1512-Pos Board B421

# Human Sperm Rotation is Regulated by Asymmetrically Positioned Flagellar Control Units

Nadja Mannowetz[1], Melissa R. Miller[1], Samuel J. Kenny[2], Steven A. Mansell[1], Michal Wojcik[2], Robert S. Zucker[1], Ke Xu[2], Polina V. Lishko[1].

[1]Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, CA, USA, [2]Department of Chemistry, University of California, Berkeley, Berkeley, CA, USA.

To fertilize an egg, spermatozoa have to overcome the tenacious egg's protective vestment. CatSper, the principal calcium channel of human sperm is indispensable for this process since it initiates the asymmetrical bending of the sperm tail via calcium influx termed hyperactivation. Apart from hyperactivation, human sperm also rotate, which enables them to swim against the liquid flow in the fallopian tube and reach the egg. However, the mechanistic details how the influx of calcium ions triggers hyperactivation and rotation have not been identified yet. CatSper is pH-dependent and for its full activation the intracellular pH must be alkaline. Alkalinization can be accomplished by either proton transporters or a faster mechanism, such as the voltage-gated proton channel Hv1. CatSper, Hv1 and regulatory proteins must be spatially compartmentalized to guarantee effective regulation of calcium influx into the sperm tail via CatSper. With this work we characterize nanodomains along the tail of human sperm, which consist of Hv1, CatSper and its regulatory protein ABHD2. With super-resolution microscopy we show that CatSper and ABHD2 form four symmetrically positioned longitudinal lines spanning the sperm tail, whereas Hv1 forms only two asymmetrical longitudinal lines. Inhibition of Hv1 leads to a decrease in sperm rotation underpinning its role and the specific structural arrangement in this motility patterns. In conclusion, Hv1, CatSper, and ABHD2 are organized in distinct regulatory nanodomains, which control hyperactivated motility and rotation thus ensuring fertilization.