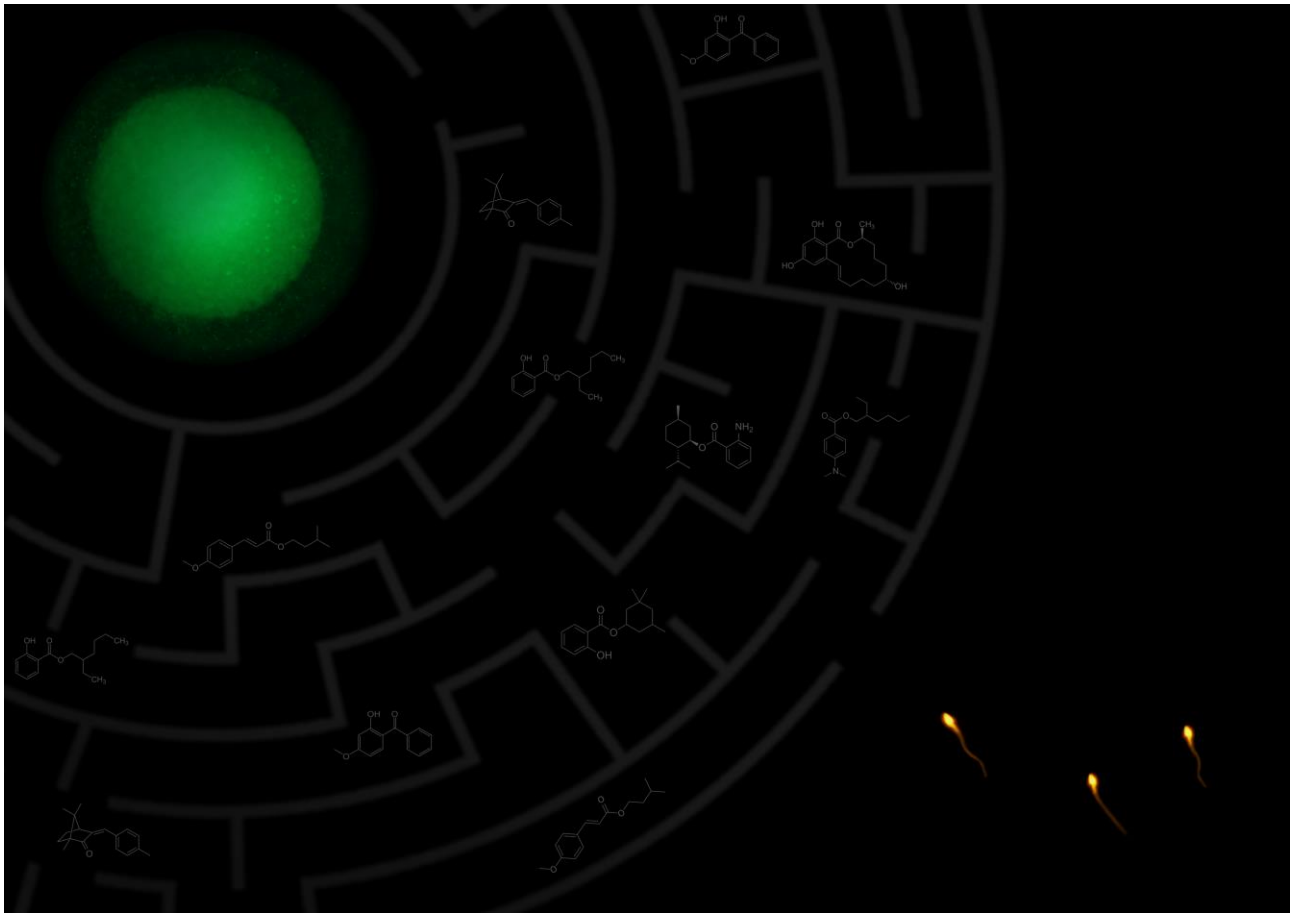
UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

Do endocrine disrupting chemicals affect human sperm cell function?



PhD thesis defense · Anders Rehfeld

Date · Wednesday, September 27th 2017 at 1 pm

Location · Nielsine Nielsen auditorium in the Panum Tower

Reception · After the defense at the Department of Growth and Reproduction, Rigshospitalet, 5064

Summary of PhD thesis

Human male infertility is common in the industrialized part of the world, but the causes are unknown in about a third of the cases. Intra cytoplasmic sperm injection (ICSI), a method developed to treat male infertility due to sperm dysfunction, is increasingly used in both the U.S. and Europe. As the increased use of ICSI has occurred during just a few decades, generic factors cannot be responsible. This suggests that sperm function may be adversely affected by environmental factors, e.g. endocrine disrupting chemicals (EDCs), and that this could in part account for the many unexplained cases of male infertility.

For human sperm cells to be able to successfully and naturally fertilize the egg, the function of the sperm cells must be precisely regulated during their journey through the female reproductive tract. Many sperm functions are controlled via the intracellular Ca^{2+} concentration, e.g. sperm motility and the chemotaxis towards the egg. In human sperm cells, all channel-mediated Ca^{2+}-influx has so far been found to occur via the CatSper Ca^{2+} channel only expressed in sperm cells. CatSper is activated by the endogenous ligand progesterone, released by the cumulus cells surrounding the egg, leading to a rapid Ca^{2+}-influx into the sperm cell.

The ligand binding sites responsible for CatSper activation have recently been found to be promiscuous and capable of binding diverse classes of ligands, such as steroids, odorants, menthol and analogous of cyclic nucleotides. This led us to hypothesize that EDCs could similarly bind the ligand binding sites responsible for CatSper activation and that this may be a direct mode of action by which EDCs could affect human sperm cell function.

This PhD thesis provides evidence that multiple EDCs can indeed activate CatSper, induce a Ca^{2+}-influx in the human sperm cells, and thereby interfere with human sperm cell function. These findings are in line with those published by others during the course of this PhD project. Furthermore, we provide evidence that EDCs can act synergistically in mixtures to activate CatSper. Future studies are needed to show whether these effects take place *in vivo* and if exposure to these EDCs can adversely affect human fertility.