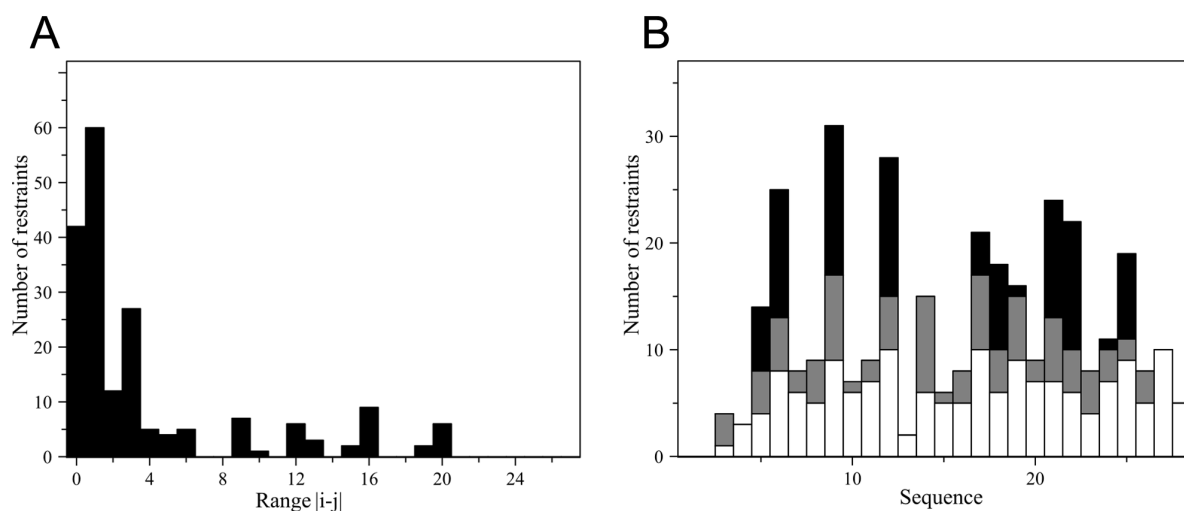**Supplementary Figures**

**Fig S1. Statistics of NMR distance restraints obtained for Tk-hefu**

Left panel, the distribution of distance restraints for the given distance between the residues in the amino acid sequence of Tk-hefu (|i-j|). Right panel, residue-based distance restraint statistics. The number of short-range (|i-j|<2, white), medium-range (1<|i-j|<5, gray) and long-range (|i-j|>4, black) restraints is plotted against the residue number. This figure is a standard output of the CYANA software.

Fig S2. Activity of Tk-hefu mutants on K$_v$1.1, K$_v$1.2 and K$_v$1.6 channels
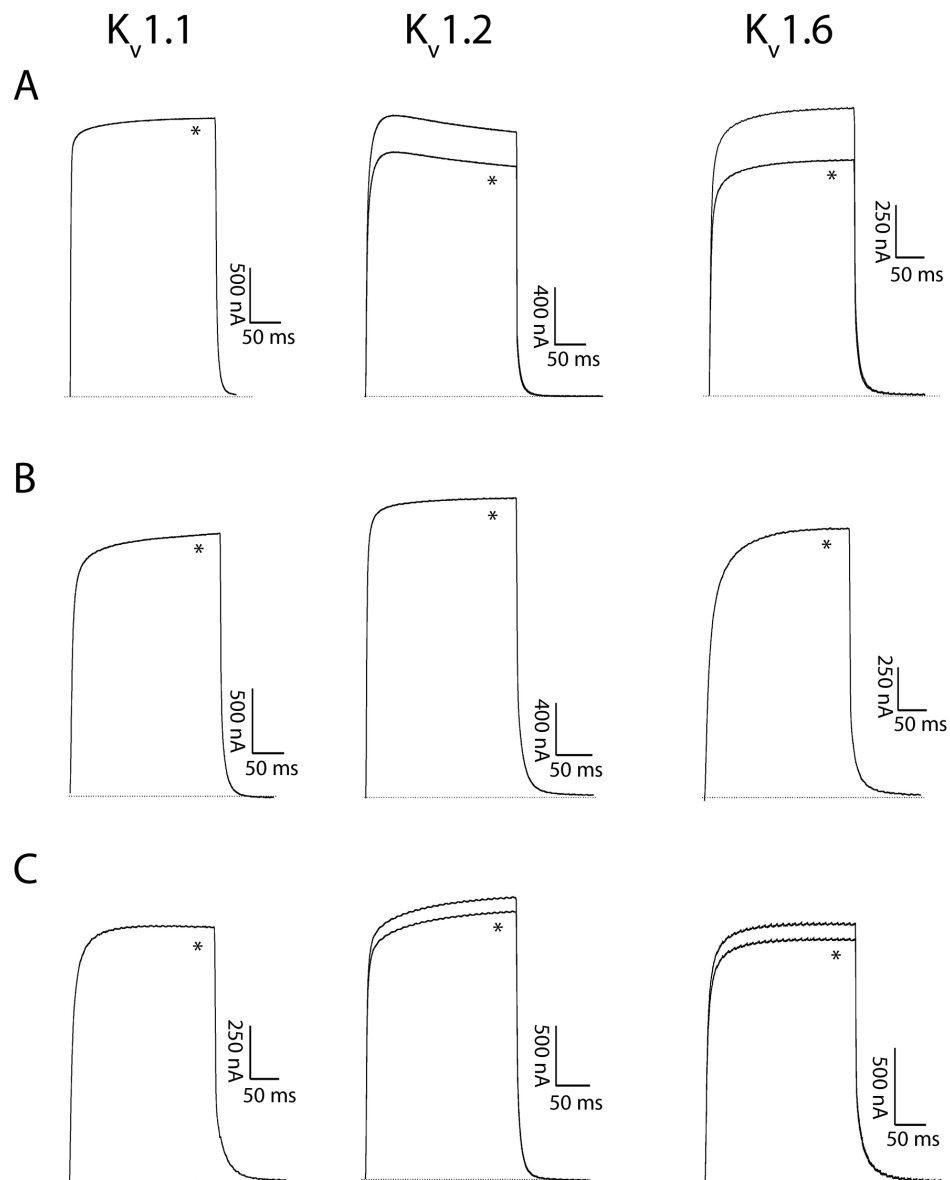
Traces shown are representatives of at least three independent experiments (n ≥ 3). The dotted line indicates the zero current level. Asterisks (*) distinguish the steady-state current after application of 40 μM Tk-hefu-2 (A), Tk-hefu-3 (B), or Tk-hefu-4 (C).

Fig S3. Time course of $K_v1.3$ current inhibition with Tk-hefu-2 and the recovery of inhibition upon washout
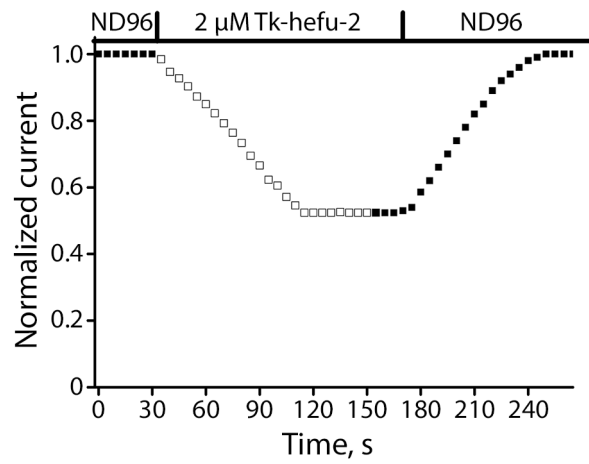
Shown is a representative experiment with 2 μM Tk-hefu-2. Closed squares, ND96 conditions; open squares, application of Tk-hefu-2. The time course of a representative experiment is shown to indicate the rate of washin and washout. The binding of Tk-hefu-2 was reversible.