# Exquisite Control of Channel Function

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Killer strains of *Saccharomyces cerevisiae* infected with a small RNA virus secrete a deadly toxin that kills uninfected yeast. The toxin associates with the extracellular domain of TOK1, an outward-rectifier $K^+$ channel located on the plasma membranes of uninfected yeast, and promotes unchecked $K^+$ efflux, which causes cell death. How infected yeast remains immune has remained a mystery, although some evidence has pointed to an intracellular mechanism that spares infected yeast cells. Sesti *et al.* showed that in the presence of extracellular toxin, TOK1 channels remain inactive in infected cells. In fact, they found that the insensitivity of the channel is conferred by interaction of the toxin with the intracellular portion of the channel in such infected cells. Toxin treatment of the intracellular side of TOK1 channels (in inside-out membrane patch assays) revealed that the channels were stabilized in the closed conformation. Similar results in *Xenopus* membranes that heterologously expressed TOK1 indicated that TOK1 was also the direct intracellular target of the toxin. Experiments with a mutant toxin that did not kill yeast but that could still confer resistance to externally applied wild-type toxin suggests a role for the mutant protein in large-scale pharmaceutical productions where the yeast-killing phenomenon is a concern.

F. Sesti, T. M. Shih, N. Nikolaeva, S. A. N. Goldstein, Immunity to K1 killer toxin: Internal TOK1 blockade. *Cell* **105,** 637-644 (2001). [Online Journal]