Welcome!

Welcome to the inaugural issue of the UCSF Male Reproductive Health Research Newsletter! Since becoming Director of Male Reproductive Health in the Department of Urology UCSF, Dr. James Smith has set forth ambitious and exciting clinical care and research goals for our division.

Our research program centers on the desire to help men and boys with cancer become fathers after surviving cancer treatment.

Our multidisciplinary team focuses on several keys areas:

A) Continued development of our fertility preservation program for adults and children;

B) Basic science research on sperm physiology and sperm stem cells;

C) Clinical research on the reproductive effects of new cancer therapies; and

D) Health services research exploring costs of reproductive care and disparities in access to care.

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Working with Dr. Polina Lishko, Assistant Professor in the UC Berkeley MCB Department, we are making strides in understanding some of the basic mechanisms underlying sperm function. We look at how certain proteins called "ion channels" are required for normal sperm function. Specifically, we are interested in how these channels contribute to a sperm's ability to swim, also called sperm motility. To do this, we compared genetic and electrical activity data collected from sperm of men with normal fertility to sperm from men suffering from infertility. By doing this, we have identified two new ion channel proteins so far that are key for normal sperm movement and function. Having a better understanding of the role of ion channels play in infertility will enable us to start developing better tools for more precisely diagnosing the type of infertility. With a more precise diagnosis we can better treat and develop new therapies for men coping with infertility. The success of this work and our plans for the future has recently led to funding by the National Institutes of Health.


The Link Between Sperm Ion Channels and Fertility
Unfortunately, for many men with an infertility diagnosis, we are not always able to diagnose the underlying cause of their infertility. While treatments like micro-TESE and in vitro fertilization have allowed many men with low or zero sperm counts to start families, we aim to develop new ways to help men conceive naturally. Further, men who survive cancer but who suffer from infertility as a result of their cancer treatment could benefit from these new treatments. In both cases, better understanding the process by which sperm develop, called spermatogenesis, will enable us to better help these men become fathers. In particular, we are interested in the role of sperm stem cells and the environment they develop in.

Sperm stem cells ultimately grow to be mature sperm, so it is important to understand what is wrong with them to understand their role in causing infertility. In partnership with Dr. Nam Tran, a reproductive endocrinologist and stem cell biologist in the UCSF Obstetrics, Gynecology, & Reproductive Sciences Department, we have made several key advances in understanding what can go wrong during sperm development that causes infertility. With this knowledge, we hope to build a set of tools that enable us to more precisely diagnose and eventually treat this type of infertility.


Tyrosine kinase inhibitors (TKI) are part of a class of cancer treatments called “targeted cancer therapies” which offer many cancer patients new ways of fighting their disease. While much is known about the reproductive effects of traditional cancer treatments such as chemotherapy and radiation, relatively little is known about the reproductive effects of TKI drugs. In collaboration with Dr. Polina Lishko, we have investigated the effects of these drugs on sperm both in the lab and in men taking TKI drugs as part of their cancer treatment. We have also assessed patient’s understanding of the potential effects of these drugs on their fertility and potential barriers to seeking fertility preservation care prior to their cancer treatment.

In surveying patients who are being treated with TKI therapy, we have found that that many patients are not warned about the potential for harmful effects of TKI drugs on their fertility. Fertility consultation is not offered to the majority of patients and many patients are dissatisfied with their decisions and regret their choice to not seek fertility care. Additionally, some of the key reasons for not seeking fertility care include a lack of awareness of the possible effects of TKI drugs on fertility and a lack of referrals to fertility specialists.

In the laboratory, we studied how the drugs affect the sperm cell’s ability to fertilize an egg. Our preliminary findings suggest that certain drugs hamper this ability. These results are the first evidence that suggest that these drugs might harm male fertility. As we investigate this effect further, we aim to educate both patients and doctors about the potential effects of these drugs on fertility given our initial laboratory results and the interest patients have demonstrated in becoming fathers.

Improvements in treatments for many cancers and serious non-cancer conditions in children have led to dramatic improvements in pediatric cancer survival rates. Unfortunately, many of these treatments are associated with potentially permanent sterilization rendering them unable to father children in the future. For post-pubertal boys (approximately age 13) and adults, fertility preservation with frozen semen is highly successful. Unfortunately, for pre-pubertal boys this approach is not possible because they are not yet producing sperm. Considering that more than 7,500 boys are diagnosed with cancer annually in the United States, this is a significant unaddressed issue.

To help address this issue, we opened our experimental ‘Pedi-LIFE’ program in 2014 at the UCSF Benioff Children’s Hospital San Francisco and Oakland. We now have one of the few programs in the United States that offers fertility preservation for boys facing potentially sterilizing medical or surgical treatment. As part of this study, we take a small testicular biopsy prior to boys starting potentially sterilizing treatment. A portion of this biopsy is used for clinical use and a second portion for sperm stem cell research. The clinical portion is frozen for potential long-term use by the patient. In collaboration with our partner, Dr. Tran, we seek to turn sperm stem cells into mature sperm in a laboratory setting. Demonstrating the ability to trigger sperm stem cells to develop into functional sperm would allow prepubertal a chance at fatherhood. Advances in fertility techniques over the past 20-30 years have led to the now commonplace technologies in which eggs from the mother can be combined with sperm from the father using techniques called in-vitro fertilization (IVF) and (ICSI) intracytoplasmic sperm injection. Thus, using sperm generated in the laboratory in conjunction with techniques like IVF and ICSI, the boys in our program will have a chance to become fathers in the future. We are also working on techniques to transplant testicular sperm stem cells back to patients after they complete cancer treatment as a way to restore sperm production.


“I was devastated when I learned of my 10 year old son’s cancer... Saving my son’s life is the most important thing, but I also want him to be able to lead a normal life. The [cancer] treatment may make him sterile so I asked my oncologist if there was anything that could be done to preserve his fertility. I was referred to urologist Dr. James Smith. I am happy to be able to take part in this research study as I hope to be a Grandfather someday.”

- Father of a 10 year-old with medulloblastoma
We have collaborated for over 7 years with Dr. Patricia Katz, faculty member in the UCSF Philip R. Lee Institute for Health Policy Studies, exploring the high costs and disparities in access to reproductive care. Together, we have examined the utilization of reproductive care by couples seeking reproductive therapy, socioeconomic disparities in reproductive care, time costs of reproductive care, and out of pocket infertility treatment costs. We have found that the financial cost of fertility treatment for couples using IVF frequently exceeds $20,000. Couples also routinely spend more than 125 hours actively undergoing fertility treatment. Financial strain is strongly related to how much couples spend and how couples finance their care. Households that need to tap into long-term savings or go into debt most often experienced the highest financial strain.

We have recently used advanced geospatial mapping techniques to explore disparities in access to male infertility care across the country. Using this technique, we measured the probability of male infertility in couples seeking Assisted Reproductive Technologies (ART) such as IVF. The national male infertility diagnosis was 17%; however, some areas had significantly greater and lesser probabilities. Future studies will explore the reasons underlying these differences.

In order to provide fertility care for all patients and in particular, cancer patients, access to reproductive care must be improved. Since many common fertility treatments are poorly covered by insurance even for cancer patients, patients need to be aware of these high costs. As a faculty member in the Institute for UCSF Institute for Health Policy Studies, Dr. Smith sees many areas for investigation to help improve access to care and help formulate and guide future infertility and fertility preservation health policies.


