Characterizing the developmental timeline of pediatric ovaries: insights from ovarian tissue donated during fertility preservation

Authors: Elizabeth L. Tsui1,*, Samantha A. Ayala2, Courtney J. Harris1, Erin E. Rowell1, and Monica M. Laronda1,3

1Stanley Manne Children’s Research Institute, Ann & Robert H. Lurie Children’s Hospital of Chicago, USA 60611, 2Department of Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, USA 60611, 3Department of Biological Sciences, University of Illinois at Chicago, IL 60607, 4Division of Pediatric Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago, USA 60611

Introduction
This study was motivated by the desire to further understand the pediatric ovary across an important early reproductive transition, puberty. Previous work has focused primarily on fetal-onatal or perinatal transitions, leaving a gap in our understanding of the structural development accompanying hormonal and phenotypic changes that define puberty. Recent work uncovered the research potential of tissue derived from ovarian tissue cryopreservation (OTC) to answer fundamental questions in ovarian biology, especially with respect to the understood pediatric population. In OTC, a patient undergoes unilateral oophorectomy to isolate and cryopreserve the superficial 2-3mm of ovarian tissue (cortex) containing dormant primordial follicles (PMFs). This tissue will be used for future autologous re-transplantation upon loss of ovarian function and desire for conception and/or hormone restoration.

Purpose
The purpose of this work was to utilize specimens derived from OTC to describe gross morphologic changes in isolated ovaries and identify sub-anatomical features that distinguish pre-pubertal and post-pubertal ovaries at the histologic level using the ovarian surface epithelium as a constant reference point. In doing so, this work provides added context for current and future studies that use this tissue and contributes to the overall body of work describing human ovarian development.

Methods
Human ovarian tissue collection. Pre-pubertal and post-pubertal samples were prospectively collected from 77 participants (31 pre-pubertal, 24 post-pubertal) undergoing ovarian tissue cryopreservation (OTC) for fertility preservation between 2018 and 2021. Pre-pubertal participants were defined as individuals displaying no physical signs of pubertal development ( Tanner 1), and post-pubertal participants were defined as Tanner 2-5. At oophorectomy, a 3-4 mm biopsy was taken for routine pathology and evaluated by Lurie Children’s Hospital (LCH) pathologists. Participants whose tissue was found to contain evidence of malignancy was excluded from this study.

Discussion and Conclusions
• Width and weight of the ovary remains static during pre-puberty but rises rapidly following the pubertal transition to its post-pubertal plateau

• Sub-anatomic pubertal development is characterized by:
  • competition of compartmentalization
  • complete development of the tunica albuginea
  • reduced abundance of primordial and total follicles in the cortical region
  • significant loss of follicles

• Standard pathology, metrics gathered during tissue processing, and tissue that would normally be discarded during OTC processing can be used for basic research regarding important aspects of pediatric biology that are not yet well understood.

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Contact Information: elizabeth.tsui@northwestern.edu
Lab Website: larondalab.org
FNP Website: https://tinyurl.com/3ans94r