Following Gene Duplication, Paralog Interference Constrains Transcriptional Circuit Evolution

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background

Why certain gene duplicates have been maintained over evolutionary time ？

- Some models
- Neofunctionalization model：one of the duplicates evolves a new function that can be selected for and maintained over time
- Subfunctionalization models：

  duplication-degeneration-complementation

However

many transcriptional regulators depend on a cooperative network of protein-protein and protein–nucleic acid interactions.

In these instances, loss of one or more ancestral molecular interactions will often give rise to competitive interference between gene duplicates (paralog interference).

Paralogy：

One of a set of homologous genes that have diverged from each other as a consequence of gene duplication.

Orthology ：

Orthology describes genes in different species that derive from a single ancestral gene in the last common ancestor of the respective species.

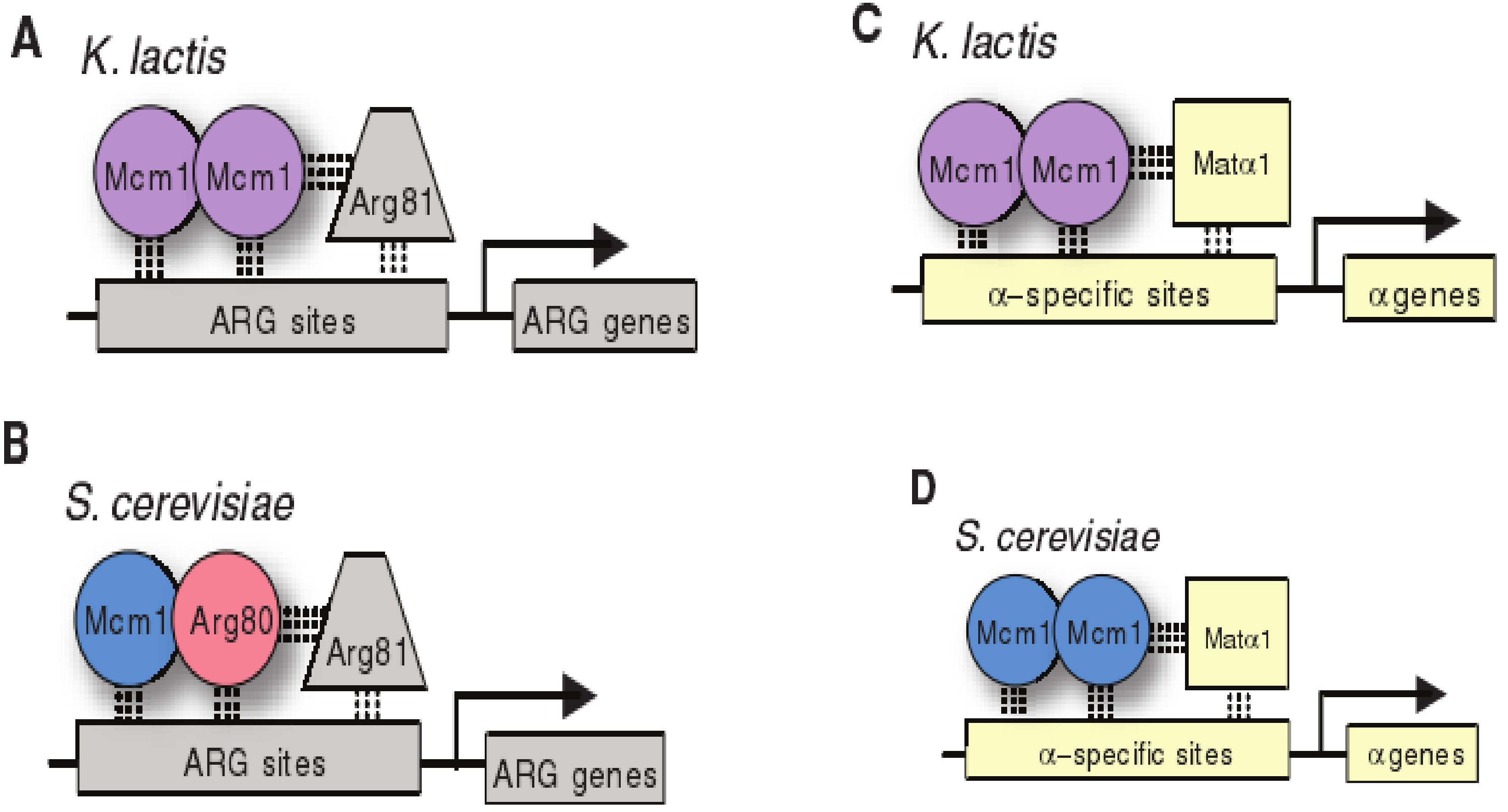
New idea

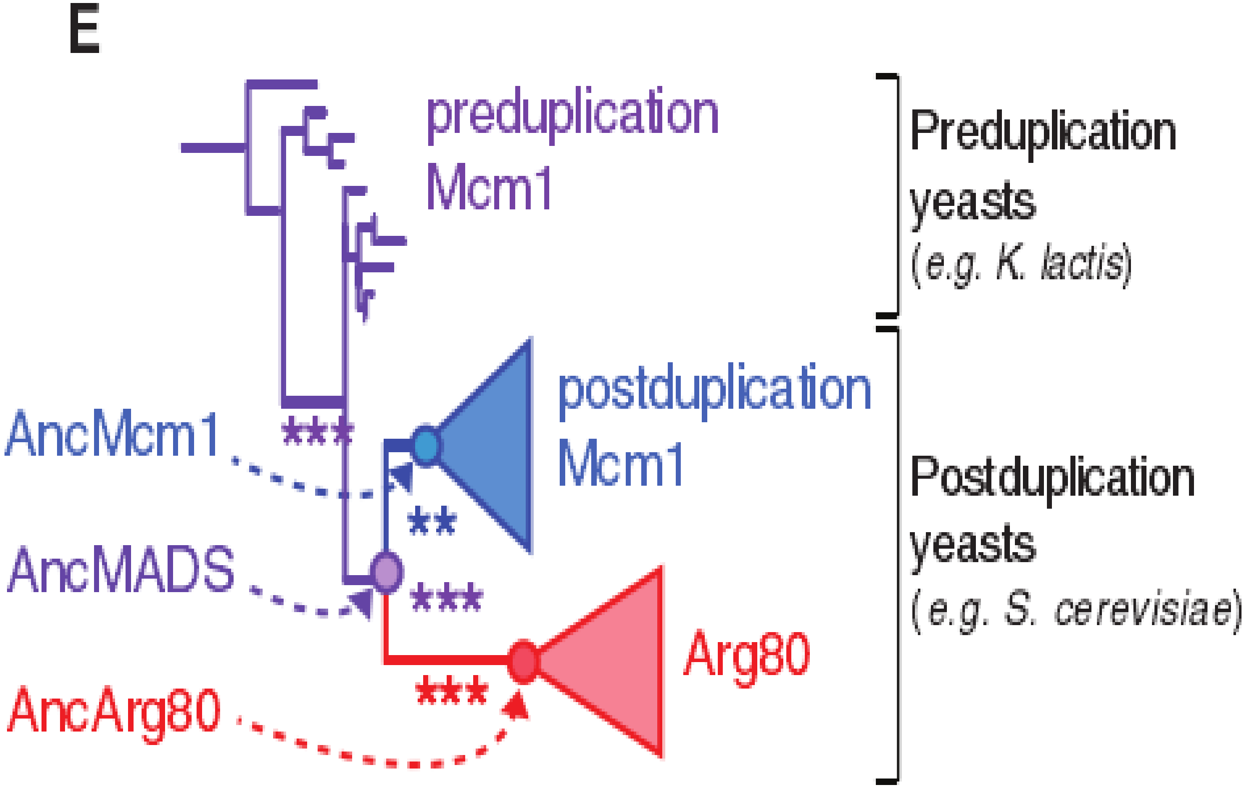
paralog interference is a common constraint on gene duplicate evolution

paralog interference → detrimental effects → evolutionarily bypassed for the paralogs

For example

Function and evolution of MADS-box proteins in hemiascomycete yeasts.



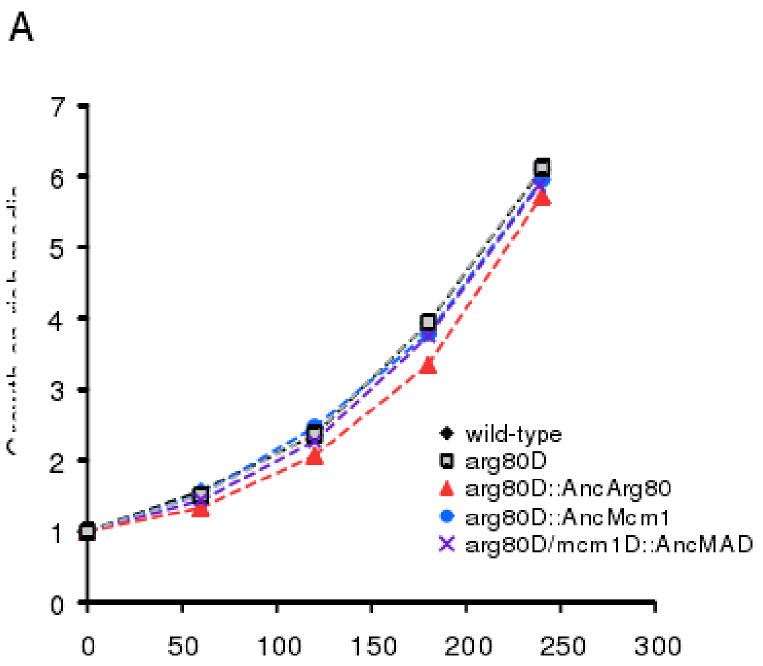


evolution of MADS-box proteins in hemiascomycete yeasts.

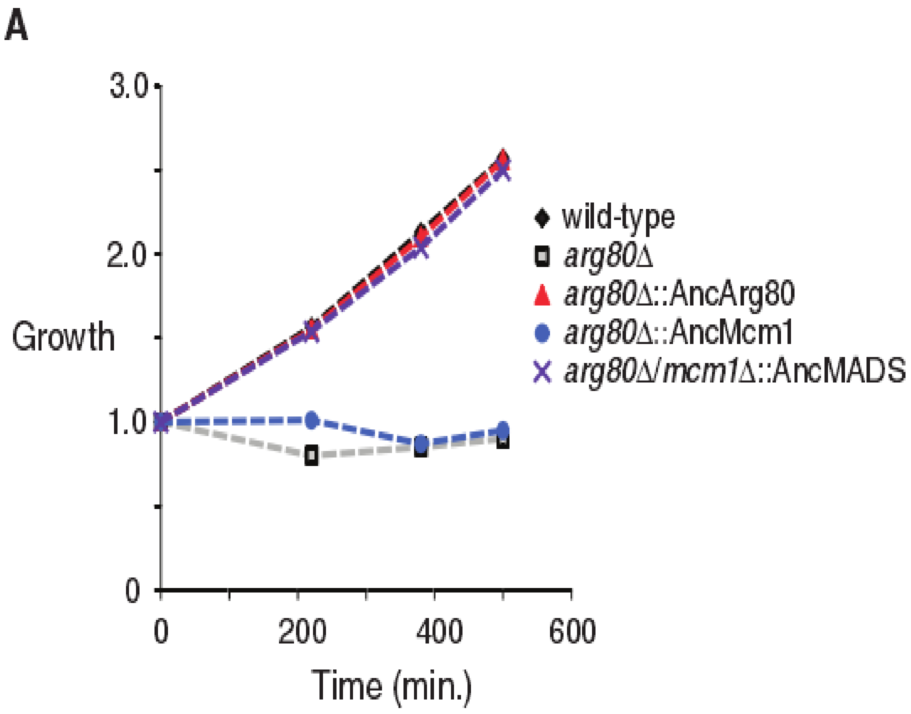
AncMcm1: most recent common shared ancestor of all postduplication Mcm1 paralogs;

AncArg80: most recent common shared ancestor of all postduplication Arg80 paralogs;

AncMADS: most recent shared common ancestor of all Mcm1 and Arg80 paralogs.

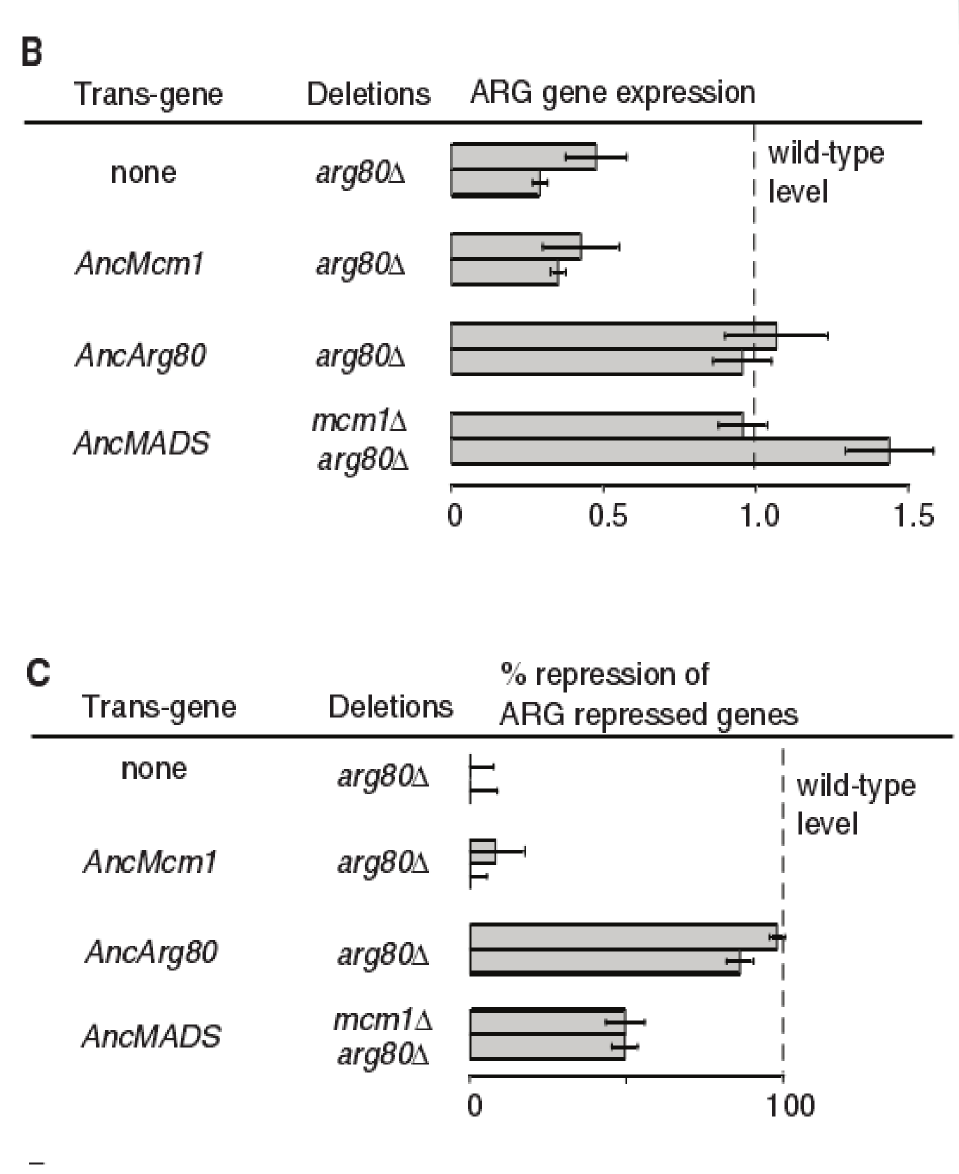


Growth on rich-media

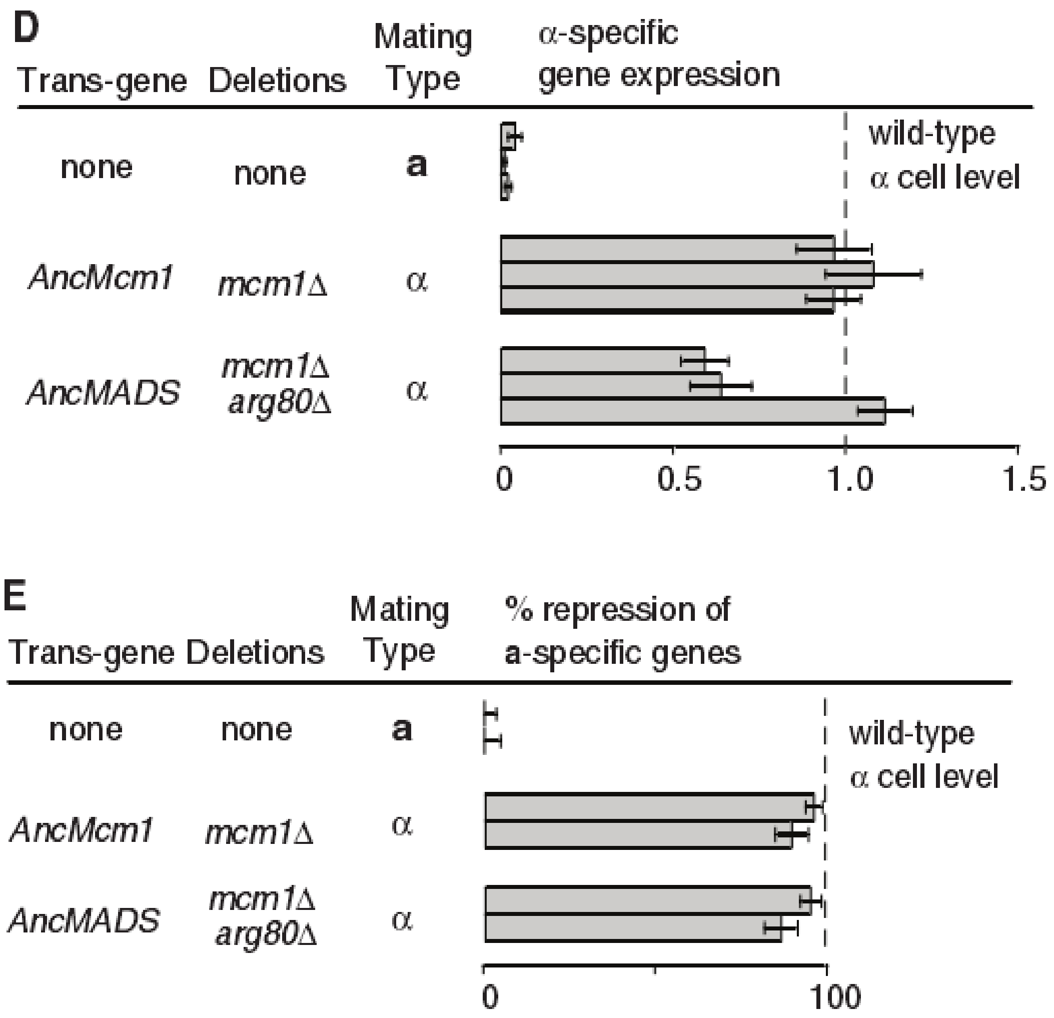


Ornithine as a sole nitrogen source

The pre-duplication ancestral gene complements both paralogs



Gene(ARG gene) expression profiling of ancestral MADS-box proteins in S. cerevisiae quantified with NanoString

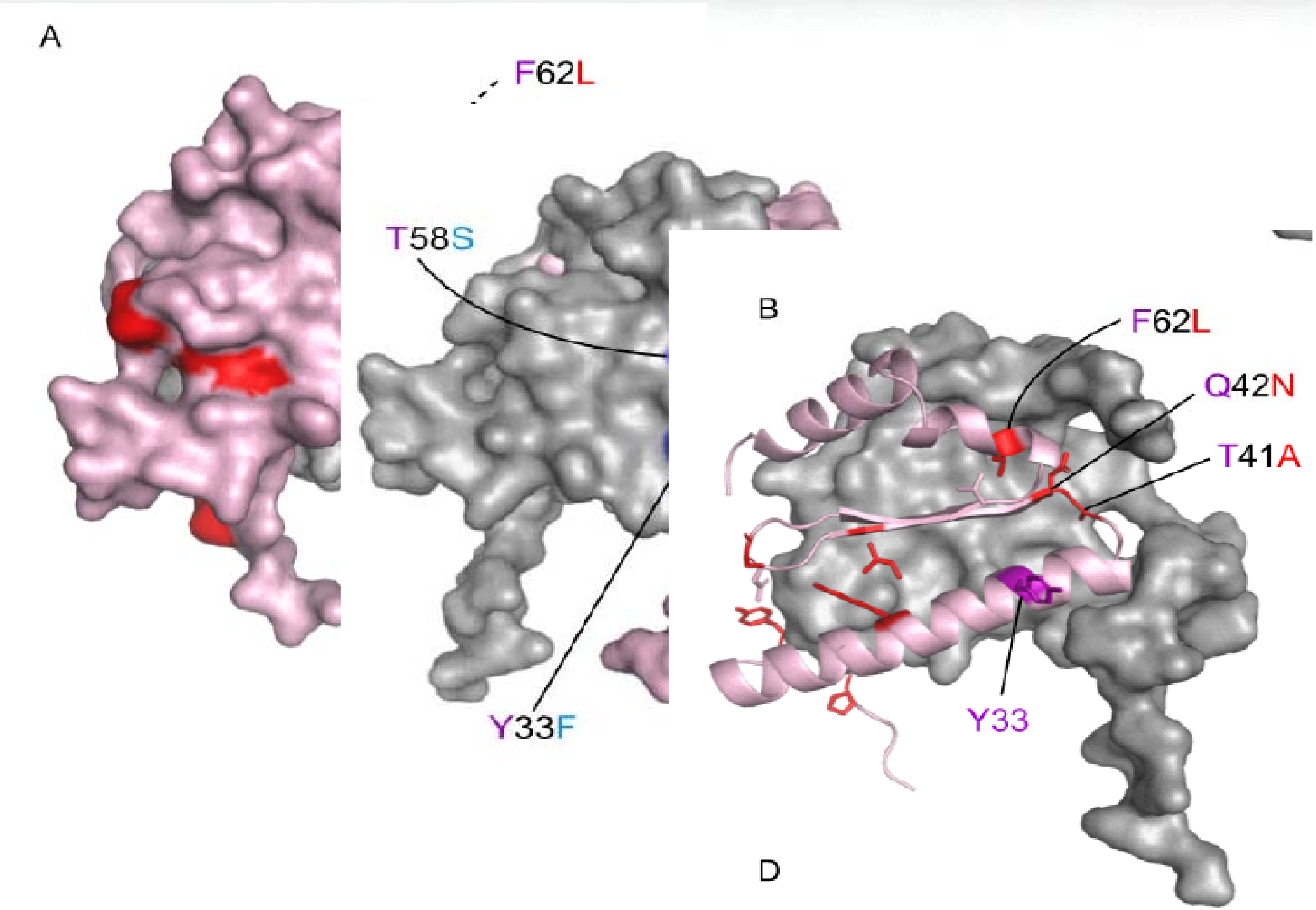


Gene(α-specific gene) expression profiling of ancestral MADS-box proteins in S. cerevisiae quantified with NanoString

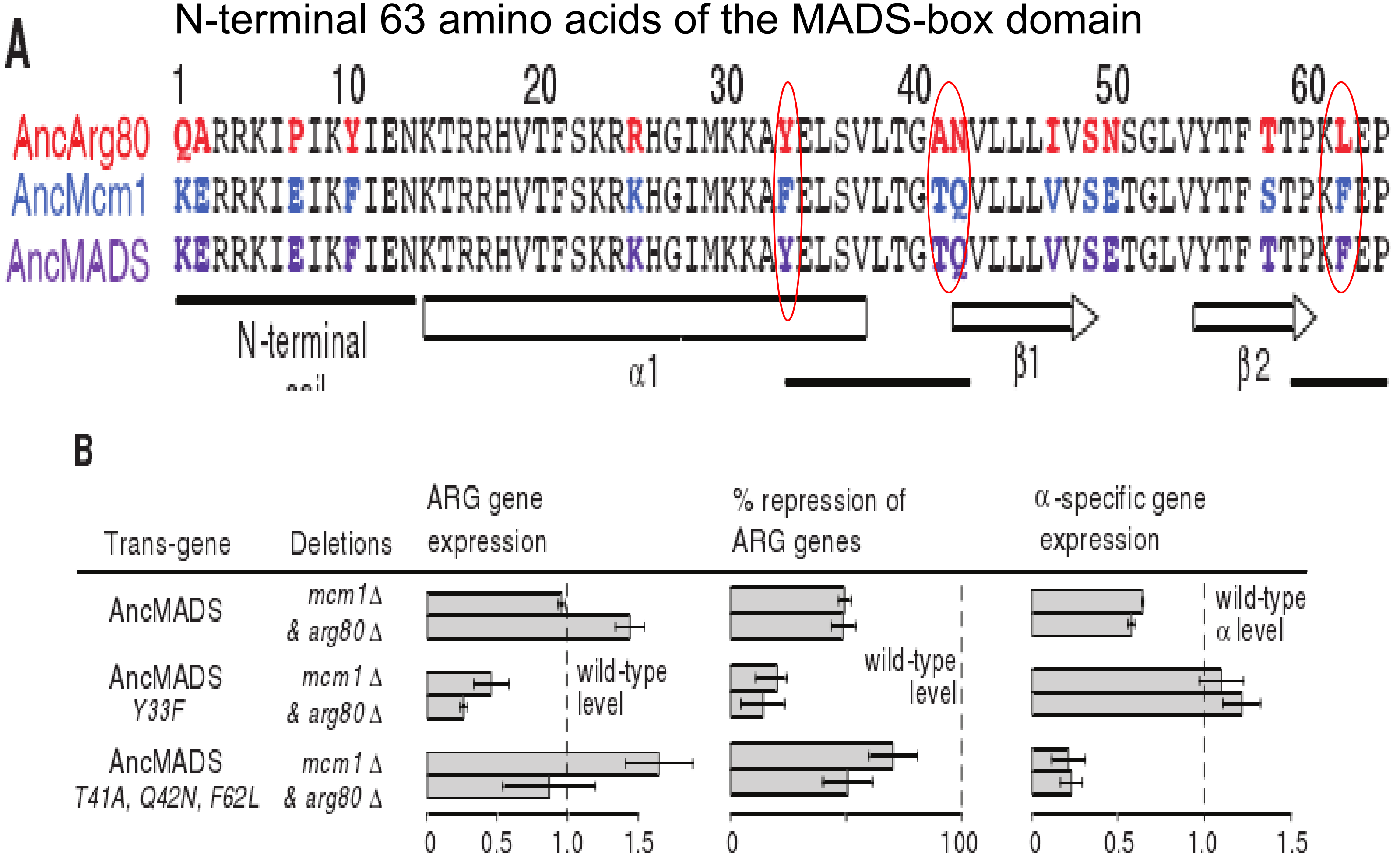
Summary

The postduplication MADS-box proteins (AncArg80 and AncMcm1) failed to complement deletions of the sister paralogs..

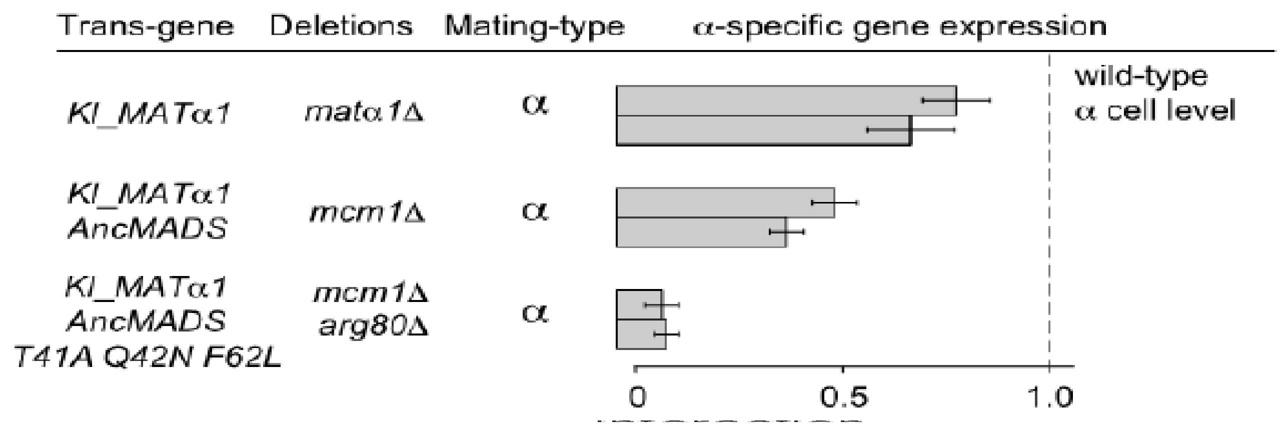
But the capacity of the preduplication ancestral MADS-box protein to complement the functions of both daughter genes in a modern species, combined with the inability of the postduplication ancestors to do the same, shows that AncMcm1 and AncArg80 acquired degenerative mutations that necessitated the retention of both paralogs over evolutionary time.

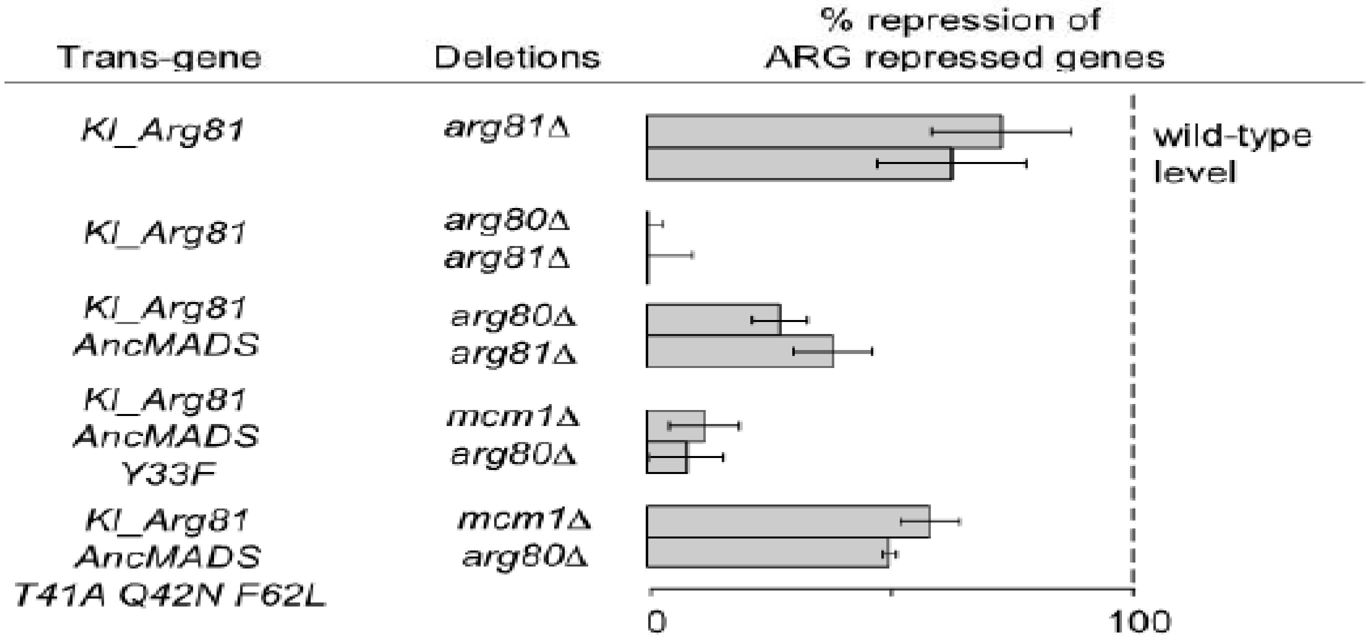

A
F62L
T58S
Y33F
B
F62L
Q42N
T41A
Y33
D

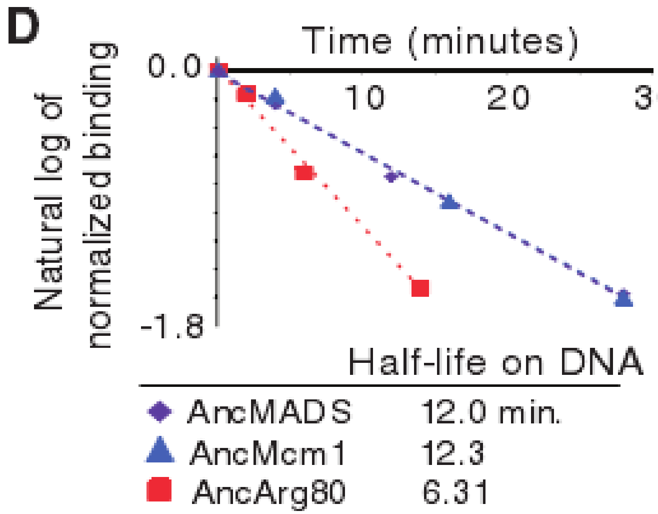
N-terminal 63 amino acids of the MADS-box domain



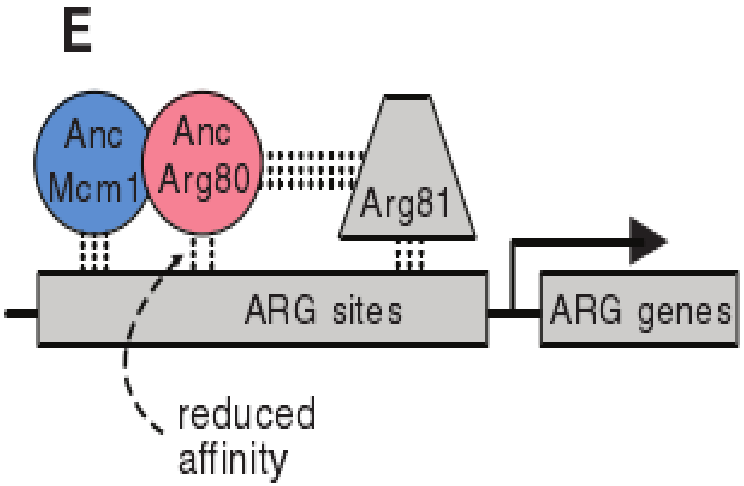
Gene expression profiling to determine the impact of mutants on the function of preduplication AncMADS protein


Trans-gene
Deletions
Mating-type
α-specific gene expression
Kl_MATα1
matα1Δ
α
Kl_MATα1 AncMADS
mcm1Δ
α
Kl_MATα1 AncMADS T41A Q42N F62L
mcm1Δ arg80Δ
α
wild-type α cell level
0
0.5
1.0

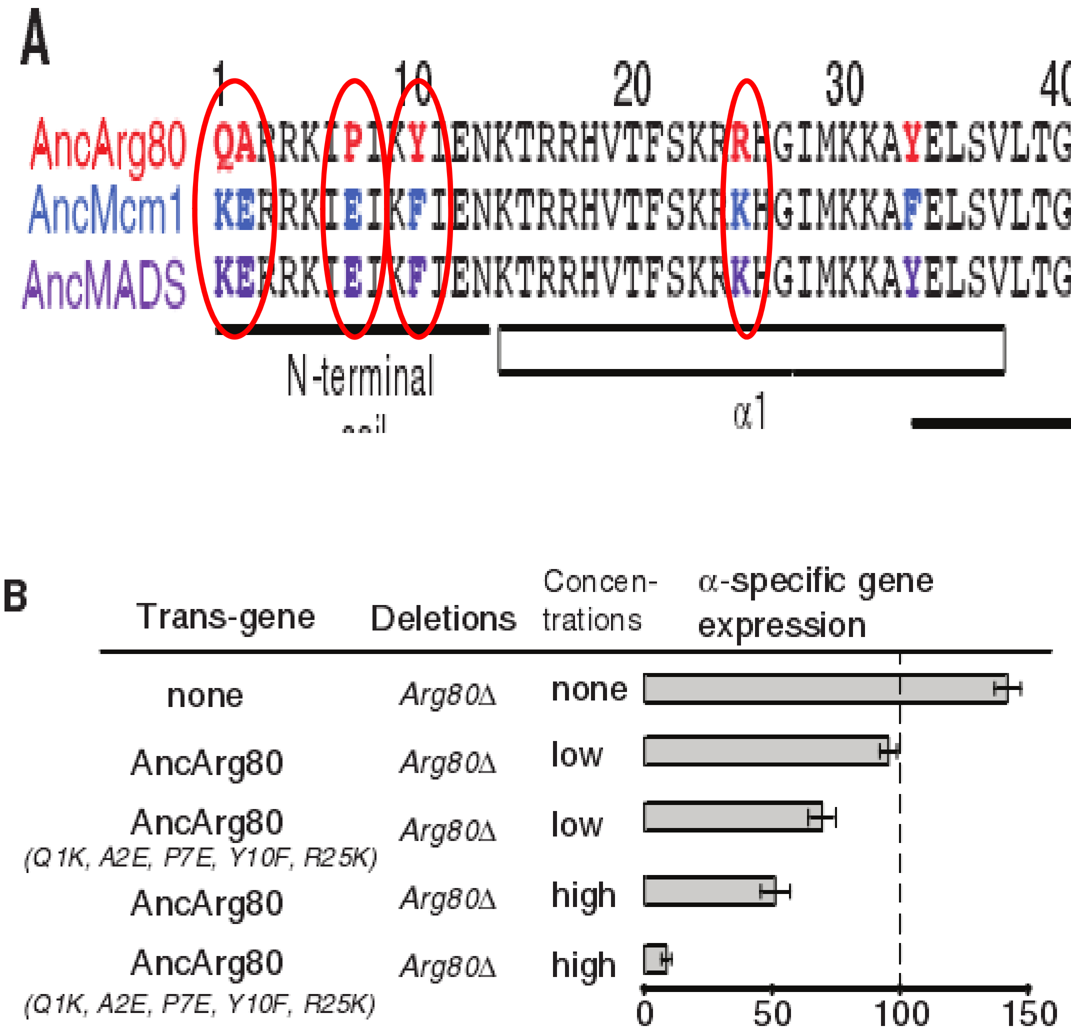

Trans-gene
Deletions
% repression of ARG repressed genes
Kl_Arg81
arg81Δ
Kl_Arg81
arg80Δ arg81Δ
Kl_Arg81 AncMADS
arg80Δ arg81Δ
Kl_Arg81 AncMADS Y33F
mcm1Δ arg80Δ
Kl_Arg81 AncMADS T41A Q42N F62L
mcm1Δ arg80Δ
wild-type level
0
100



The half-life of AncArg80 was significantly lower than the half-lives of AncMADS and AncMcm1



soon after the duplication decrease in Arg80 DNA-binding affinity



Competitive interference between Mcm1 and Arg80.

Conclusion

Although in some cases, this interference can be exploited, for example, by using it to repress gene expression.

we propose that a more common outcome is the minimization of this interference in gene duplicates that persist over evolutionary time.

Whether such minimization is generally accompanied by an increase in regulatory complexity, as seen here, remains to be determined.

Thanks for your attention!