*The **CatSper** Male Contraceptive*

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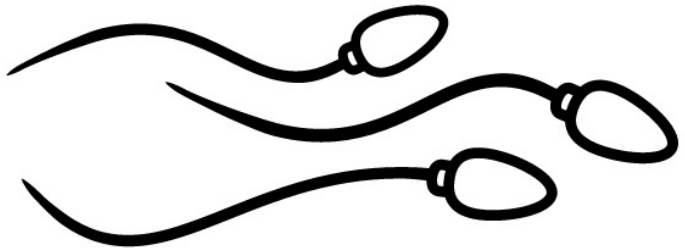


120+ Million Unintended Pregnancies
Occur globally each year

Men lack contraceptive options to equally participate in family planning

MOST EFFECTIVE

Less than 1 pregnancy per 100 women in a year

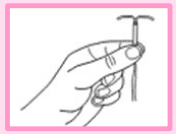
6-12 pregnancy per 100 women in a year

18 or more pregnancy per 100 women in a year

LEAST EFFECTIVE

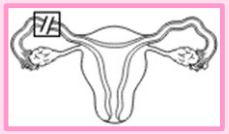
REVERSIBLE

- Implant
- Intrauterine Device (IUD)



PERMANENT

- Female Sterilization



- Vasectomy

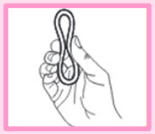
REVERSIBLE

- Injectable

- Pill

- Patch

- Ring



- Diaphragm

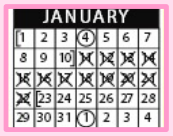
REVERSIBLE

- Female Condoms

- Sponge

- Spermicide

- Fertility Awareness



- Male Condoms

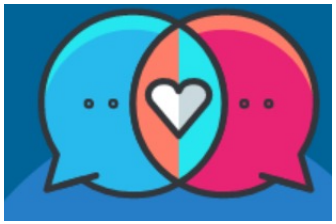
WE FILL THE GAP

We aim to develop the new generation of male contraceptives

- First-in-Class
- New MOA
- Minimal off-target
- Non-hormonal
- Reversible

Society is ready for the next male contraceptive – **Science needs to catch up!**

81%
Of men say they would use a non-conventional male birth control[1]

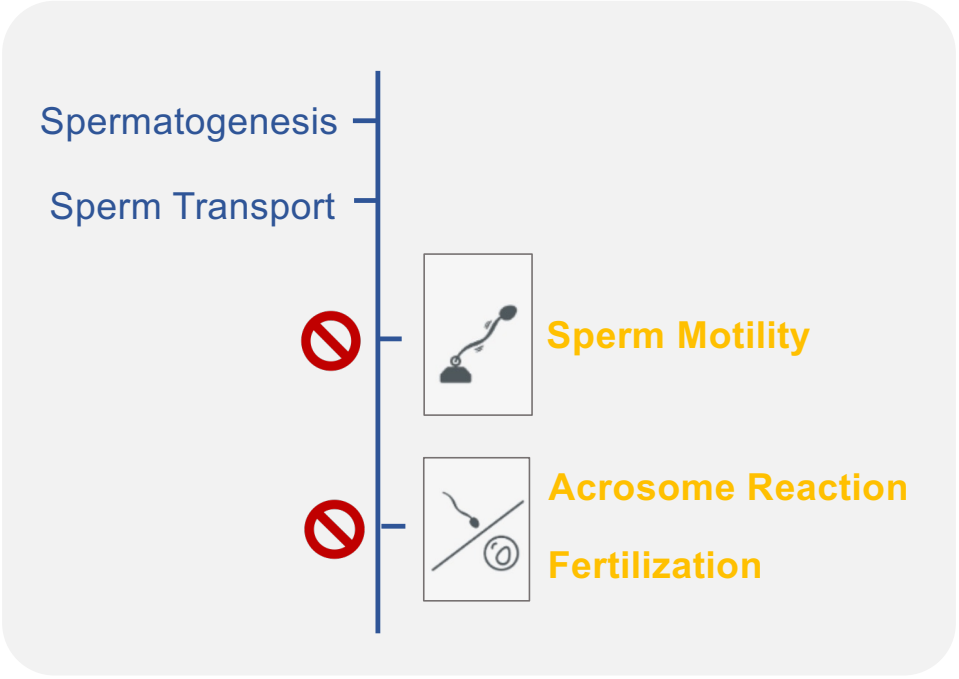


U.S. Contraceptive Market Size Worth $10 Billion by 2027[2]

According to Global Market Insights
"If a new male contraceptive method is approved in the next five years, the market is projected to be about $1 billion by 2024 and could grow at a rate of 6% over the next 10 years[3]"
AND birth control methods are covered by insurance plans

[1]Consumer Research Study, Male Contraceptive Initiative (2019); [1]Windsperger AP., et al. 2012; Grand View Research. Dec 2020; [3]Ugalmugle et al., 2019.

What is the ideal target for a male contraceptive?



Ideal Target :

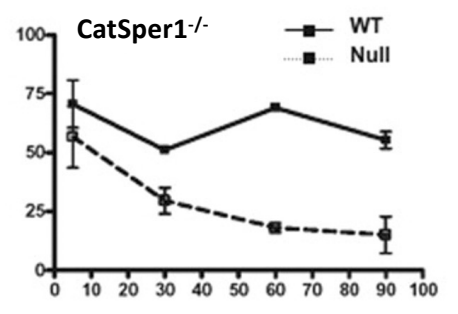
Non-hormonal

Reversible

Minimal off-target

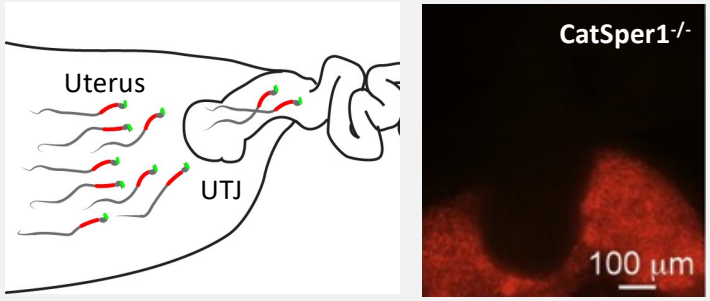
CatSper is necessary for sperm motility and egg fertilization

1. Sperm motility endurance



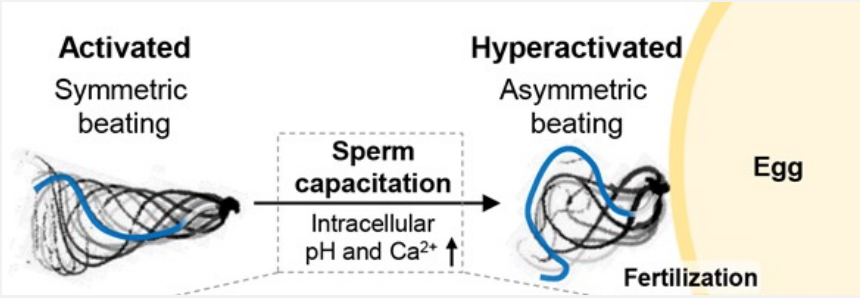
Similar results for CatSper2$^{-/-}$, 3$^{-/-}$, and 4$^{-/-}$

2. Crossing Utero Tubal Junction (UTJ)



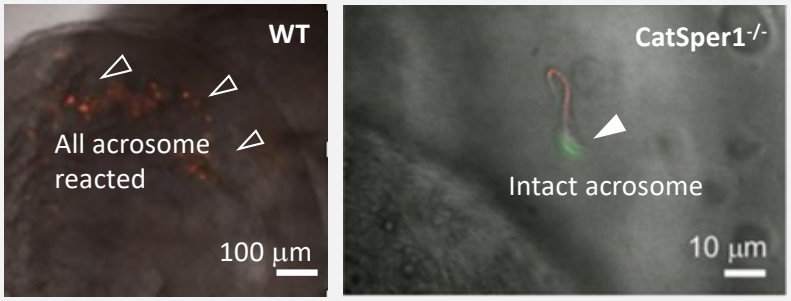
No sperm in the tubule when mated with CatSper1$^{-/-}$ male

3. Hyperactivated asymmetric beating



No asymmetric beating develops in CatSper$^{-/-}$ sperm

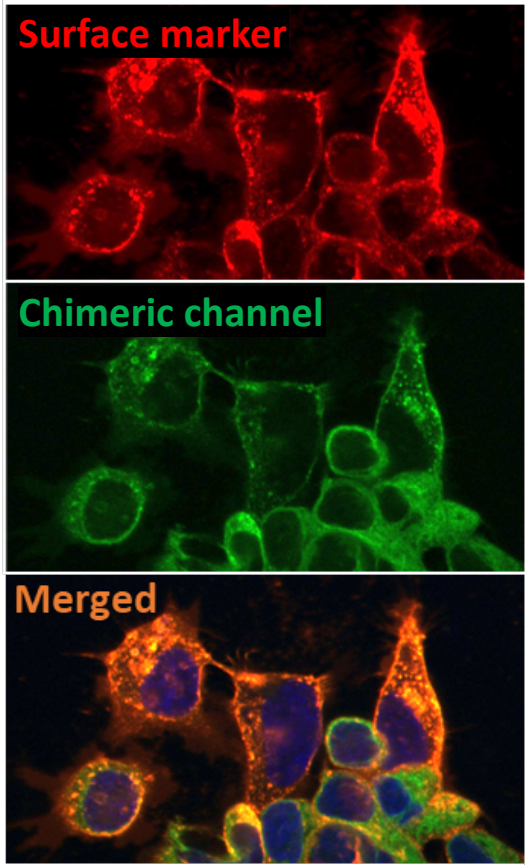
4. Acrosome reaction

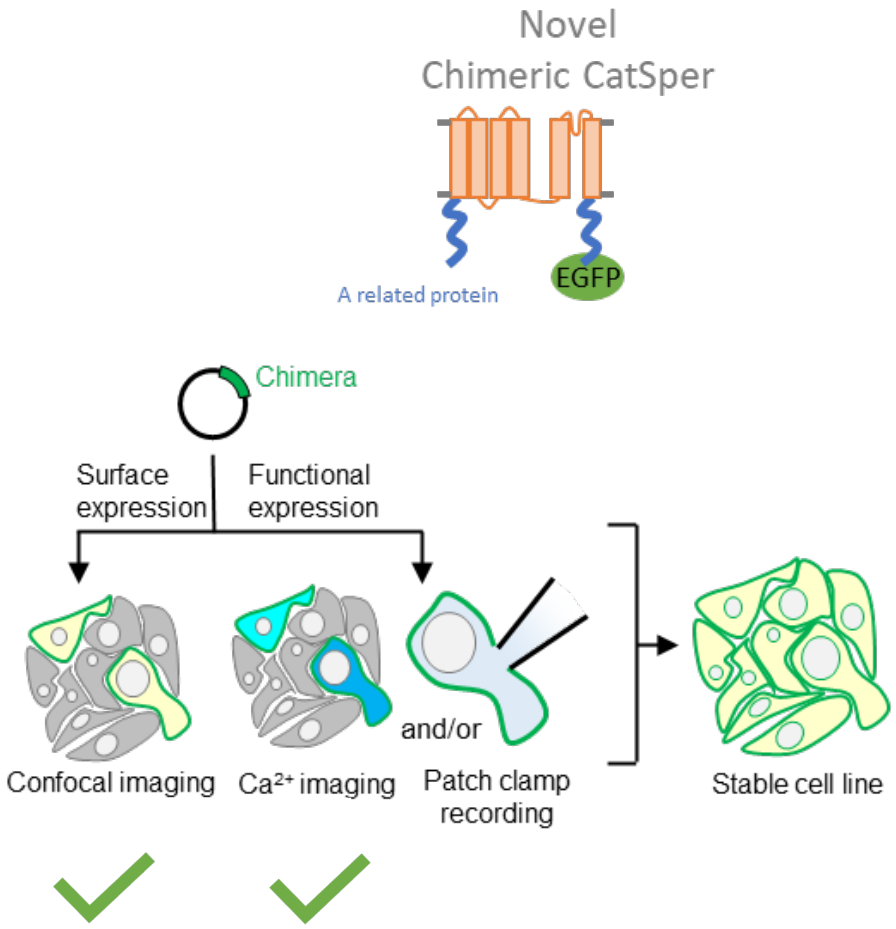


No acrosome reaction when mated with CatSper1$^{-/-}$ male

We developed the technology for CatSper drug screening

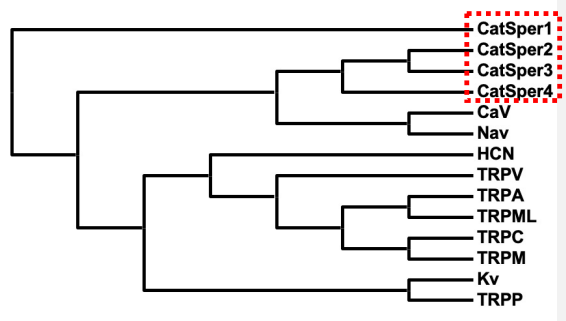
Chimeric CatSper-EGFP



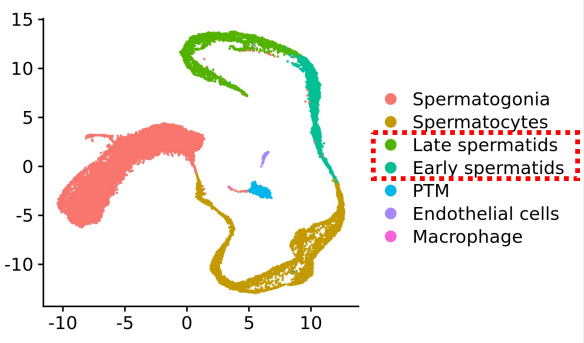


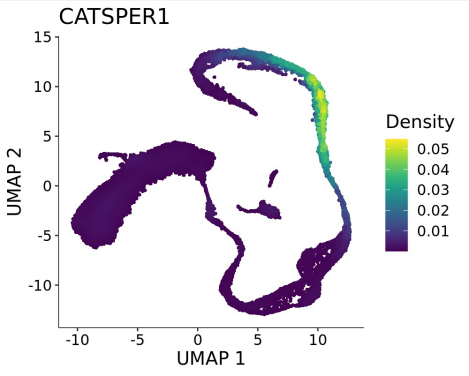
CatSper inhibition is expected to have minimum or non-existent side effects

CatSper underwent rapid evolution and functional divergence compared to other Ca^{+2} channels



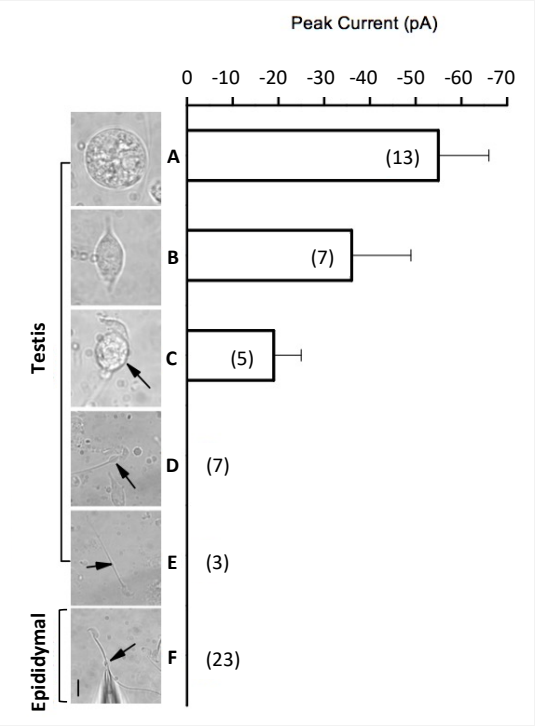
CatSper is only expressed in post-meiotic male germ cells





Similar results for CatSper2, 3, and 4

CatSper is the primary Ca^{2+} channel in sperm cells



The Team

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Associate Professor
Dept. of Cellular & Molecular Physiology
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CatSper Global Authority

Melisa Lopez-Anton, PhD

Blavatnik Fellow at Yale University
Scientist in Cancer Biology
Entrepreneur

Entrepreneur / Science

High-impact Scientific Publications

nature COMMUNICATIONS

A novel gene required for male fertility and functional CATSPER channel formation in spermatozoa

Jean-Ju Chung[1,2], Betsy Navarro[1,2], Grigory Krapivinsky[1,2], Luba Krapivinsky[1,2] & David E. Clapham[1,2]

Cell

Structurally Distinct Ca^{2+} Signaling Domains of Sperm Flagella Orchestrate Tyrosine Phosphorylation and Motility

Jean-Ju Chung,[1,2,8] Sang-Hee Shim,[4,6,7] Robert A. Everley,[3] Steven P. Gygi,[3] Xiaowei Zhuang,[4,5,*] and David E. Clapham[1,2,*]

Cell

Dual Sensing of Physiologic pH and Calcium by EFCAB9 Regulates Sperm Motility

Authors
Jae Yeon Hwang, Nadja Mannowetz, Yongdeng Zhang, ..., Joerg Bewersdorf, Polina V. Lishko, Jean-Ju Chung

eLife

3D in situ imaging of the female reproductive tract reveals molecular signatures of fertilizing spermatozoa in mice

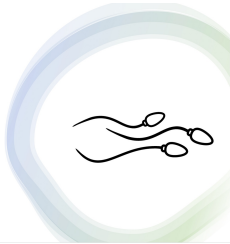
Lukas Ded[1,2], Jae Yeon Hwang[1], Kiyoshi Miki[3], Huanan F Shi[1], Jean-Ju Chung[1,4*]

Research Awards for this Project

MCI Male Contraceptive Initiative

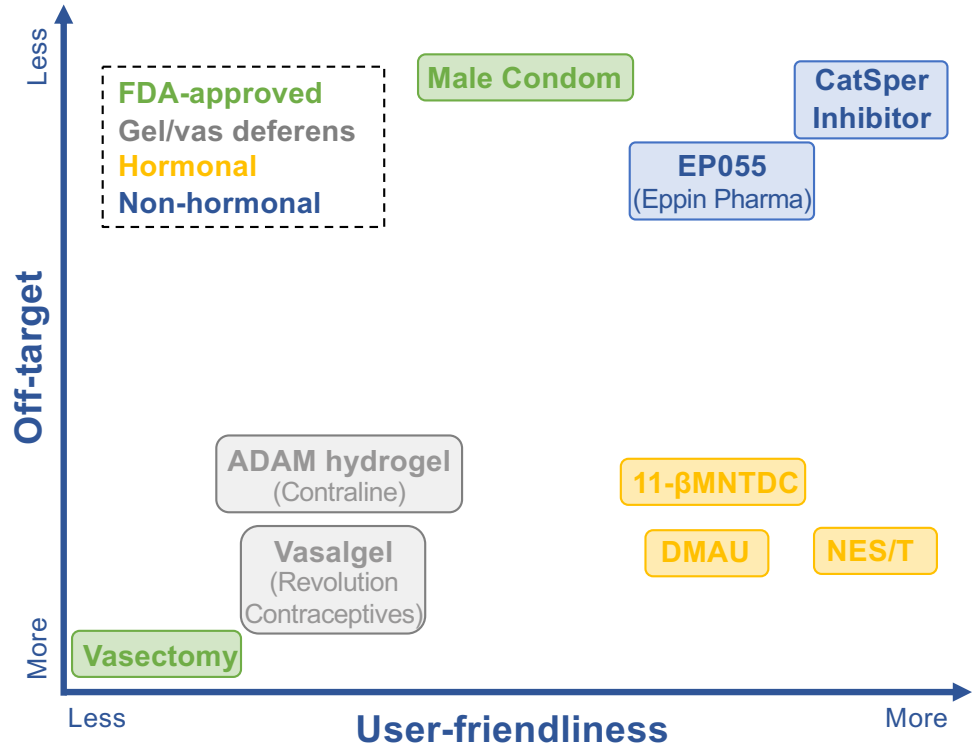
David Sokal Innovation Awards (2021)

$150K over two years



CatSper Inhibitor compares favorably to current and future male birth control methods

Technical Value Proposition

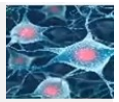


High unmet need

Phase III				
Phase II	DMAU	NES/T		
Phase I	11-βMNTDC			
Pre-IND	EP055 (Eppin Pharma)	ADAM hydrogel (Contraline)	Vasalgel (Revolution Contraceptives)	
Drug Discovery	CatSper Inhibitor			

Discovery Process and Future Plans with Blavatnik Fund

Cell Biology

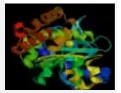


- ✓ In house expertise on CatSper
- ✓ Cell-based assay for CatSper Ca^{+2} channel FLIPR-HTS
- ✓ Assays for two other Ca^{+2} channel FLIPR-HTS (counter-screening)
- Generation reporter cell lines
- Ready-to-go assay characterization

High-Throughput Screening (In house YCMD)

- Pilot screening
- Primary screening
- Data analysis for hit identification
- Hit confirmation

Compound Profiling and Hit Follow-up



- Activity Determination (EC_{50}/IC_{50})
- Preliminary SAR analysis
- Assays and tests on two related targets
- Cardiac safety profiling and liability screen

ADME and Formulation

- *In vitro* ADME and preformulation (6 compounds)
- Formulation development and ASD development (1 compound)
- Mouse PK study (1 compound)

$100K

$200K