

 FUNGAL PATHOGENESIS

## Escaping elimination

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Chytridiomycosis — an infectious disease caused by the fungal pathogen *Batrachochytrium dendrobatidis* — is a key factor in the ongoing global decline in amphibian populations; however, the molecular mechanisms that are involved in the pathogenesis of *B. dendrobatidis* are unclear. In a recent study published in *Science*, Fites *et al.* now show that *B. dendrobatidis* releases soluble mycotoxins that inhibit the proliferation of lymphocytes from the African clawed frog *Xenopus laevis* by inducing caspase-mediated apoptosis.

The authors found that co-culturing with live *B. dendrobatidis* cells inhibited the proliferative capacity of *X. laevis* splenocytes. This inhibitory effect was also observed when the splenocytes were separated from

*B. dendrobatidis* by a cell-impermeable membrane or when splenocytes were incubated with *B. dendrobatidis* culture supernatants. Further dissecting the mechanism involved, the authors showed that *B. dendrobatidis* supernatants activated apoptosis signalling in splenocytes, and this was decreased by a pan-caspase inhibitor. A caspase activity assay showed that *B. dendrobatidis* supernatants induce both intrinsic and extrinsic caspase signalling pathways in splenocytes.

Importantly, *B. dendrobatidis* supernatants retained their capacity to inhibit lymphocyte proliferation after heat, acid or proteinase K treatment, which suggests that the stimulatory factors involved are not proteins. This, together with the finding that *B. dendrobatidis* zoospores (which lack cell

walls) did not inhibit lymphocyte proliferation, led the authors to hypothesize that the released inhibitory factors may be cell wall components. In agreement with this, inhibiting *B. dendrobatidis* cell wall synthesis significantly decreased the negative effect of the fungus on lymphocyte proliferation. However, treatment of *B. dendrobatidis* supernatants with chitinases or  $\beta$ -glucanases had no effect on proliferating lymphocytes.

As proliferation of mammalian epithelial cells is also inhibited by *B. dendrobatidis* supernatants, the authors conclude that the released factors are broad-spectrum cytotoxins; however, the identity of these inhibitory factors remains to be determined.

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**ORIGINAL RESEARCH PAPER** Fites, J. S. *et al.*  
The invasive chytrid fungus of amphibians paralyzes lymphocyte responses. *Science* **342**, 366–369 (2013)

