I am the current pediatric urology fellow at the University of California, San Francisco and will be joining the faculty at USF in September of this year. My goal is to apply my basic science background to studying the mechanisms of cryptorchidism and the biological impact of orchiopexy surgery, one of the most common surgeries performed by pediatric urologists.

I started my basic science career during medical school, when I joined Dr. Laurence Baskin's lab at the University of California, San Francisco. I worked on utilizing optical projection tomography, a novel 3D imaging technique at the time, to elucidate the three-dimensional morphology of the developing human fetal penis. That year, we were featured on the cover of the Journal of Urology, describing the “double zipper” hypothesis of male urethral formation. The study has since become an often-cited resource and a cornerstone for our understanding of urethral formation and thus hypospadias.

I had the privilege to continue my residency training at UCSF, and therefore had the opportunity to continue to work closely with Dr. Baskin and Dr. Gerald Cunha. During my research year in residency, I worked on a study describing the immunohistochemical ontogeny of the developing human testis. We published what we believe to be the most comprehensive ontological map to date of testicular development, encompassing all major cell populations in the testis from fetal development through mini-puberty, pre-puberty, and puberty.

In my fellowship research year, I am working on our current projects in the Baskin lab by applying our understanding of testicular development to abnormalities in development such as disorders of sexual differentiation. Furthermore, I am exploring my own independent research by focusing on cryptorchidism and the impact of temperature on testicular development and dysgenesis.

As an independent surgeon-scientist, my research goals are to understand the impact of surgical correction on malignancy potential, androgen synthesis, and fertility potential on undescended testis. The long-term goal is to elucidate the molecular mechanisms of temperature on testicular dysgenesis to find pathways that may help us better understand other testicular developmental pathologies and improve clinical outcomes for these patients.
Yi Li SPU Project Summary

Orchiopexy is the most common surgery performed by pediatric urologists. Patients who have delayed orchiopexy have increased risk of malignancy, decreased rates of fertility and decreased testosterone production. Currently, we do not understand how the small difference in ambient temperature causes this dysgenesis. Furthermore, we do not know whether dysgenic testis that have been surgically corrected recover any steroidogenic function or fertility potential over time. Clinically, we do not know if there is a point where surgically correcting the location of a testis has benefit over testicular removal, especially in the setting of increased malignancy risk.

In this study, we propose the development of a xenograft model to study human cryptorchid testis tissue at various ambient temperatures to determine if exposing these dysgenic gonads to lower temperature results in net increase or decrease in germ cell number and Leydig cell function. We will plan to obtain biopsies of human cryptorchid testes at various ages and ectopic locations. This tissue will be analyzed at baseline, then grafted into an athymic mouse renal capsule (simulating a high temperature environment, i.e., abdominal testes) and ear pinna (simulating a low temperature environment, i.e., scrotal testes). The tissue will be grown for eight weeks and then harvested and analyzed.

The first aim of this study will be to evaluate the impact of ambient temperature on human cryptorchid germ cell recovery. We hypothesize that testis tissue grafted at lower temperatures will show increase in germ cell numbers. We hypothesize that younger and less ectopic testes will increase in germ cell number being exposed to decreased temperature, while older and more ectopic testes will not.

The second aim of this study is to validate a mechanism to study androgen synthesize potential in this xenograft model. We will graft human testis tissue into athymic mice and then treat the mice with human chorionic gonadotropin to stimulate androgen production in the prepubertal testis tissue. Androgen synthesis will be evaluated with testosterone assay, seminal vesical weights, and immunohistochemical analysis of androgen synthesis markers. We hypothesize that testis tissue grafted at lower temperatures will show increased ability to respond to HCG stimulation.

The goal of this study is to establish a new xenograft model for studying the impact of temperature on human testicular tissue and provide greater insight into the biological effects on human cryptorchid testis after orchiopexy surgery. Better understanding of the impact of this surgery will help us to better counsel patients and to make better surgical decisions for this common pathology and may pave the way for further research into other causes of testicular dysgenesis in patients with disorders of sexual differentiation.