha Nimmagadda, Vasantha Padmanabhan, Ariella Shikanov, Molly B. Moravek



A Mouse Model to Investigate the Reproductive Consequences of Testosterone Administration After Suppressing Puberty in Transgender Boys.

Cynthia Dela Cruz[1,2], Hadrian M. Kinnear[3,4], Prianka H. Hashim[1], Faith L. Chang[5], Likitha Nimmagadda[5], Vasantha Padmanabhan[1,6], Ariella Shikanov[1,3,5], Molly B. Moravek[1,7,8]

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The effect of pubertal suppression with gonadotropin-releasing hormone agonist (GnRHa) prior to initiating testosterone (T) treatment in transmasculine adolescents on future reproductive capacity is largely unknown. Our objective was to develop a mouse model to investigate the reproductive consequences of T administration following pubertal suppression with GnRHa, mimicking hormone therapy in peripubertal transmasculine adolescents. A pilot study was first undertaken to assess the effectiveness of the GnRHa in arresting the female mice's pubertal development. To achieve pubertal suppression, prepubertal C57BL/6N female mice (n=7 mice/group) were subcutaneously implanted with GnRHa (Goserelin acetate implant 3.6mg) on postnatal day (PND) 26. Controls underwent sham surgery. Animals were sacrificed on PND 34, PND 46, and PND 52. PND of the vaginal opening and first estrus, daily vaginal cytology to assess estrous cyclicity, weekly and terminal blood for LH and FSH assessment, organ weights, and corpora lutea counts were recorded. GnRHa treatment resulted in earlier vaginal opening ($p<0.0001$) and first estrus ($p<0.0001$). FSH levels in animals sacrificed on PND 46 were suppressed throughout GnRHa treatment ($p=0.0006$). This suppression was not evident at PND 52. Vaginal cytology showed a persistent diestrus until PND 46 but not until PND 52. A decrease in total ovarian weight ($p=0.0015$) and uterine weight ($p<0.0001$) was observed on PND 46 relative to controls. GnRHa treatment also resulted in lower terminal LH levels at both PND 34 ($p<0.0001$) and PND 46 ($p=0.0042$). Additionally, ovaries from GnRHa-treated animals showed an absence of corpora lutea at all timepoints. These findings indicate that our pubertal suppression paradigm reliably suppresses puberty for at least 21 days (PND 46). We then compared control, T-treated (0.45mg/subcutaneous) and GnRHa+T-treated (n=4/group) mice. GnRHa treatment began on PND 26. Weekly T enanthate (0.45 mg) or vehicle injections were initiated on PND 46 and continued for 6 weeks, and animals were sacrificed on PND 92. T-treated mice showed an increased uterine mass ($p=0.005$) and preputial gland and lower ovarian mass ($p=0.01$) relative to controls. GnRHa + T-treated mice showed an increase in the preputial gland and decreased ovarian mass ($p=0.002$) compared to controls. Findings from this study indicate

that GnRH agonist treatment arrests puberty with subsequent T treatment maintaining acyclicity during the entire treatment period. The increase in uterine mass observed in T-treated animals and the decrease in ovarian mass in both T-treated and GnRHa + T-treated groups are similar to findings in adult transgender men. These preliminary findings suggest that this is an appropriate mouse model for investigating the impact of gender-affirming hormone therapy in peripubertal transmasculine adolescents.