Kaupp *BMC Pharmacology and Toxicology* 2015, **16**(Suppl 1):A20
http://www.biomedcentral.com/2050-6511/16/S1/A20

BMC Pharmacology & Toxicology

MEETING ABSTRACT Open Access

Ultrasensitive signal detection by a guanylyl cyclase chemoreceptor

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From 7th International Conference on cGMP Generators, Effectors and Therapeutic Implications
Trier, Germany. 19-21 June 2015

Background

Sperm navigate to the egg in a gradient of a chemoattractant for fertilization – a mechanism called chemotaxis. In sea urchin, the chemoattractant peptide binds to a chemoreceptor guanylyl cyclase (GC) on the sperm surface. Activation of the GC initiates a sequence of signaling events that eventually results in Ca2+ influx and a change in swimming direction. We studied the GC properties that allow sperm to track the chemoattractant with single-molecule precision on a millisecond time scale. A high density (9•103 GC molecules/μm2) and a subnanomolar ligand affinity provide a high ligand-capture efficacy. The sperm surface represents an almost perfect absorber. The peptide-induced GC activity is terminated by multiple dephosphorylation steps, which provide a means of precise lifetime control and, thereby, reduces "molecular noise". Several experiments suggest that GC undergoes autodephosphorylation. Future experiments need to clarify, whether the GC entertains phosphatase and kinase activity, possibly in the kinase-homology domain (KHD).

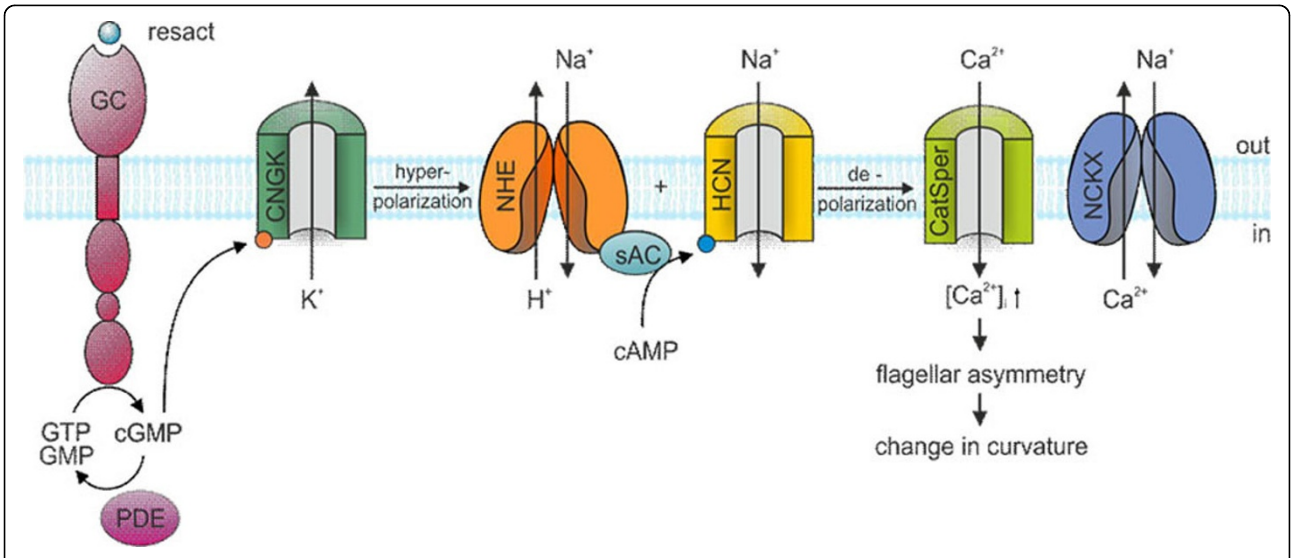

Figure 1 Cellular signaling during chemotaxis in sea urchin sperm. The signaling events are initiated by binding of the ligand to the receptor GC. The rise of cGMP opens K^+-selective cyclic nucleotide-gated channels (CNGK). The ensuing hyperpolarization activates a voltage-dependent Na^+/H^+ exchanger (NHE) and a pacemaker channel (HCN). The resulting alkalization by NHE and depolarization by HCN opens a sperm-specific Ca^{2+} channel (CatSper). Ca^{2+} is exported by a Na^+/Ca^{2+}-K^+ exchanger (NCKX).

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The turnover of cGMP synthesis of 72 cGMP molecules/sec or about 11 cGMP molecules/GC*/lifetime is sufficient to open a few cGMP-gated channels and to produce a unitary voltage response of about 2 mV. The receptor GC can bind the ligand over six orders of magnitude of concentrations. The shallow binding curve might reflect negative cooperativity among binding sites; alternatively receptor population might be composed of a mixture of receptors with a range of $K_{1/2}$ values.

Published: 2 September 2015

doi:10.1186/2050-6511-16-S1-A20
Cite this article as: Kaupp: Ultrasensitive signal detection by a guanylyl cyclase chemoreceptor. *BMC Pharmacology and Toxicology* 2015 **16**(Suppl 1):A20.