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**: Implant, Intrauterine Device (IUD), Female Sterilization

- **Reversible**: Male Condoms, Sponge, Spermicide, Fertility Awareness

- **Permanent**: Vasectomy

- **Least Effective**: Pill, Patch, Ring, Diaphragm

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**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

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

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”

AND birth control methods are covered by **insurance plans**

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What is the ideal target for a male contraceptive?

Ideal Target:
- Non-hormonal
- Reversible
- Minimal off-target

- Sperm Motility
- Acrosome Reaction
- Fertilization
CatSper is necessary for sperm motility and egg fertilization

1. Sperm motility endurance

![Graph showing sperm motility endurance](image1.png)

Similar results for CatSper2/−, 3/−, and 4/−

2. Crossing Utero Tubal Junction (UTJ)

![Diagram showing crossing UTJ](image2.png)

No sperm in the tubule when mated with CatSper1/− male

3. Hyperactivated asymmetric beating

![Diagram showing hyperactivated asymmetric beating](image3.png)

No asymmetric beating develops in CatSper/− sperm

4. Acrosome reaction

![Diagram showing acrosome reaction](image4.png)

No acrosome reaction when mated with CatSper1/− male
We developed the technology for CatSper drug screening
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

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

Similar results for CatSper 2, 3, and 4
The Team

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CatSper Global Authority

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High-impact Scientific Publications

- Cell
  A novel gene required for male fertility and functional CATSPER channel formation in spermatozoa
  Authors: Jean-Ju Chung, Nima Niazi, Brigitte Krapapoly, Luba Krapapoly, and David E. Clapham

- Cell
  Structurally Distinct Ca²⁺ Signaling Domains of Sperm Flagella Orchestrate Tyrosine Phosphorylation and Motility
  Authors: Jean-Ju Chung, Xiaowei Shi, Robert A. Sanders, Steve Y. Sagi, and David E. Clapham

- eLife
  Dual Sensing of Physiologic pH and Calcium by EFCAB9 Regulates Sperm Motility
  Authors: Jae Yoon Hwang, Nadia Mannowitz, Yongpeng Zhang, Jingjing Dong, Polina V. Lishko, and Jean-Ju Chung

- eLife
  3D in situ imaging of the female reproductive tract reveals molecular signatures of fertilizing spermatozoa in mice
  Authors: Lukas Ded, Jae Yoon Hwang, Kiyoshi Miki, Huanan Shi, and Jean-Ju Chung

Research Awards for this Project

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)

**Off-target**

- Less
  - FDA-approved Gel/vas deferens
    - Hormonal
    - Non-hormonal
  - Male Condom
  - EP055 (Eppin Pharma)
  - CatSper Inhibitor

- More
  - ADAM hydrogel (Contraline)
  - 11-βMNTDC
  - DMAU
  - NES/T
  - Vasalgel (Revolution Contraceptives)

**User-friendliness**

- Less
- More
## 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)