CatSper channels

Overview: CatSper channels (CatSper1–4; nomenclature as agreed by NC-IUPHAR, Clapham and Garbers, 2005) are putative 6TM, voltage-gated, calcium-permeant channels that are presumed to assemble as a tetramer of α-like subunits and mediate the current ICatSper. In mammals, CatSper subunits are structurally most closely related to individual domains of voltage-activated calcium channels (CaV) (Ren et al., 2001). CatSper1 (Ren et al., 2001), CatSper2 (Quill et al., 2003) and CatSper3 and 4 (Lobley et al., 2003; Lin et al., 2005; Qi et al., 2007), in common with a recently identified putative 2TM- auxiliary CatSperf protein (Liu et al., 2007) and a putative 1TM-associated CatSperγ protein (Wang et al., 2009), are restricted to the testis and localized to the principle piece of sperm tail.

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>CatSper1</th>
<th>CatSper2</th>
<th>CatSper3</th>
<th>CatSper4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensembl ID</td>
<td>ENSG00000175294</td>
<td>ENSG00000166762</td>
<td>ENSG00000152705</td>
<td>ENSG00000188782</td>
</tr>
<tr>
<td>Activators</td>
<td>Constitutively active, weakly facilitated by membrane depolarization, strongly augmented by intracellular alkalization</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Blockers</td>
<td>Cd2+ (200 μM), Ni2+ (300 μM), ruthenium red (10 μM)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Functional characteristics</td>
<td>Calcium-selective ion channel (Ba2+ &gt; Ca2+ &gt;&gt; Mg2+ &gt;&gt; Na+); quasi-linear monovalent cation current in the absence of extracellular divalent cations; alkalization shifts the voltage dependence of activation towards negative potentials (V0, at pH 6.0 = +87 mV; V0 at pH 7.5 = +11 mV)</td>
<td>Required for ICatSper</td>
<td>Required for ICatSper</td>
<td>Required for ICatSper</td>
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</table>

CatSper channel subunits expressed singly, or in combination, fail to functionally express in heterologous expression systems (Quill et al., 2001; Ren et al., 2001). The properties of CatSper1 tabulated above are derived from whole cell voltage-clamp recordings comparing currents endogenous with spermatozoa isolated from the corpus epididymis of wild-type and Catsper1−/− mice (Kirichok et al., 2006). ICatSper is also undetectable in the spermatozoa of Catsper2−/−, Catsper3−/− or Catsper4−/− mice, and CatSper 1 associates with CatSper3, 3 or 4 in heterologous expression systems (Qi et al., 2007). Moreover, targeted disruption of Catsper1, 2, 3 or 4 genes results in an identical phenotype in which spermatozoa fail to exhibit the hyperactive movement (whip-like flagellar beats) necessary for penetration of the egg cumulus and zona pellucida and subsequent fertilization. Such disruptions are associated with a deficit in alkalization- and depolarization-evoked Ca2+ entry into spermatozoa (Carlson et al., 2003; 2005; Qi et al., 2007). Thus, it is likely that the CatSper pore is formed by a heterotetramer of CatSpers1–4 (Qi et al., 2007). CatSper channels are required for the increase in intracellular Ca2+ concentration in sperm evoked by egg zona pellucida glycoproteins (Xia and Ren, 2009). The driving force for Ca2+ entry is principally determined by a mildly outwardly rectifying K+ channel (KSper) that, like CatSpers, is activated by intracellular alkalization (Navarro et al., 2007). KSper is not yet identified, but its properties are most consistent with mSlo3, a protein detected only in testis (Navarro et al., 2007).

Further Reading


References


