eLife's transparent reporting form

We encourage authors to provide detailed information *within their submission* to facilitate the interpretation and replication of experiments. Authors can upload supporting documentation to indicate the use of appropriate reporting guidelines for health-related research (see EQUATOR Network), life science research (see the BioSharing Information Resource), or the ARRIVE guidelines for reporting work involving animal research. Where applicable, authors should refer to any relevant reporting standards documents in this form.

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Sample-size estimation
- You should state whether an appropriate sample size was computed when the study was being designed
- You should state the statistical method of sample size computation and any required assumptions
- If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

> Sample size of each averaged data is stated in the related figure legends.

Replicates
- You should report how often each experiment was performed
- You should include a definition of biological versus technical replication
- The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
- If you encountered any outliers, you should describe how these were handled
- Criteria for exclusion/inclusion of data should be clearly stated
- High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

> Information about the number of replicates can be found in the related figure legends and in the Methods section denoted "Electrophysiological data analysis". The number of replicates used for the electrophysiology experiments is also summarized in Supplementary Tables 1 and 6 and can be found in the source data files to the related figures. Each electrophysiology experiment was performed on at least 4-5 individual cells.

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Statistical reporting

- Statistical analysis methods should be described and justified
- Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
- For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
- Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

Statistical analysis methods are described in the Methods, in sections denoted "Electrophysiological data analysis" and "Analysis of KCNQ1-KCNE1 MD simulations". Electrophysiological recordings are presented followed by the averaged data expressed as mean +/- SEM. Threshold for statistical significance ($P < 0.001$) between KCNQ1 (or KCNE1) WT and mutants in terms of the specified parameter is given in the figure legends or table footnotes. MD data are presented as time series data or as averaged data calculated over four individual MD simulations.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

Group allocation

- Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
- Indicate if masking was used during group allocation, data collection and/or data analysis

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

Not applicable.

Additional data files ("source data")

- We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
- Where provided, these should be in the most useful format, and they can be uploaded as "Source data" files linked to a main figure or table
- Include model definition files including the full list of parameters used
- Include code used for data analysis (e.g., R, MatLab)
- Avoid stating that data files are "available upon request"

Please indicate the figures or tables for which source data files have been provided:

Source data files containing numerical data that are represented as graphs in the paper were uploaded for the following figures and figure supplements: Figure 2, Figure 2-figure supplement 1, Figure 2-figure supplement 2, Figure 2-figure supplement 3, Figure 3-figure supplement 3, Figure 3-figure supplement 4, Figure 5, Figure 5-figure supplement 1, Figure 7, Figure 7-figure supplement 1, Figure 8. In addition, the structural models presented in the paper together with the structural restraints have been deposited in PDB-Dev (PDBDEV_00000042). The experimental restraints and starting model coordinates used for docking, as well as representative snapshots from the MD simulations have been deposited under: https://doi.org/10.5281/zenodo.3598943. The models and MD simulation data will be released upon acceptance of this paper.