Kfc1 is a novel meiotic regulator required for meiosis that engages in a function specific interaction with Kar4

1679B

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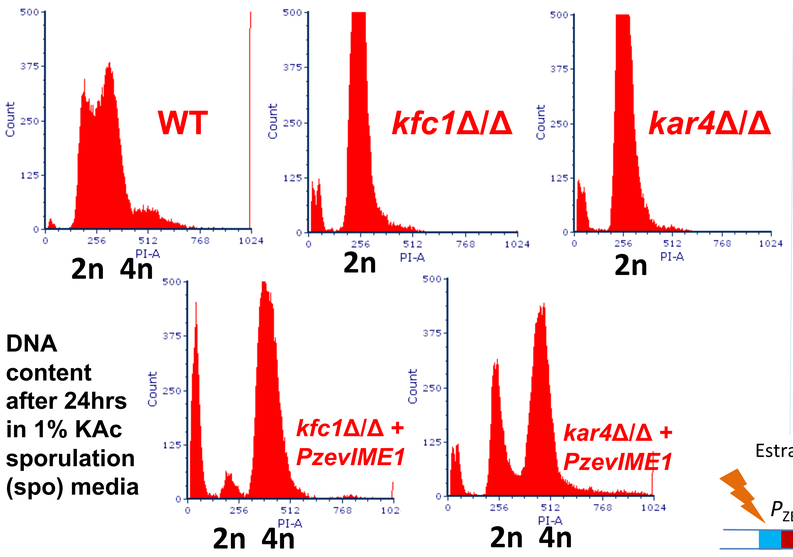
Abstract: Ygl036w is a previously uncharacterized protein with no annotated function or discernable domains except for several intrinsically disordered regions. High throughput studies from our lab and others showed that Ygl036w interacts with the meiotic proteins Kar4 and Mum2, suggesting a role for Ygl036w in meiosis. We found that Ygl036w is essential for meiosis and required early before pre-meiotic S-phase. Previous separation of function screens identified alleles of Kar4 that were defective for two independent meiotic functions. The defect associated with the first function (Mei) is suppressed by over-expression of the master meiotic transcription factor *IME1*. Suppression of the second function (Spo) requires the over-expression of an additional gene, *RIM4*, encoding a translational regulator. Using the Mei- and Spo- alleles, we asked if Ygl036w engages in a function specific interaction with Kar4. We found that Kar4 mutants specifically defective for the Spo function are unable to interact with Ygl036w. Accordingly, we propose a new name for *YGL036w*, *KFC1* for *KAR4 Collaborator 1*. Here we further characterize the *kfc1*Δ/Δ meiotic defect at both the cellular and molecular level.

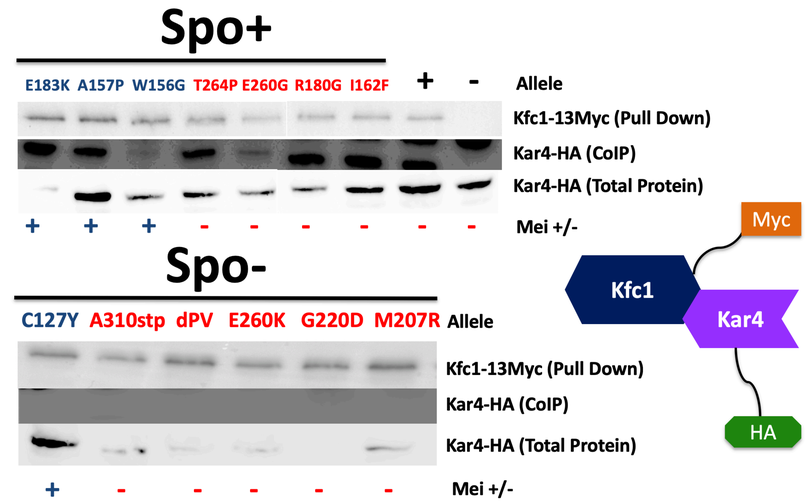
KAR4 Collaborator 1 (Ygl036) is required early in meiosis before pre-meiotic S-phase

Genotype	*KFC1* Plasmid	% Sporulation
+/+	-	29.2
*kfc1*Δ/*kfc1*Δ	-	0
*kfc1*Δ/+	-	11.5
*kfc1*Δ/*kfc1*Δ	+	17.1
*kfc1*Δ/+	+	25.1



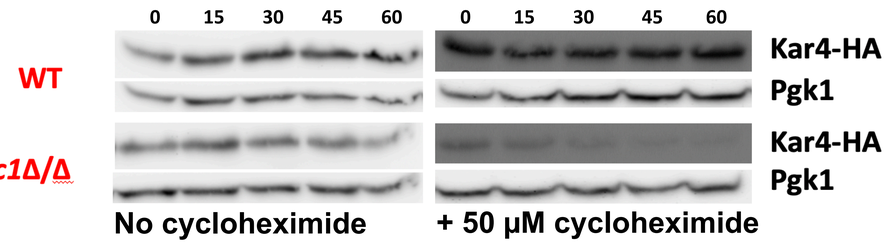
DNA content after 24hrs in 1% KAc sporulation (spo) media

Kfc1 has a function specific interaction with Kar4

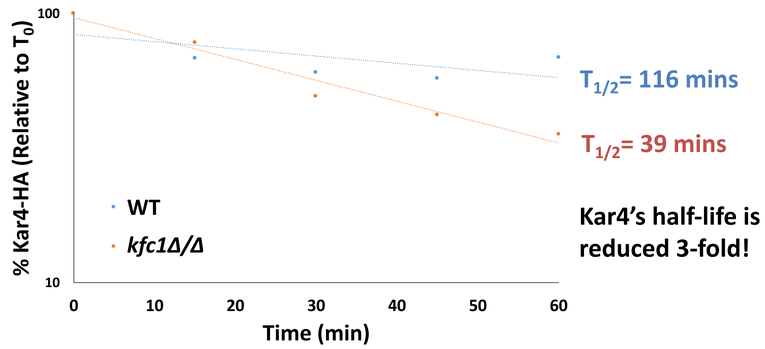


Kar4 is unstable during meiosis in kfc1Δ/Δ

Time in Spo Media (min)

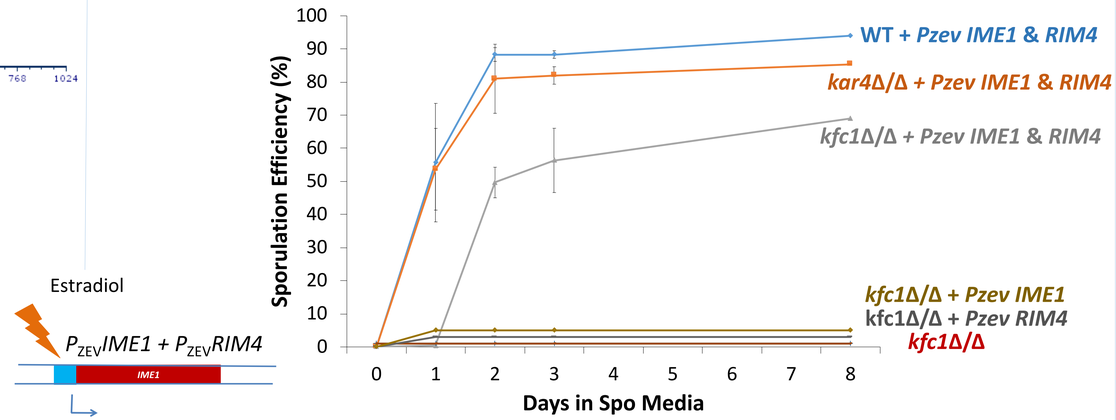


Cells were moved to Spo media for 4 hours before addition of cycloheximide.

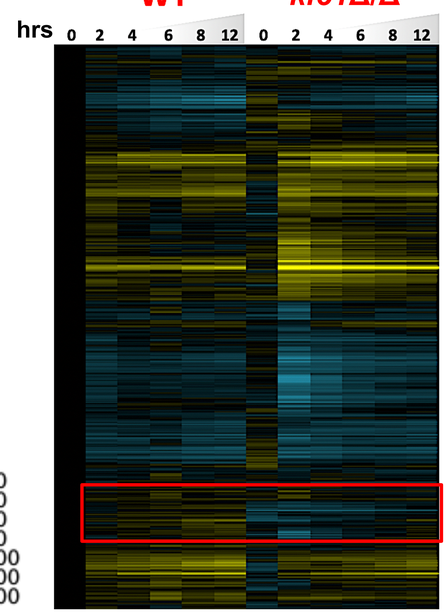


Kar4's half-life is reduced 3-fold!

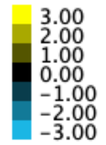
kfc1Δ/Δ meiotic defect is rescued by overexpressing both *IME1* and *RIM4*



kfc1Δ/Δ has an early transcriptional defect

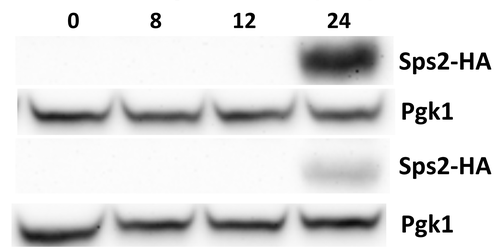


RNAseq revealed that expression of early meiotic genes including *DMC1* is reduced ≥2-fold in *kfc1*Δ/Δ



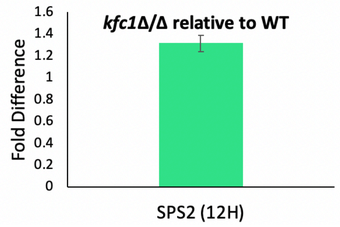
kfc1Δ/Δ has a late post-transcriptional defect

Time in Spo Media (hrs)



Spore wall protein levels reduced!

SPS2 mRNA is wild-type



mRNA levels were measured using qPCR.

Summary & Future Directions