

# MOL 231: WHY ARE HSP90 CHAPERONES SO ABUNDANT?

## Cellular effect of reducing HSP90 levels

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### HSP90 are conserved and highly abundant cellular chaperones

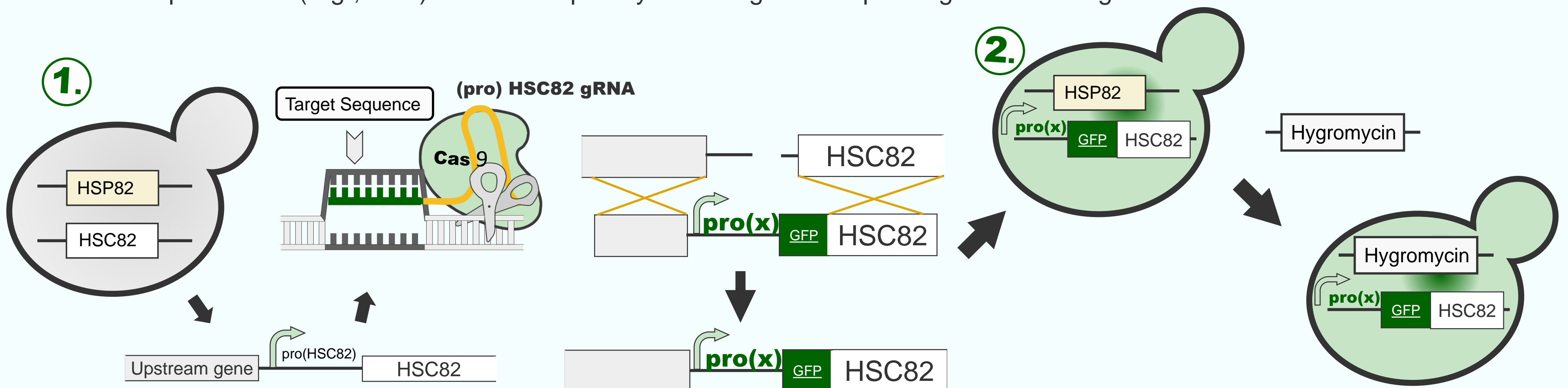
- Hsp90 is a **conserved chaperone family** activated at various stress conditions such as heat stress.
- Hsp90 chaperones **have multiple roles in maintaining protein homeostasis** including nascent polypeptide folding, misfolded protein surveillance, assembly of multiprotein complexes and in gene expression.
- Hsp90 is **one of the most abundant cellular proteins**, accounting for 1%-2% of total cellular proteome [1] and frequently overexpressed in cancer.

### Goals:

Interestingly, budding yeast (*S. cerevisiae*) can tolerate up to 20-fold reduction in Hsp90 levels [1]. In this study we aimed to establish a model system based on budding yeast to examine the effects of reduced levels of Hsp90 on cellular function.

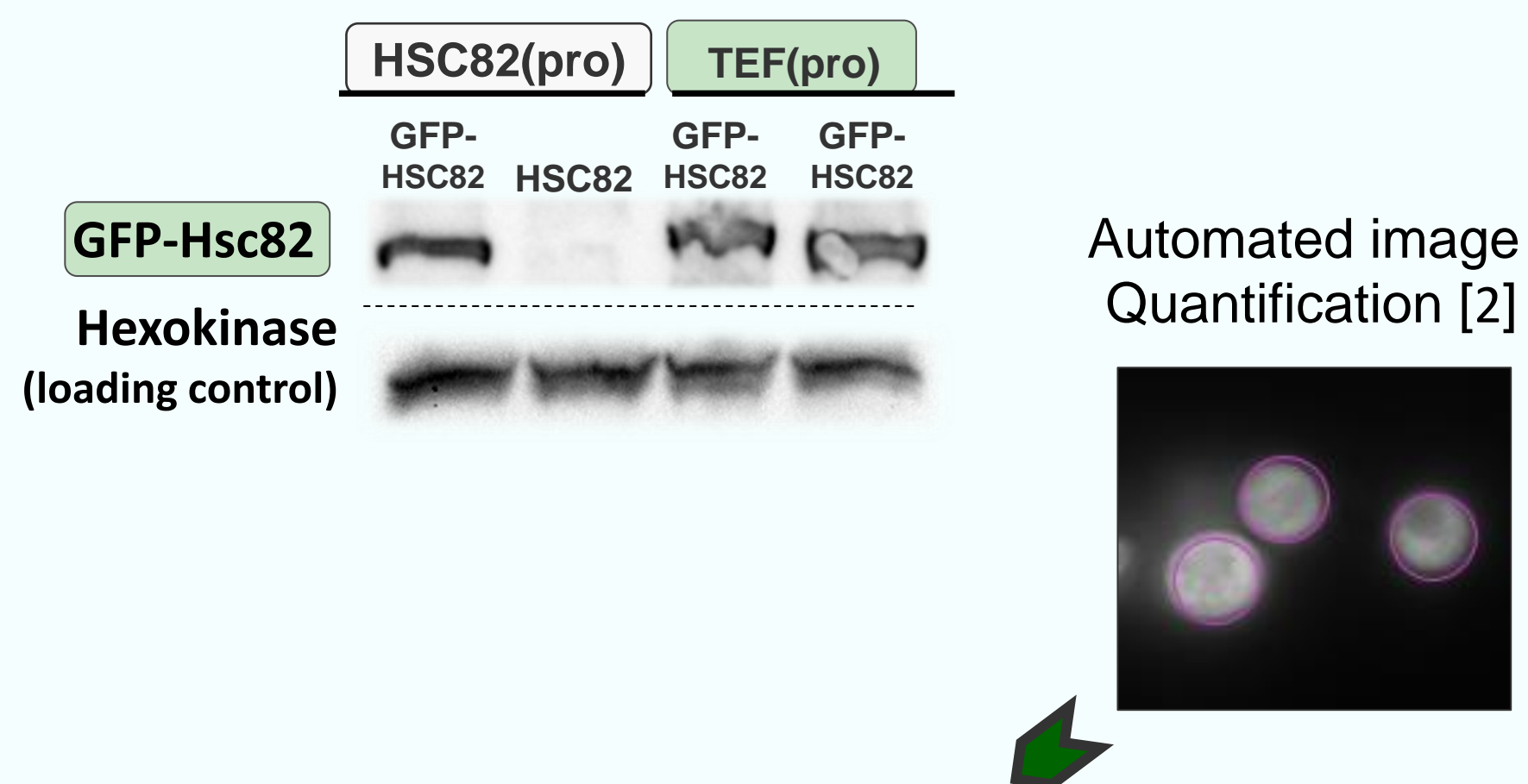
### Reducing HSP90 levels in budding yeast cells

We used CRISPR-Cas9 technology to replace original promoter of HSC82 (yeast Hsp90 coding gene) with a series of weaker constitutive promoters (e.g., TEF) and subsequently knocking out the paralogous HSP82 gene.

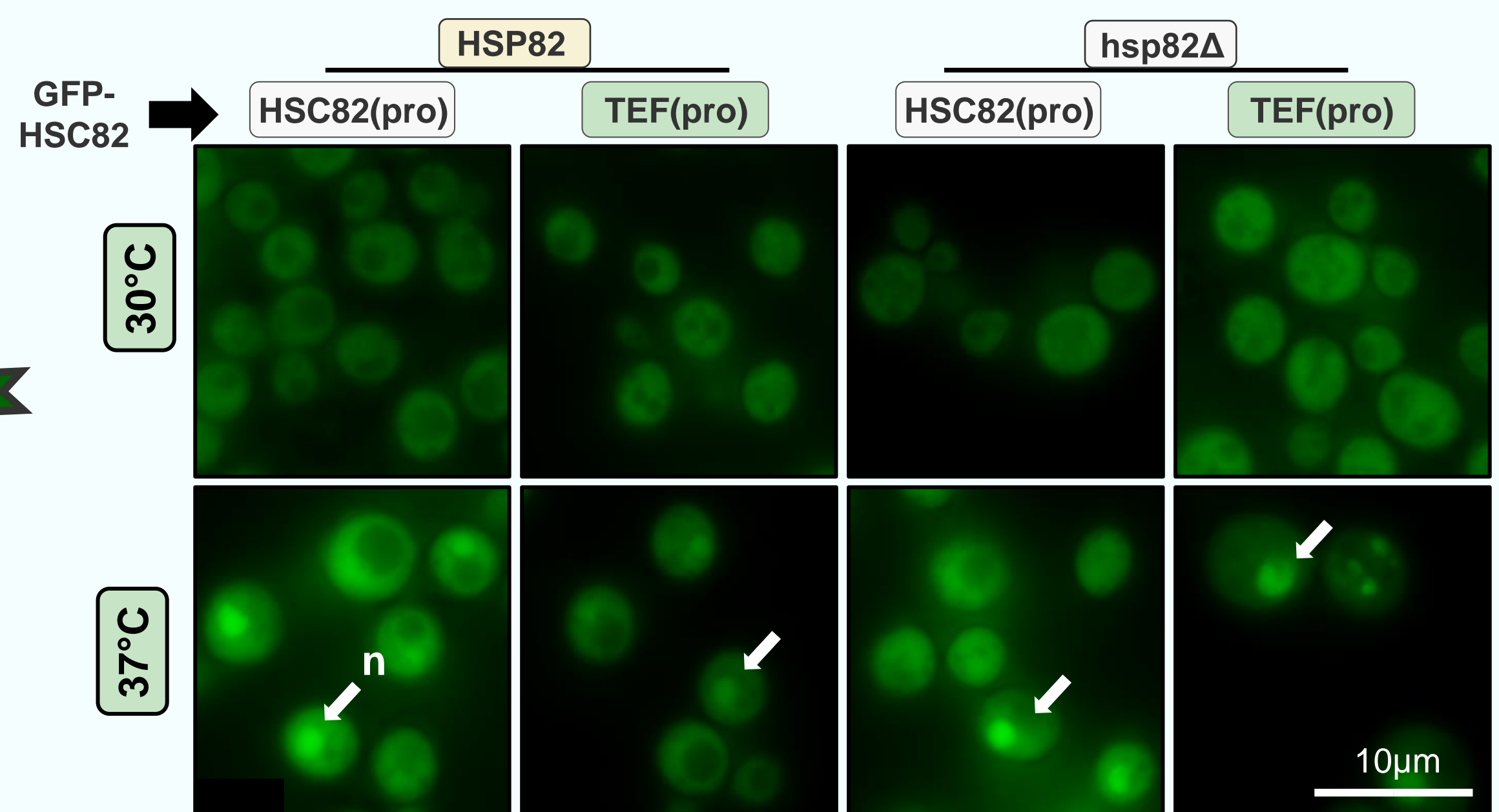


### Low Hsp90 levels affects cell fitness in heat stress

#### Expression of GFP-tagged full-length Hsp90



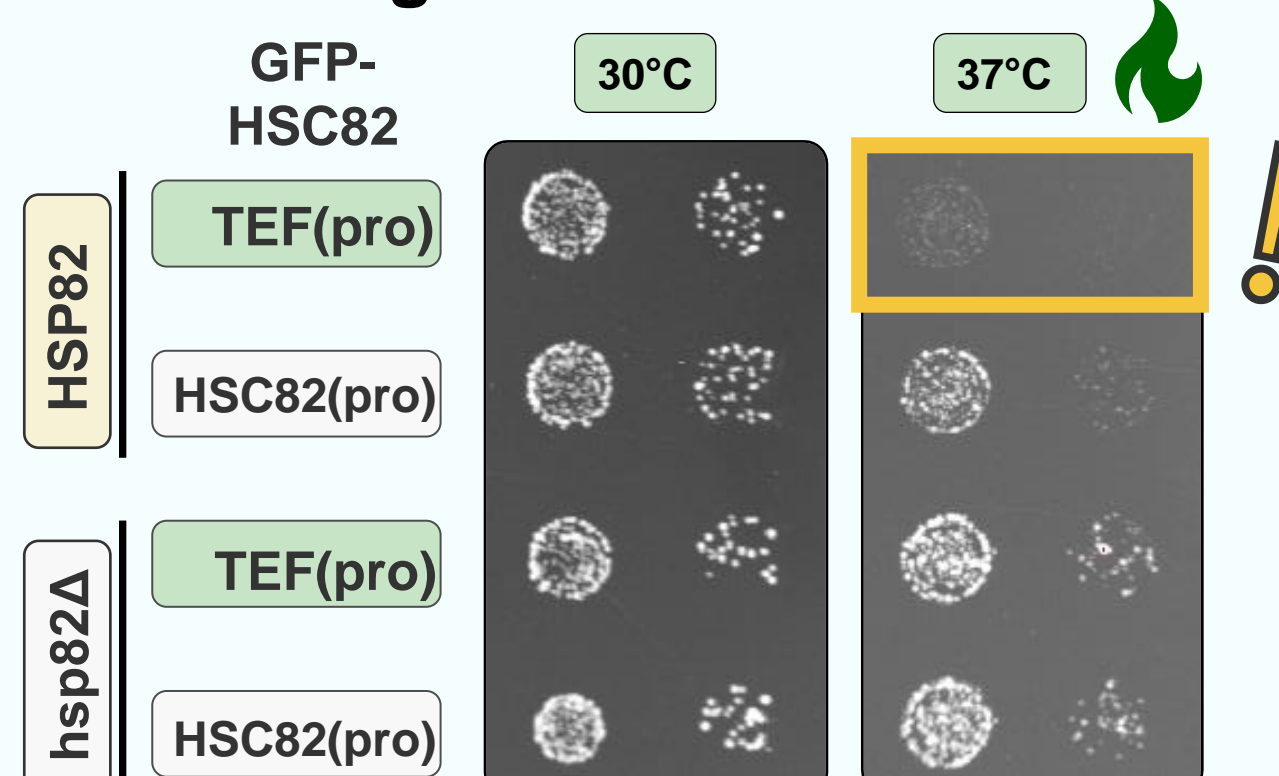
#### Heat stress induces nuclear accumulation of Hsp90



### Conclusions

- We created a yeast model system to systematically analyze cellular impact of Hsp90 deprivation.
- Our results suggest that high Hsp90 levels are important during heat stress
- Hsp90 redistributes to the nucleus during heat stress

#### Low Hsp90 levels inhibit cell growth in heat stress



#### TEF promoter results in ~ 2-fold reduced expression of Hsp90 in heat stress conditions (37°C)

