

## Restoring Physiology in Protein Deficient Cells with Small Molecules

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Many human diseases arise from the deficiency of critical protein function. Small molecules which can partially replicate protein function represent a potentially empowering alternative treatment to these diseases. In this vein, the small molecule natural product amphotericin B has recently been shown to restore growth to yeast deficient in potassium uptake. Herein, we report the robust restoration of vigorous and sustainable growth upon treating a yeast strain lacking a highly regulated iron transporting protein complex with the inherently less selective and non-regulated tropolone natural product hinokitiol. Several lines of evidence demonstrate that this restoration is due to the capacity of hinokitiol to bind and transport iron. Collectively, these findings suggest this rescue phenomenon is general, and substantially brighten the prospect of treating diseases caused by missing proteins with imperfect small molecule surrogates.

