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Pharmacological analysis of the regulatory mechanisms of sperm hyperactivation by ouabain

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Mammalian sperm activate their motility upon ejaculation, but sperm motility needs further change to whiplash-like motility to penetrate and fertilize the egg. This specialized motility is called "hyperactivation". It was reported that extracellular Na^+ is involved in regulation of hyperactivation. Na^+/K^+ ATPase (NKA) plays a major role in the regulation of cellular Na^+ homeostasis. The catalytic subunit of NKA is an α subunit, and there are $\alpha 1$ and $\alpha 4$ subunits in sperm. The sensitivity of these two α subunits to ouabain, a specific NKA inhibitor, is quite different, that is, 10^{-6} M ouabain inhibits NKA $\alpha 4$ while $>10^{-5}$ M ouabain inhibits both the $\alpha 1$ and $\alpha 4$. Therefore, this difference of sensitivity enables us to distinguish the physiological role of NKA α subunits on sperm function by pharmacological approach. In this symposium, I will introduce my latest study which showed, by utilizing this pharmacological property of ouabain, that the NKA $\alpha 1$ subunits is necessary for the maintenance of motility while the $\alpha 4$ subunit is necessary for the hyperactivation-associated change in flagellar movement. These results suggest that NKA $\alpha 4$ subunit is an attractive target for the male contraception.