

# Zn<sup>2+</sup>-binding and molecular determinants of tetramerization in voltage-gated K<sup>+</sup> channels

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The N-terminal, cytoplasmic tetramerization domain (T1) of voltage-gated K<sup>+</sup> channels encodes molecular determinants for subfamily-specific assembly of  $\alpha$ -subunits into functional tetrameric channels. Crystal structures of T1 tetramers from *Shaw* and *Shaker* subfamilies reveal a common four-layered scaffolding. Within layer 4, on the hypothetical membrane-facing side of the tetramer, the *Shaw* T1 tetramer contains four zinc ions; each is coordinated by a histidine and two cysteines from one monomer and by one cysteine from an adjacent monomer. The amino acids involved in coordinating the Zn<sup>2+</sup> ion occur in a HX<sub>5</sub>CX<sub>20</sub>CC sequence motif that is highly conserved among all *Shab*, *Shaw* and *Shal* subfamily members, but is not found in *Shaker* subfamily members. We demonstrate by coimmunoprecipitation that a few characteristic residues in the subunit interface are crucial for subfamily-specific tetramerization of the T1 domains.