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**Natural genetic diversity of yeast aids in identification of genes involved in ionic liquid (IL) tolerance**

Mining yeast genomes for tolerance to ILs yields insight into cellular defense mechanisms and strategies to improve strain performance.

**The Science**

Microbes from nature represent a range of biological variation that can be exploited to identify traits that contribute to a particular phenotype. In this study, researchers examined natural diverse isolates of *Saccaromyces cerevisiae* for tolerance to ILs and identified two genes associated with this outcome. Analysis of specific gene variants suggests that tolerance may be governed in part by the degree to which ILs can be pumped out of cells.

**The Impact**

An understanding of the cellular mechanisms of IL tolerance can enable rational engineering approaches to design robust microbial strains that efficiently convert biomass to biofuels. The range of natural biological variation present among diverse microbial isolates is an important resource that can contribute to identification of biological mechanisms of interest.

**Summary**

ILs are promising deconstruction solvents for the conversion of lignocellulosic biomass to biofuels. However, many conversion microbes are sensitive to the toxic effects of residual solvent. One approach to circumventing this problem is to identify genetic traits that contribute to IL tolerance and engineer them into biofuel-producing strains for improved performance. Researchers examined the growth of 136 *S. cerevisiae* genome-sequenced strains in media containing 1-ethyl-3-methyl imidazolium chloride ([C2C1im]Cl) in order to gauge natural phenotypic variation among yeast from diverse ecological niches. The best performing strain was analyzed and compared to an IL-sensitive strain to determine the genetic basis for tolerance. From a screened library of genomic DNA fragments, two genes were associated with improved IL tolerance: *SGE1*, which encodes a plasma membrane multidrug efflux pump, and a previously uncharacterized gene (designated here as *ILT1*), encoding a predicted membrane protein. Comparison of *SGE1* sequences across strains implicated two single nucleotide polymorphisms (SNPs) that associated with IL tolerance and sensitivity. The phenotypic effects of the SNPs were confirmed by CRISPR/Cas9 genome editing of a [C2C1im]Cl-sensitive strain. Interestingly, the SNPs were determined to affect Sge1 protein stability and cell surface localization, potentially impacting the amount of toxic ILs that cells can pump out of the cytoplasm. These results demonstrate the wealth of biological function inherent in nature that may be exploited for biocatalyst strain improvement and provide further clues on the cellular mechanisms of IL tolerance.

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**Publications**

Higgins, D.A. et al., “Natural variation in the multidrug efflux pump *SGE1* underlies ionic liquid tolerance in yeast.” *Genetics* (2018), DOI:10.1534/genetics.118.301161.

**Related Links**

<http://www.genetics.org/content/early/2018/07/24/genetics.118.301161>

**PM Recommendation for SC Web Publication**

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