Anesthetic preconditioning protects *S. cerevisiae* from a lethal heat stress.

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Background/Introduction: Anesthetic action and preconditioning are conserved across all living organisms (1, 2). We hypothesize that anesthetics invoke a cellular stress response in yeast protective from an otherwise lethal stress. Establishing *S. cerevisiae* as a model organism for anesthetic preconditioning may allow high throughput screening for more potent, efficacious, and less toxic protective compounds. Additionally, high throughput assays may uncover molecular mechanisms of cellular protection.

Methods: Potency for protection was determined by pretreating *S. cerevisiae* with and without anesthetic compounds at varying temperatures before exposing them to a usually lethal heat stress. Cell viability was detected by optical density measurements and by colony forming unit assays.

Results and Discussion: Anesthetics dose-dependently protect *S. cerevisiae* from a lethal heat stress with the following rank order for potency: CBr4 > Propofol > TBE > HFP > TFE > Isopropanol > Ethanol and TCE > DCE > MCE (Table 1). Potency for protection correlates log-linearly with compound lipophilicity (R square 0.94). CBr4, TBE, TCE and HFP enhance protection induced by mild to moderate temperature elevation.

Conclusions: Anesthetics protect *S. cerevisiae* from a lethal heat stress and enhance protection induced by mild to moderate temperature elevation. *S. cerevisiae* may be a useful organism to characterize pharmacological requirements for anesthetic preconditioning.

References: (1) Sonner JM, Anesthesia and Analgesia 2008 Sept;107(3):849. (2) Jia B, Anesthesiology 2008 Mar;108(3):426-33.

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Table 1.

Compound	Concentration for maximum Protection ± SEM	n-value	logP
Propofol	310 ± 0µM	3	3.79

Carbon tetrabromide	33.8 ± 2.8µM	9	3.42
2,2,2-tribromoethanol	5.6 ± 0mM	9	2.1
2,2.2-trichloroethanol	31 ± 0mM	6	1.42
1,1,1,3,3,3-hexafluoroisopropanol	19.3 ± 2.8mM	6	1.66
2,2,2-trifluoroethanol	193.3 ± 28.3mM	6	0.41
2,2-dichloroethanol	100 ± 0mM	3	0.43
2-monochloroethanol	310 ± 0mM	3	0.03
Isopropanol	560 ± 0mM	3	0.05
Ethanol	1 ± 0M	3	-0.31