The *Pseudomonas aeruginosa* acyl-CoA dehydrogenase FadE2 and negative regulator of the mitochondrial UPR mediates bacterial survival during oxidative stress

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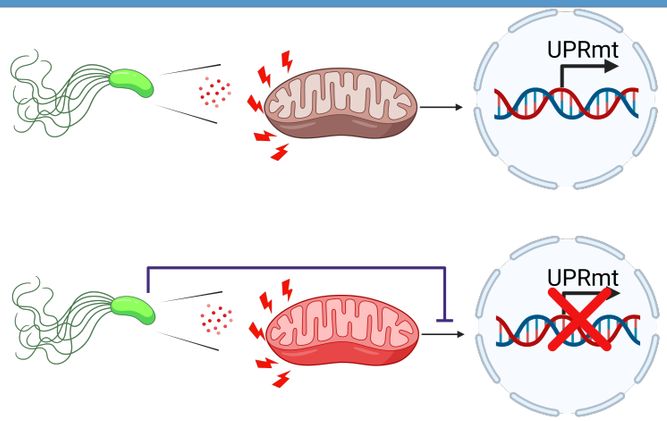
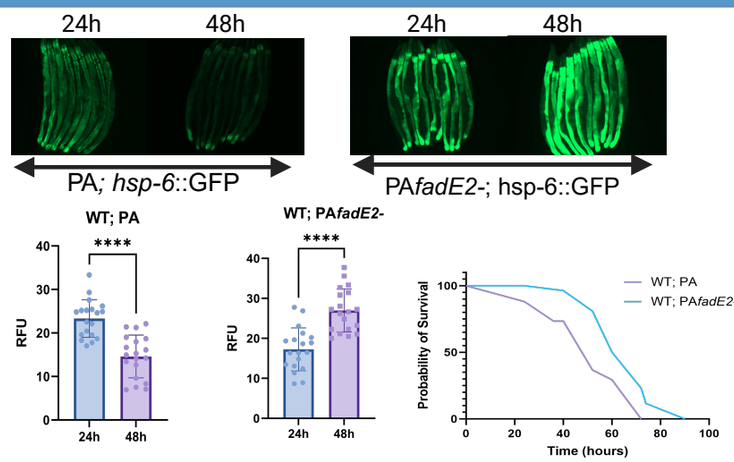
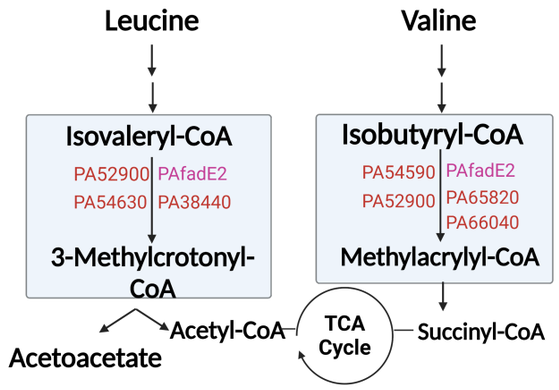
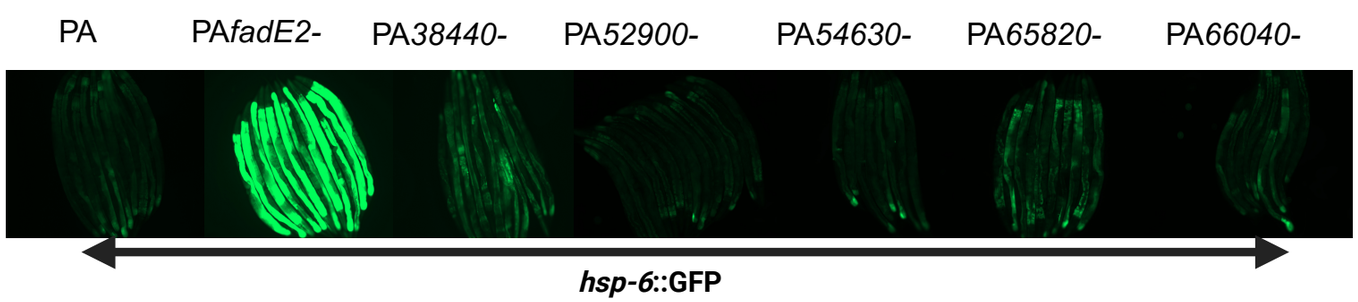
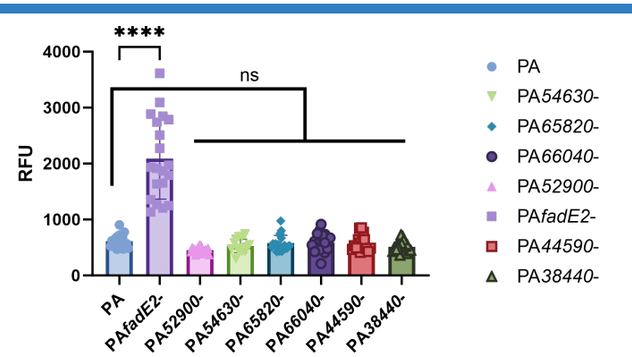




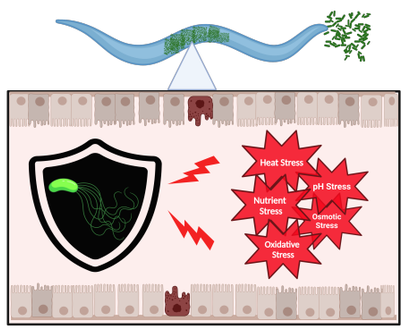


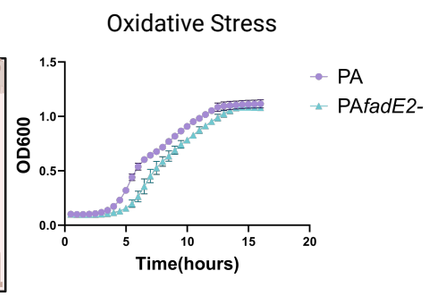
The mitochondrial unfolded protein response (UPRmt) regulates mitochondrial protective genes transcriptionally. *Pseudomonas aeruginosa* infection activates the UPRmt in *C. elegans* due to toxins targeting mitochondrial function. Intriguingly, the UPRmt is suppressed during prolonged infection. We found that the *P. aeruginosa* acyl-CoA dehydrogenase FadE2, which is involved in BCAA catabolism, is required for UPRmt suppression during *P. aeruginosa* infection.

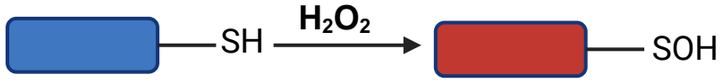




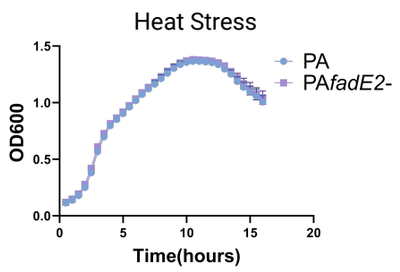
FadE2 is one of several enzymes that catabolize branched-chain amino acids and fatty acids. We wanted to see if FadE2 is unique or if losing any other acyl-CoA dehydrogenases lead to the same result. Here, we show that FadE2 is the only P. aeruginosa acyl-CoA dehydrogenase capable of suppressing the UPRmt. Therefore, what makes P. aeruginosa FadE2 unique in in its ability to repress the UPRmt?

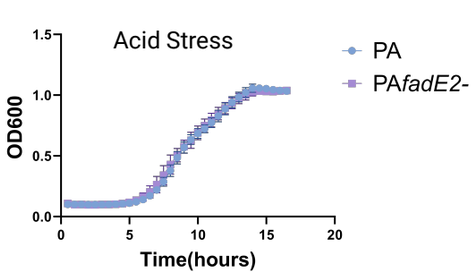


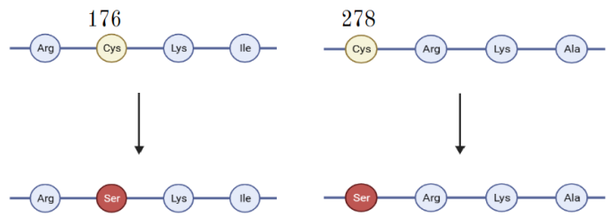


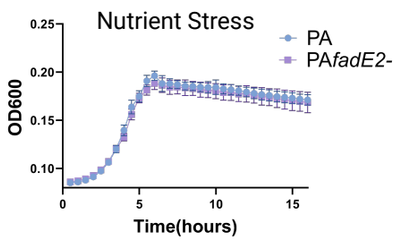


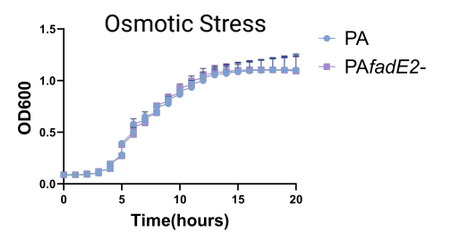
FadE2	171	181	274	284
P. aeruginosa	ACDPRCKILIF	····	LELMCKRAVSR	
E. cloacae	ACDPRCKILIF	····	LELMCKRAVSR	
A. baumanii	ACDPRCKILIF	····	LELMCKRAVSR	

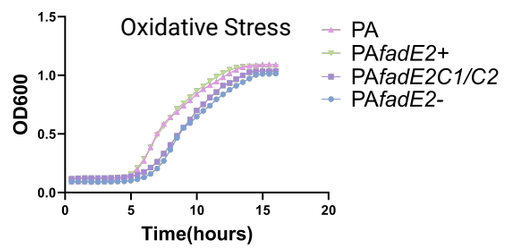




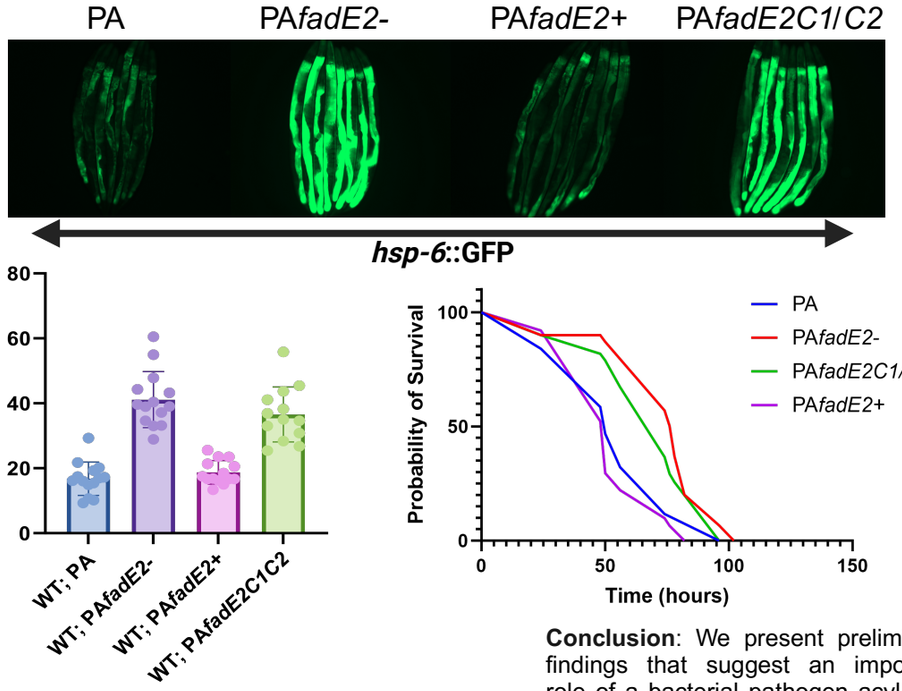








P. aeruginosa establishes itself in the intestinal lumen of C. elegans during infection, a hostile environment home to a variety of environmental stresses that the pathogen must mitigate. Consistently, we discovered that FadE2 contributes to pathogen survival specifically during oxidative stress, and may be regulated directly via an oxidative-mediated mechanism.



Conclusion: We present preliminary findings that suggest an important role of a bacterial pathogen acyl-CoA dehydrogenase, FadE2, in mediating protection during oxidative stress. We further propose that FadE2 may be modified directly via oxidation. Ultimately, the activity and regulation of FadE2 impacts the host at the level of the UPRmt stress response, which limits its survival during infection.