

## **An optogenetic arrhythmia model to study catecholaminergic polymorphic ventricular tachycardia mutations**

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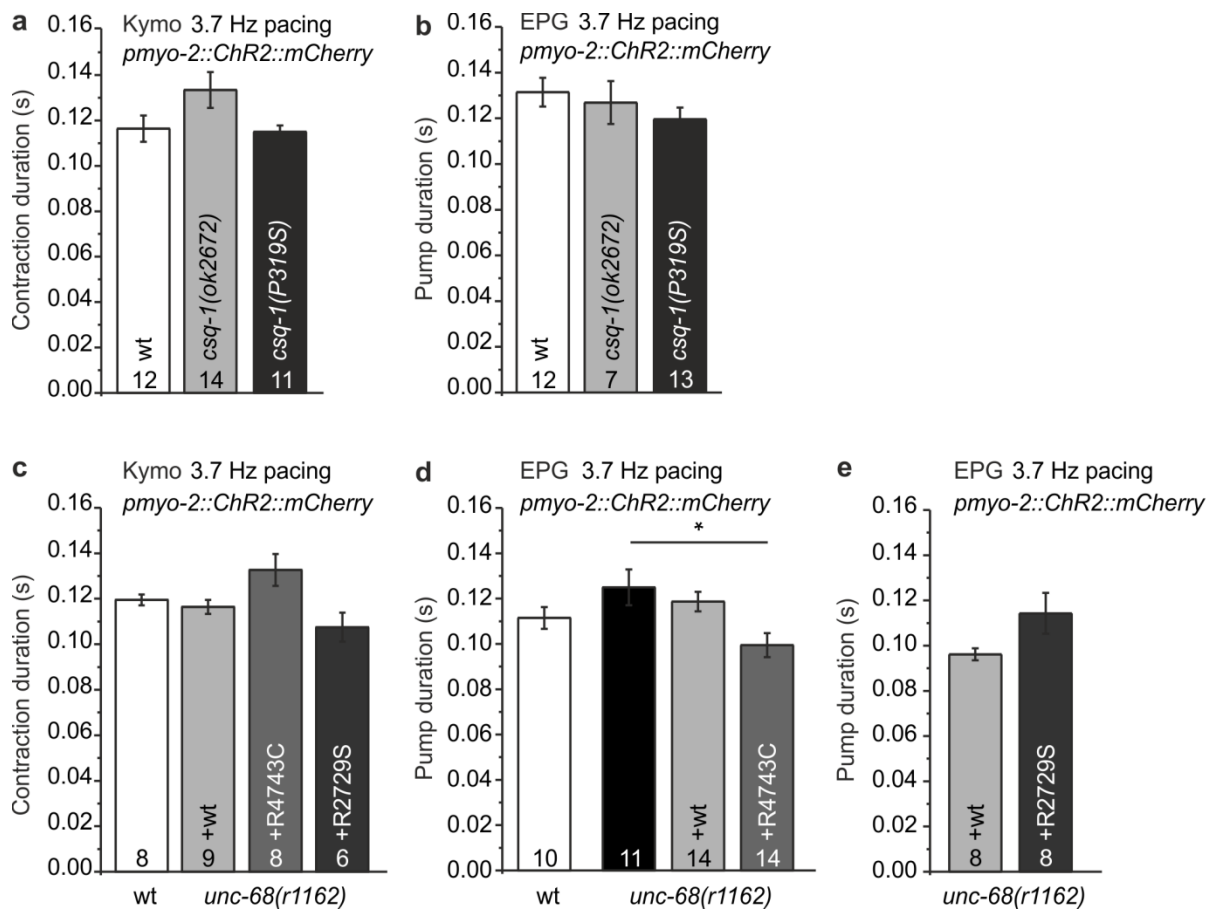
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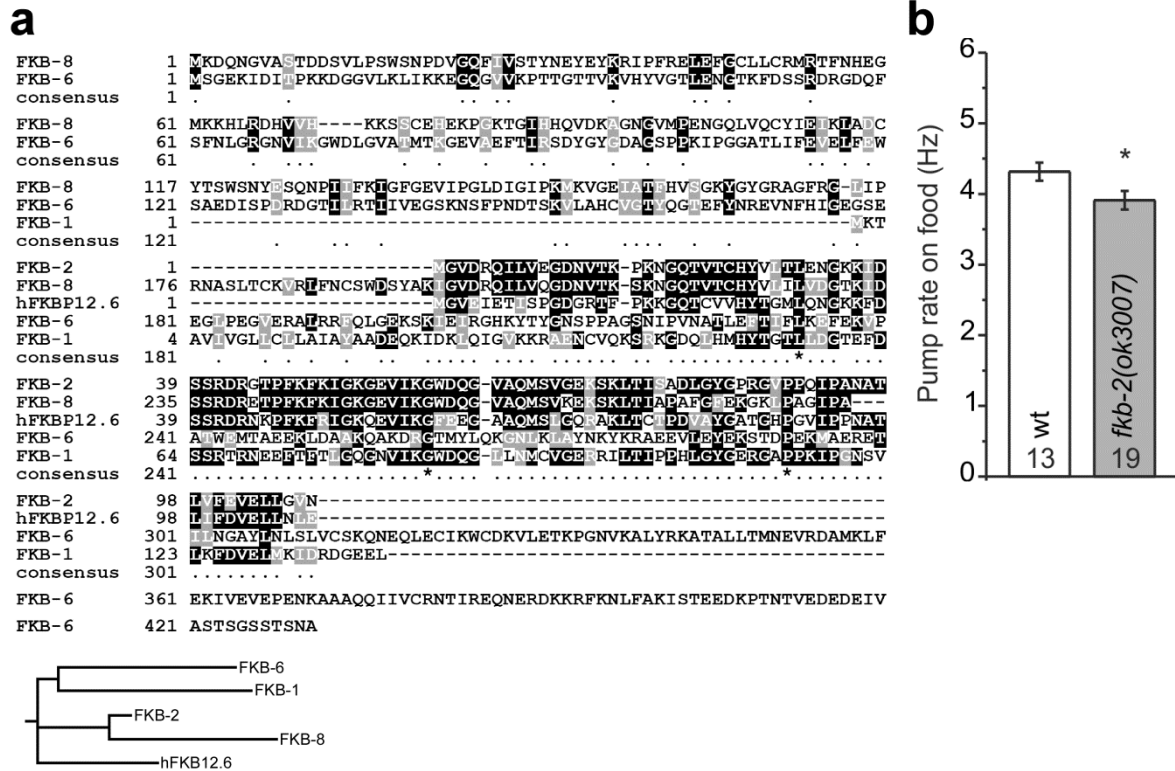
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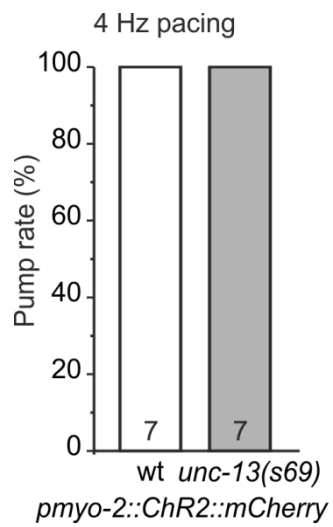
## **Supplementary Material**



**Supplementary Figure 1 | Mutations of *unc-68* and *csq-1* do not affect pharynx pump duration.** (a) Contraction duration obtained by kymographic video analysis of intact animals and (b) pump duration obtained by EPG recordings of cut-head preparations of deletion mutant *csq-1(ok2672)*X and point mutation *csq-1(gk876502)* (altering P319 to S), compared to wt (n = 11-14, n=7-13, respectively). (c) Contraction duration obtained by kymographic video analysis and (d, e) pump duration obtained by EPG recordings of intact animals of *unc-68(r1162)* deletion mutant, its rescue with *unc-68* wt fosmid as well as the R4743C and R2729S point mutant fasmids, compared to wt (n=6-12, n=10-14, n=8, respectively).

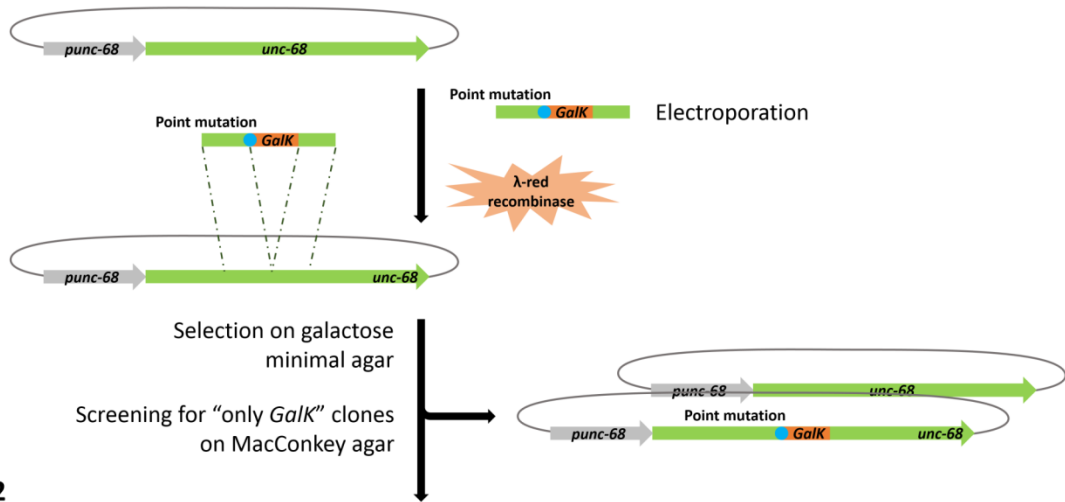


**Supplementary Figure 2 | Deletion of FKB-2, the presumptive *C. elegans* homolog of human FKBP12.6, reduces pump rate on food. (a)** Clustal-X2 alignment of *C. elegans* sequences of FKB-1, FKB-2, FKB-6 and FKB-8, with human FKBP12.6. Inset: Phylogenetic tree of the five proteins. **(b)** Food-stimulated pumping was compared in wt and *fkb-2(ok3007)* deletion mutants, by video microscopy.

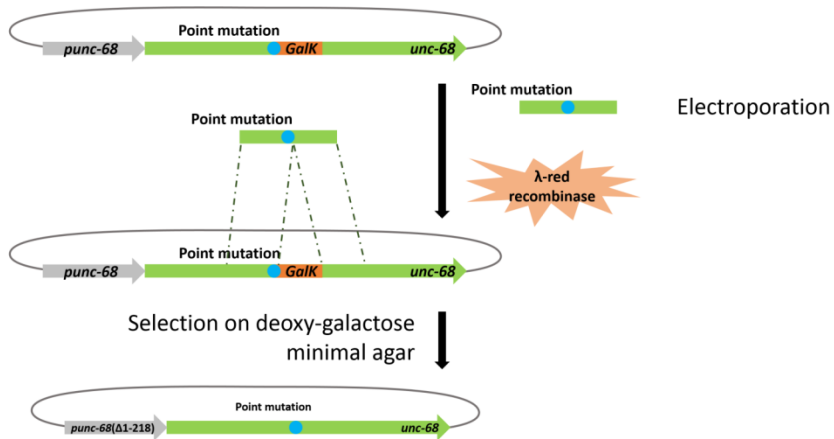


**Supplementary Figure 3 | No neuronal influence on paced pharynx pumping.** EPG recordings of cut-head preparations of *pmyo-2::ChR2::mCherry*-expressing animals containing the *unc-13(s69)* mutation compared to wt (n =7).

### Step 1



### Step 2



**Supplementary Figure S4 | Heterologous recombineering.** Insertion of point mutations into a fosmid containing *unc-68* by heterologous recombineering using SW105 cells, the recombinase  $\lambda$ -Red and *GalK* cassette for selection (see Methods for details).

## Supplementary Table 1: Primer sequences

### Primers for generation of plasmids used in this work:

oEF48:	5`-GCTCGGATCCATGACTTGGATCAAACCTTGC-3`
oEF49:	5`-GCTGGGTACCGGCAGCTCCTTTCTAGACTTCTTTCC-3`
oets3:	5`-CATCGCTGCAGGTTACAGGCATCGATTG-3`
oets4:	5`-GTTCTTCTCGGTCAGAAC-3`
oEF150:	5`-ATGCCTGCAGGTCGAAGCCTTCGGCGCGACTAATA-3`
oEF151:	5`-TTTTTCTACCGTACTAACAGTGTTCGACCAC-3`

### Primers used in this work for generation of *unc-68* point mutations in fosmids:

oEF200:	5`-TACCAGGCCTACTTCCAAACCATAAGGGATCAGTTTTGCTGTTCTTAGATTACCTGTTGA CAATTAATCATCGG-3`
oEF201:	5`-GATTGCTCAAGAACATGGAAGAGCATATCTTGTTGATCAATCCGTATACGCGGCCGCTC TAGAACTAGTGGATCC-3`
oEF202:	5`-TACAGATGTACAAAACTCAATATTTAAATATTTCCAGAATATGCTTGCATGTCCTGTTGA CAATT AATCATCGG-3`
oEF203:	5`-TTGATGAAGAAAGCCAAGTACAAAGTGATCTTTTCGATTGTTTTGAAGTTGCGGCCGCTC TAGAACTAGTGGATCC-3`
oEF15:	5`-CTTCATCGTCGTCTCCTTCC-3`
oEF16:	5`-GTGCACCTCAAATGGTTCAG-3`
oEF204:	5`-GAAGATCCAGCCGATTCAAC-3`
oEF205:	5`-TTGAGCGCAAGAGCTGTATC-3`
oEF206:	5`-AAGATCCAGCCGATTCAACC-3`
oEF207:	5`-CAATCCGTATACTGAATCTAAGAACAGC-3`
oEF208:	5`-GCTGTTCTTAGATTCAAGTATACGGAATTG-3`
oEF209:	5`-CGTCGGCAAAGAAGTGTGAG-3`
oEF210:	5`-GAATCTATCGGTGCACCTC-3`
oEF211:	5`-CCAGAATATGCTTGCATGTAACCTCAAACAATCG-3`
oEF212:	5`-CGATTGTTTTGAAGTTACATGCAAGCATATTCTGG-3`
oEF213:	5`-CCTCCGATGCAGCTTCAGC-3`

Primers used in this work for genotyping of mutants:

oEF59: 5`-CTCAGCGGTGGAAAC-3`  
oEF60: 5`-GTACTTGAACCTAGGTAC-3`  
oEF61: 5`-GTGTACTCTGTTTCGTC-3`  
oNH1: 5`-TGCGCAGACCATTTGAGGAAG-3`  
oNH2: 5`-CTCCCTCACGGGTTTCCTC-3`  
oNH3: 5`-GAAACTACCAAGCGGCAACC-3`  
oEF214: 5`-TGCGCAGACCATTTGAGGAA-3`  
oEF215: 5`-GAAGGACCTCAAATCGGACT-3`