Universität Münster

Clinic Invent

Technology Offer

Ref.-No. M09/20

High-throughput screening assay to identify CatSper modulators

Introduction

Since its market release in the early 1960s, the “contraceptive pill” has enjoyed particular popularity among family planning methods and is a prime example of blockbuster drugs. However, during the last decades, a quest for modern non-hormonal contraceptives has emerged to not only provide an alternative with fewer side effects for women, but also render pharmacological contraception accessible for men. A promising strategy for non-hormonal contraception is to affect sperm functions that are essential for fertilization, i.e. motility. The CatSper Ca^{2+} channel in the sperm flagellum takes a center stage in the control of sperm motility: It is well-established that a loss of CatSper function leads to non-syndromic male infertility. CatSper is expressed exclusively in sperm, indicating that drugs that selectively target CatSper have the potential to prevent fertilization with virtually no side effects. However, because CatSper cannot be functionally expressed in culture cells, drug-discovery attempts rely on Ca^{2+}-fluorometric readout of the activity of native CatSper in human sperm, rendering high-throughput screening campaigns, thus far, largely impossible.

Invention

We developed a novel method that overcomes this problem, enabling high-throughput drug-screening campaigns for the identification of CatSper modulators. To this end, our test transforms drug-evoked changes in the activity of CatSper into a simple sperm-motility response. This allows not only to rapidly screen large compound libraries for drugs acting on CatSper, but also the immediate grading of the inhibitory or agonistic action of the tested compounds, e.g. for the straight-forward drafting of structure-response relationships. The test layout is simple: A small number of motile human sperm, derived directly from a native ejaculate, is subjected to an assay buffer fortified with the compound to be tested. The decrease in motility of this sperm population is observed over time – in a continuous or end-point fashion, e.g. inside the wells of common multiwell assay plates. Compared to a control without drugs added, the sperm motility decreases faster or slower (or is abolished altogether) in the presence of a CatSper agonist or inhibitor, respectively. The half-life time of the sperm population provides a direct readout of the agonistic or inhibitory performance of the tested drug. Our “CatSper-modulator test” is currently the only method suitable for a high-throughput screening on an industrial scale.

Advantages of the invention

The invention provides an in vitro drug-screening assay for CatSper modulators, which is safe, reliable, rapid and simple to perform. The assay can be performed directly with the native ejaculate and no specific devices are required.

Areas of application

reproductive medicine, male non-hormonal contraceptives

Keywords

non-hormonal contraceptives, CatSper Ca^{2+} channel, CatSper modulators, high-throughput drug-screening

Development Status

completed

Commercial Opportunity

The technology is offered for in-licensing and co-development

Patent Status

PCT application filed

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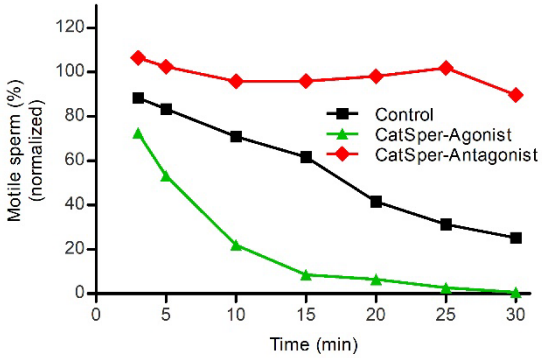

The “CatSper-modulator test“ transforms CatSper function into a sperm population motility response: In the presence of a CatSper agonist, the population motility decreases faster, while a CatSper inhibitor extends its half-life time.