

Integrated Multi-Omic data analysis and validation with yeast model show oxidative phosphorylation modulate protein aggregation in Amyotrophic Lateral Sclerosis

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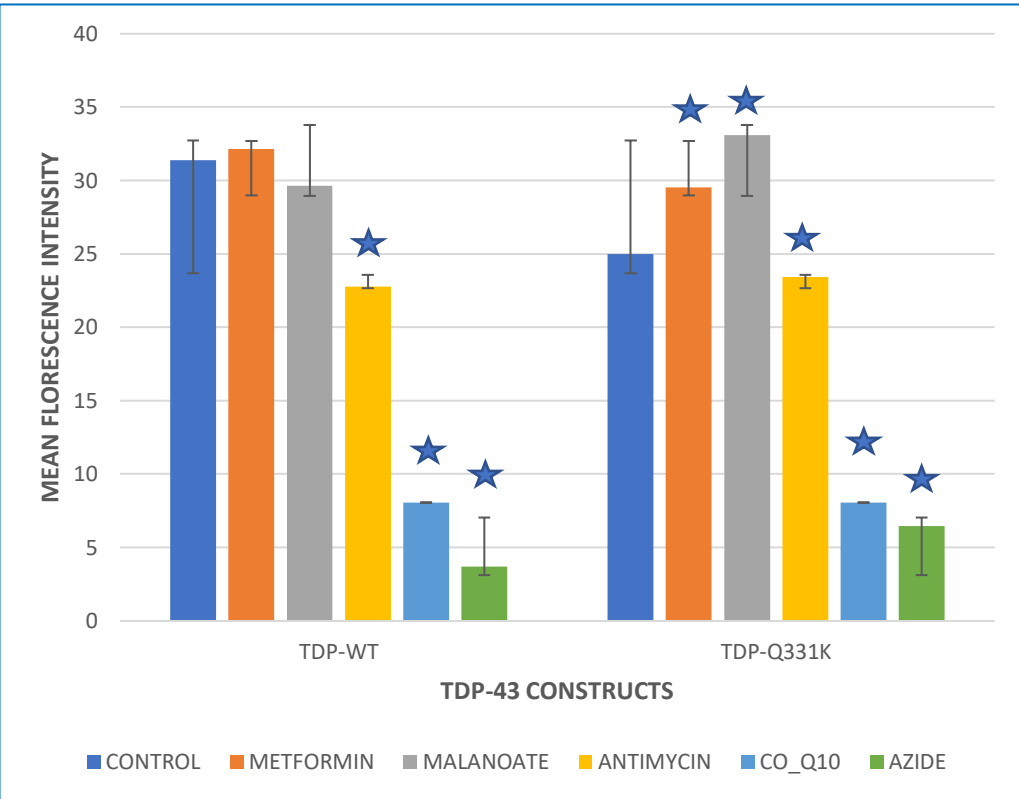
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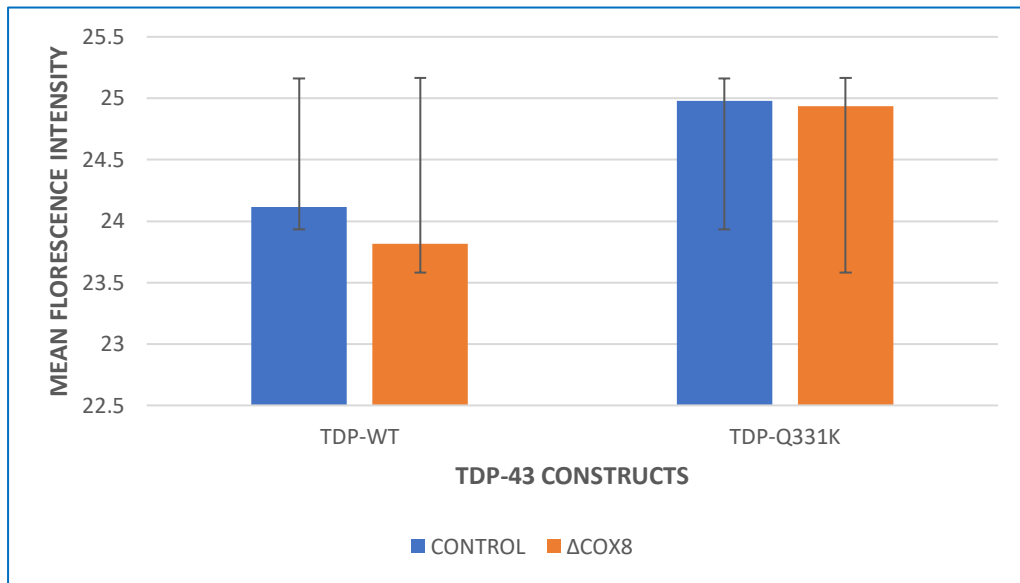
Key words: Systems Analysis, ALS, SOD1, FUS, TDP-43, Transcriptomics, Oxidative Phosphorylation, Mitochondrial Dys-function



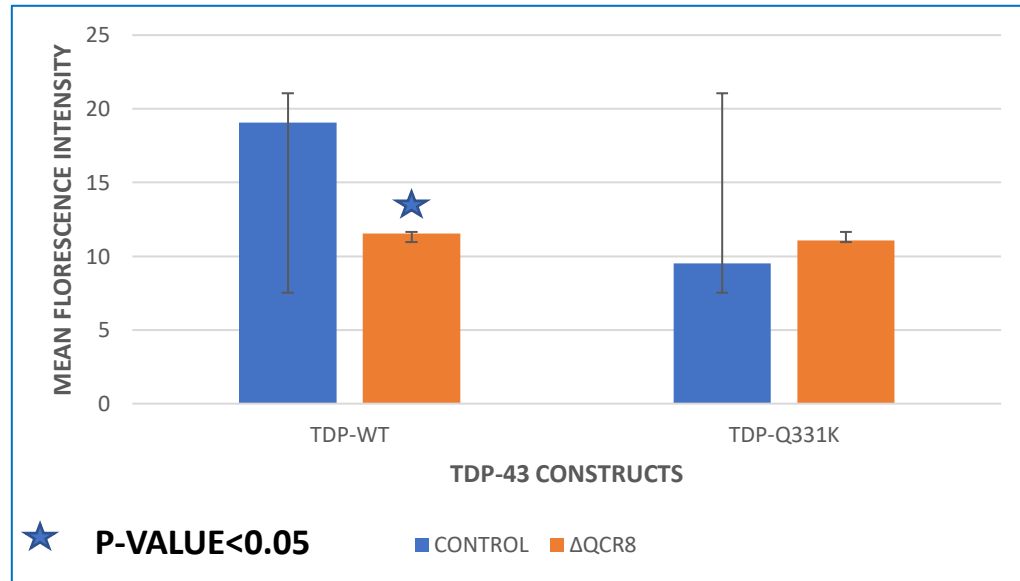
★ P-VALUE<0.05

CONDITION	TDP-WT-YFP		TDP-Q331K-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	31.390754		24.99937527	
METFORMIN (COMPLEX-I INHIBITOR)	32.15759	0.473164777	29.52789205	1.33175E-05
MALANOATE (COMPLEX-II INHIBITOR)	29.651584	0.146940429	33.07909776	9.14039E-05
ANTIMYCIN (COMPLEX-III INHIBITOR)	22.785517	5.06181E-06	23.43998771	0.009415651
CO-ENZYME Q ₁₀ (COMPLEX-III MODULATOR)	8.0400624	2.92105E-08	8.040062387	7.6214E-08
AZIDE (COMPLEX-IV INHIBITOR)	3.6834153	8.28004E-11	6.462695801	2.59137E-09

SUPPLEMENTARY FIGURE-2A: GRAPH REPRESENTING RESULTS OBTAINED FROM FLORESCENCE QUANTIFICATION OF TDP-43 TRANSFORMED YEAST CELLS TREATED WITH DIFFERENT MITOCHONDRIAL INHIBITORS.

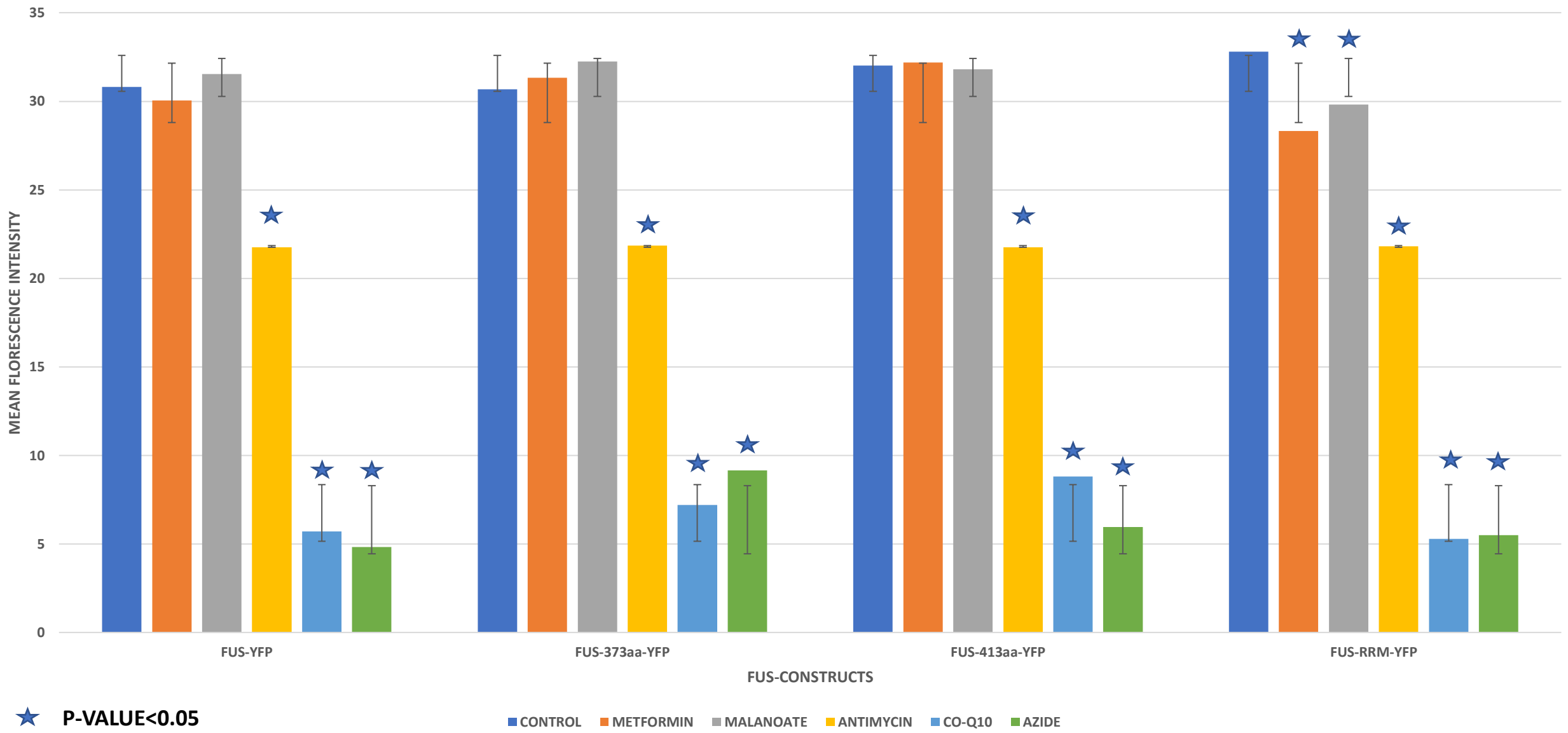


CONDITION	TDP-WT-YFP		TDP-Q331K-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	24.11395013		24.98033669	
ΔCOX8	23.81352833	0.747454	24.93348764	0.939422



CONDITION	TDP-WT-YFP		TDP-Q331K-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	19.08494		9.52045	
ΔQCR8	11.5587	0.007299	11.06827	0.487024

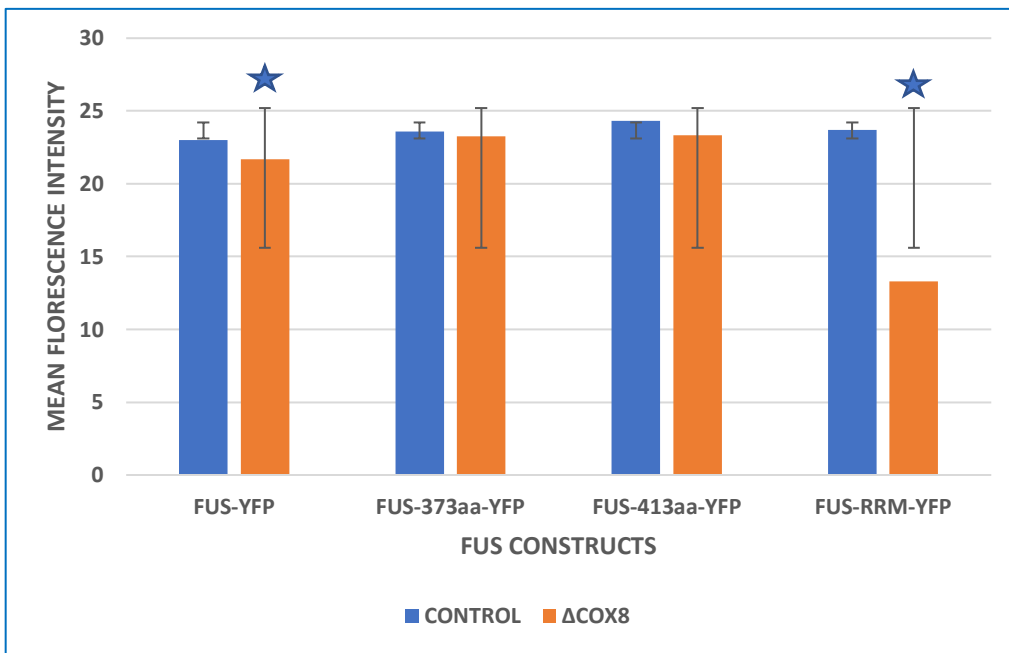
SUPPLEMENTARY FIGURE-2B: GRAPHS REPRESENTING RESULTS OBTAINED FROM FLORESCENCE QUANTIFICATION OF TDP-43 TRANSFORMED YEAST KNOCK-OUTS OF COX8 AND QCR8.



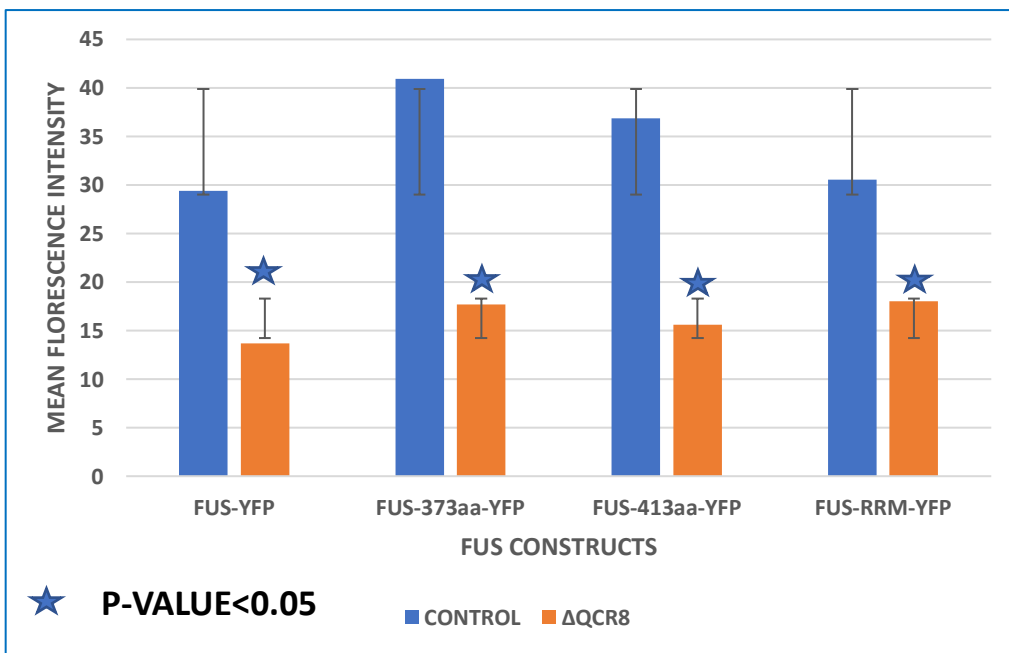
SUPPLEMENTARY FIGURE-2C: GRAPH REPRESENTING RESULTS OBTAINED FROM FLORESCENCE QUANTIFICATION OF FUS TRANSFORMED YEAST CELLS TREATED WITH DIFFERENT MITOCHONDRIAL INHIBITORS.

CONDITION	FUS-YFP		FUS-373aa-YFP		FUS-413aa-YFP		FUS-RRM-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	30.80894028		30.68367544		32.02187357		32.80759026	
METFORMIN (COMPLEX-I INHIBITOR)	30.04716245	0.667857356	31.33050623	0.749411719	32.20069529	0.831349798	28.33162029	0.004535833
MALANOATE (COMPLEX-II INHIBITOR)	31.53803457	0.751397756	32.25896932	0.427844224	31.8171661	0.730686952	29.81050558	0.020781162
ANTIMYCIN (COMPLEX-III INHIBITOR)	21.75765695	3.17953E-05	21.85716813	0.000139927	21.75807525	4.5769E-08	21.81850342	3.83468E-06
CO-ENZYME Q ₁₀ (COMPLEX-III MODULATOR)	5.70342673	6.731E-08	7.194835111	2.18976E-07	8.806479802	1.4776E-07	5.285956248	3.80501E-08
AZIDE (COMPLEX-IV INHIBITOR)	4.831598448	1.38991E-08	9.1606332	5.10418E-06	5.954019342	2.39987E-09	5.495334774	9.36801E-08

SUPPLEMENTARY FIGURE-2D: TABLE REPRESENTING RESULTS OBTAINED FROM FLORESCENCE QUANTIFICATION OF FUS TRANSFORMED YEAST CELLS TREATED WITH DIFFERENT MITOCHONDRIAL INHIBITORS.



CONDITION	FUS-YFP		FUS-373aa-YFP		FUS-413aa-YFP		FUS-RRM-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	22.98053934		23.59071948		24.3247818		23.7040334	
ΔCOX8	22.98053934	0.001478902	23.59071948	0.50320515	24.3247818	0.13499719	23.7040334	6.38765E-05



CONDITION	FUS-YFP		FUS-373aa-YFP		FUS-413aa-YFP		FUS-RRM-YFP	
	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)	MEAN FLORESCENCE INTENSITY	SIGNIFICANCE (P-VALUE)
CONTROL	29.37490776		40.92742736		36.8824770		30.5248526	
ΔQCR8	13.70909795	0.00124564	17.7049148	1.42025E-05	15.6181715	2.43201E-05	18.0381337	0.00051122

SUPPLEMENTARY FIGURE-2E: GRAPHS REPRESENTING RESULTS OBTAINED FROM FLORESCENCE QUANTIFICATION OF FUS TRANSFORMED YEAST KNOCK-OUTS OF COX8 AND QCR8.