

# mTOR inhibitor GDC-0349 improves ASO induced SAMMSON knock down resulting in enhanced anti-tumor efficacy in uveal melanoma

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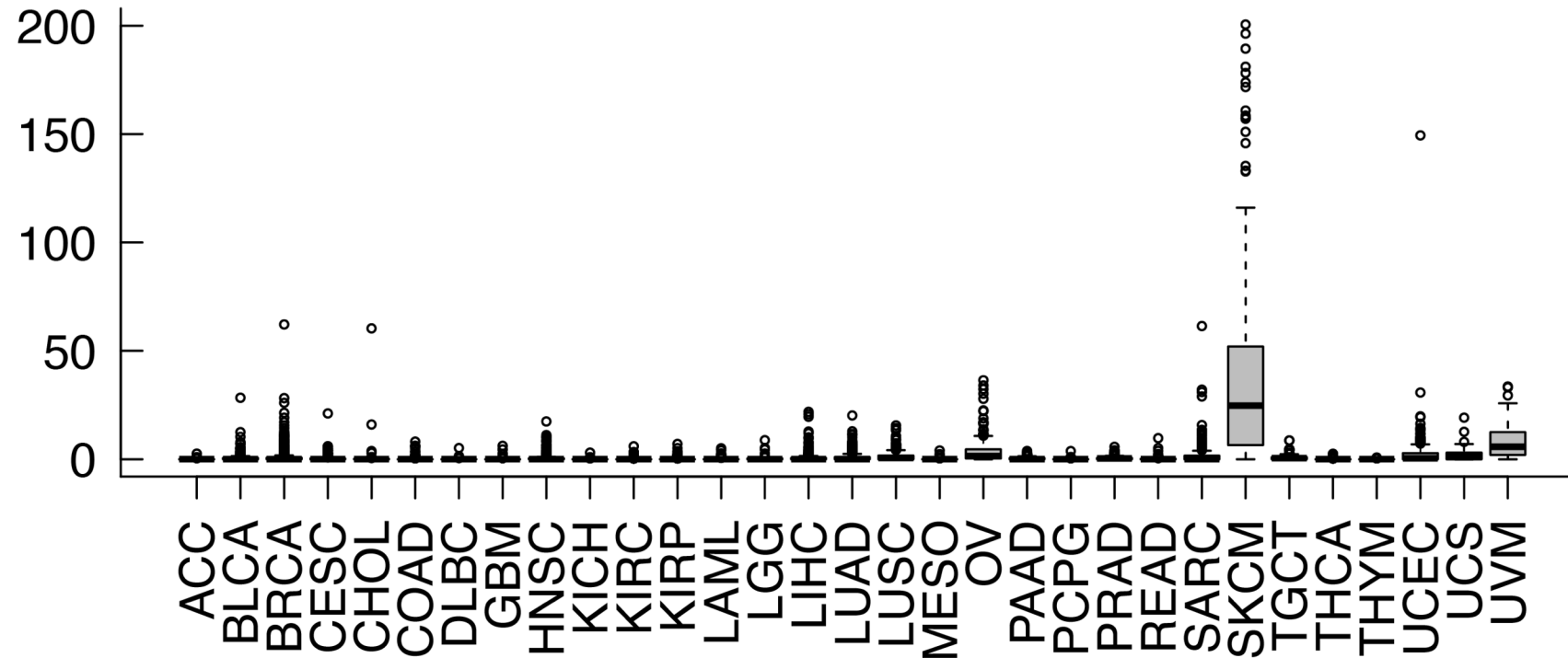


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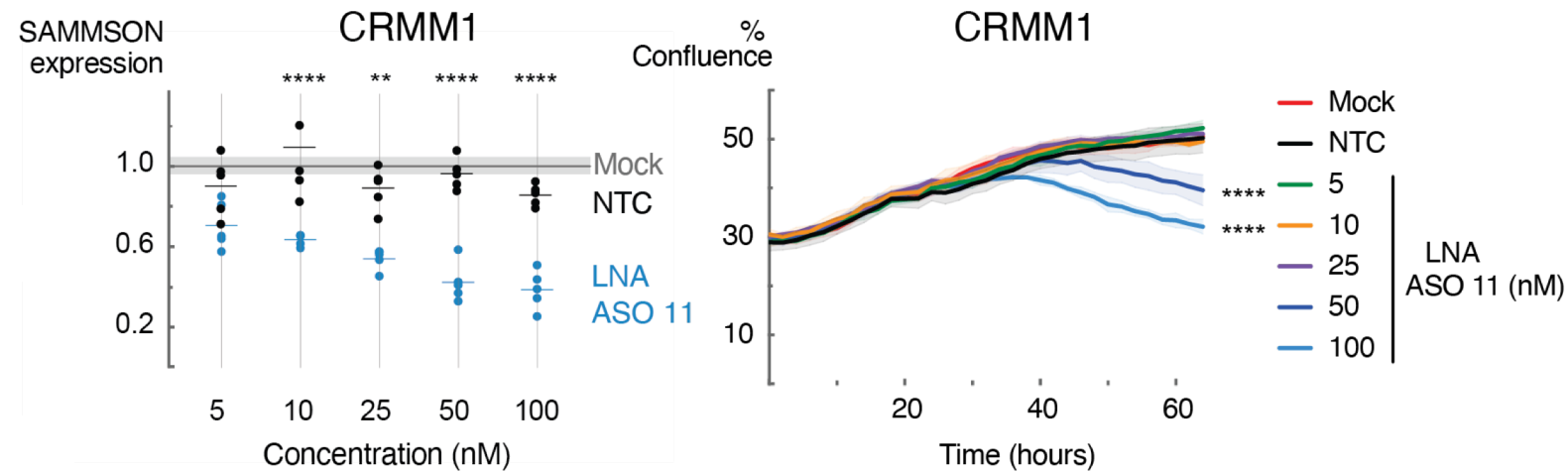
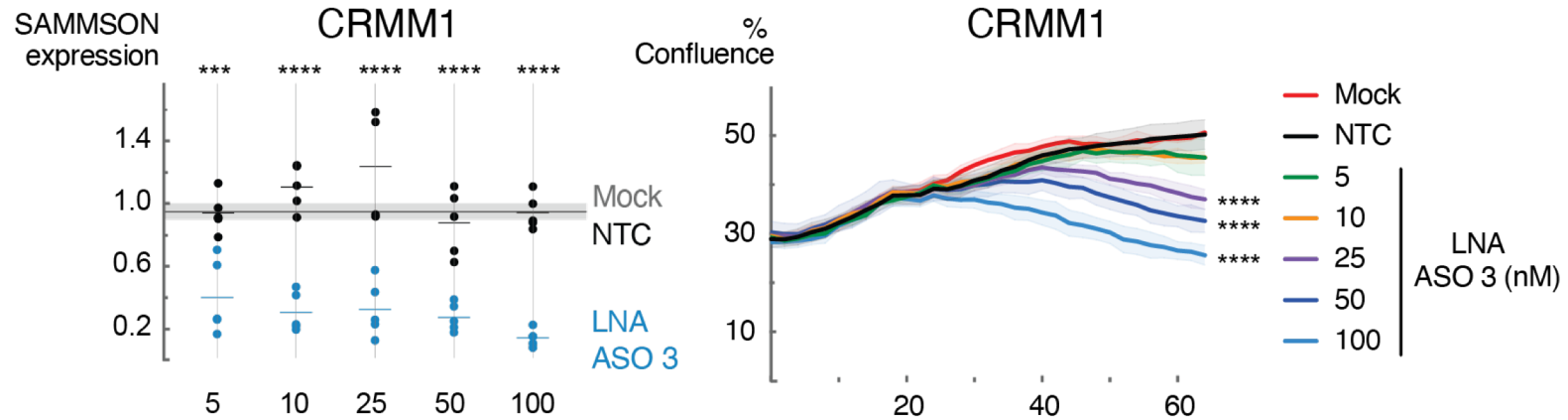


# SAMMSON lncRNA expression in uveal melanoma tumors

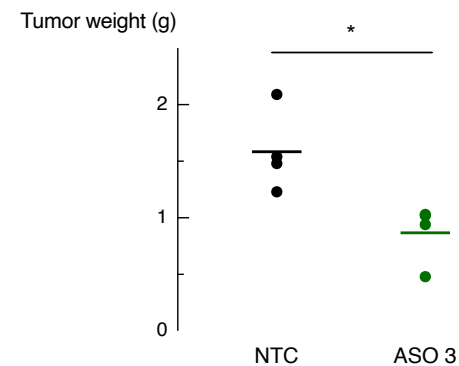
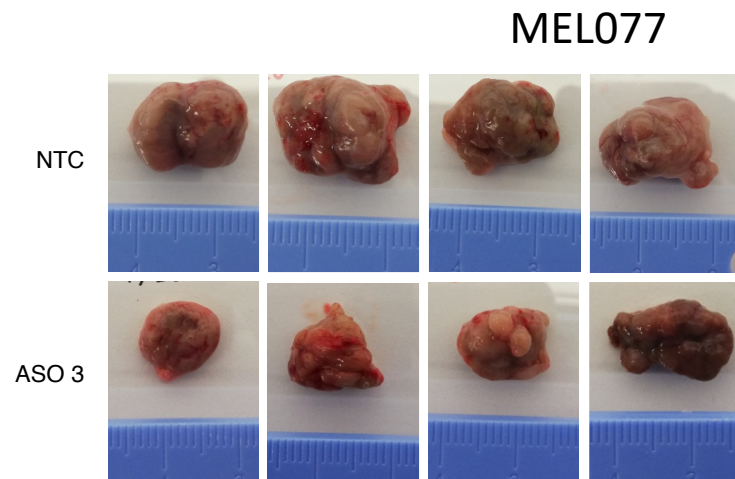
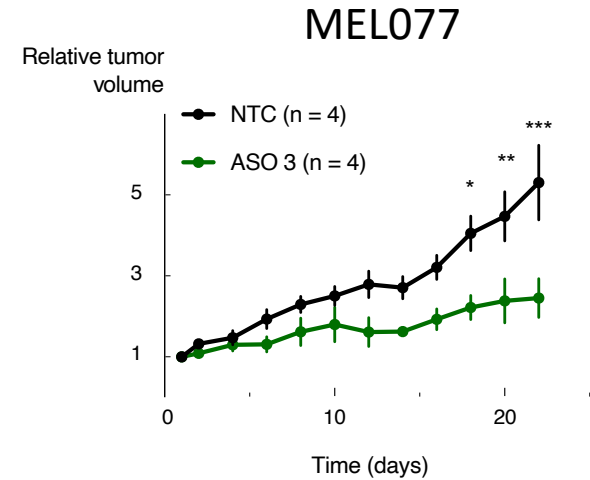
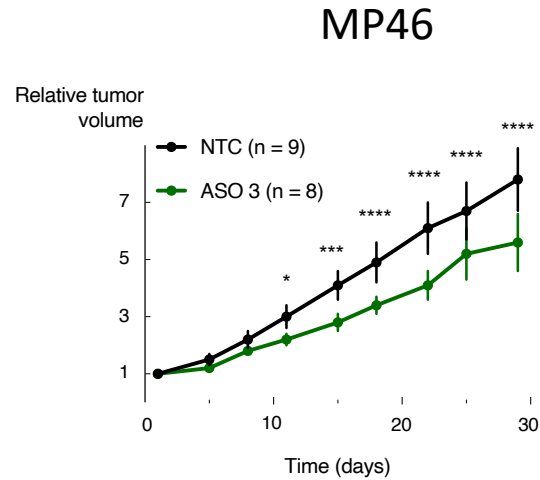
Relative SAMMSON expression



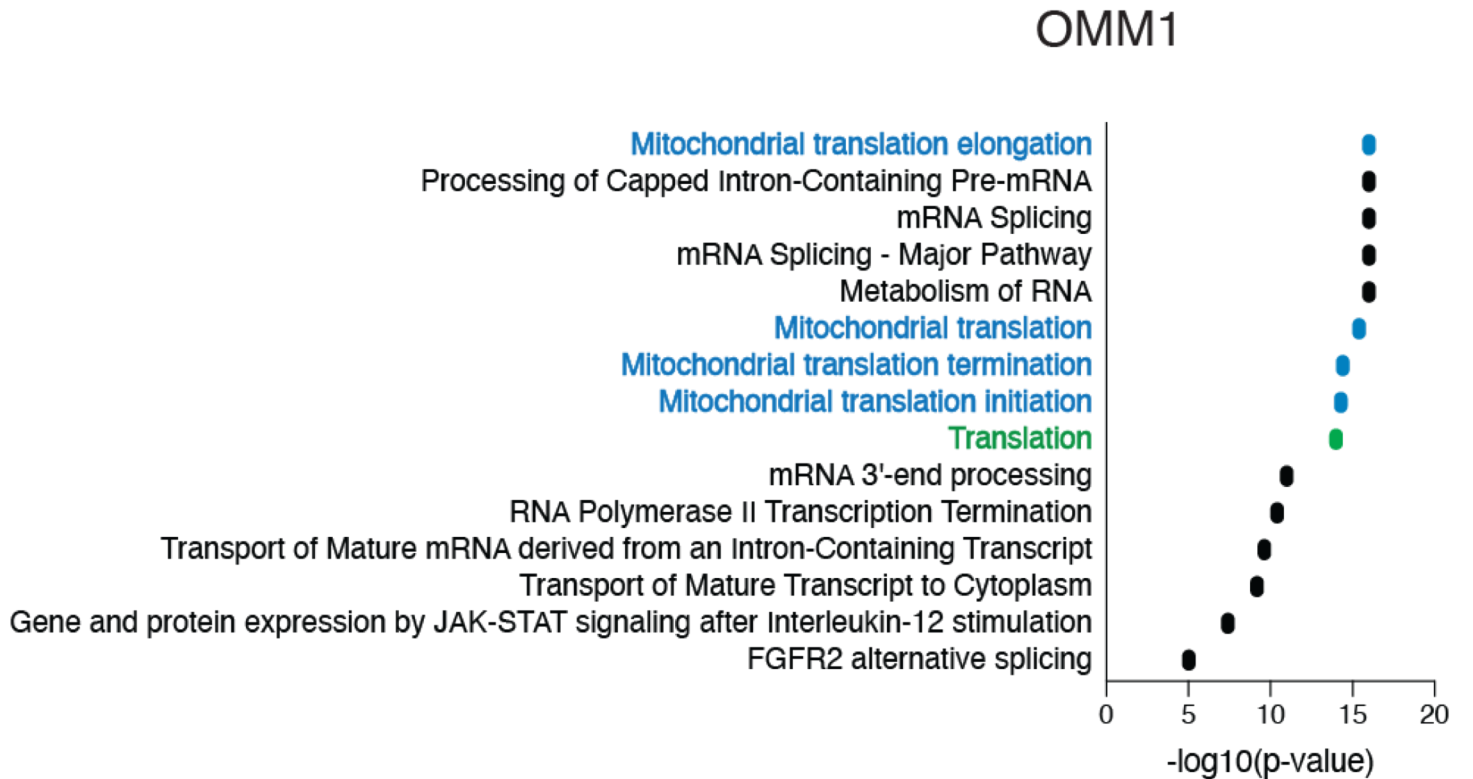
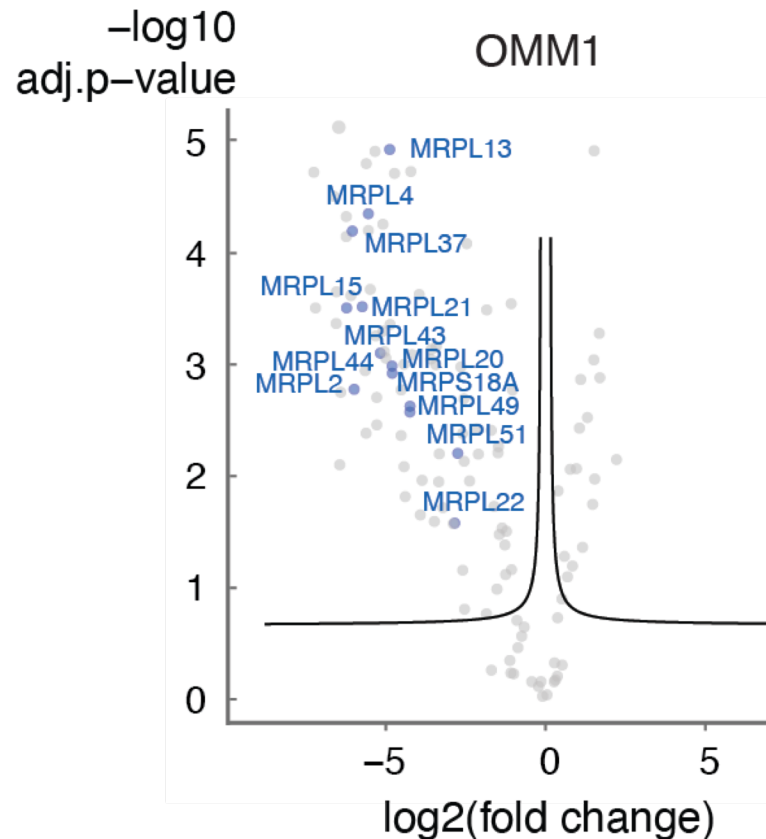
# SAMMSON knock down upon ASO treatment



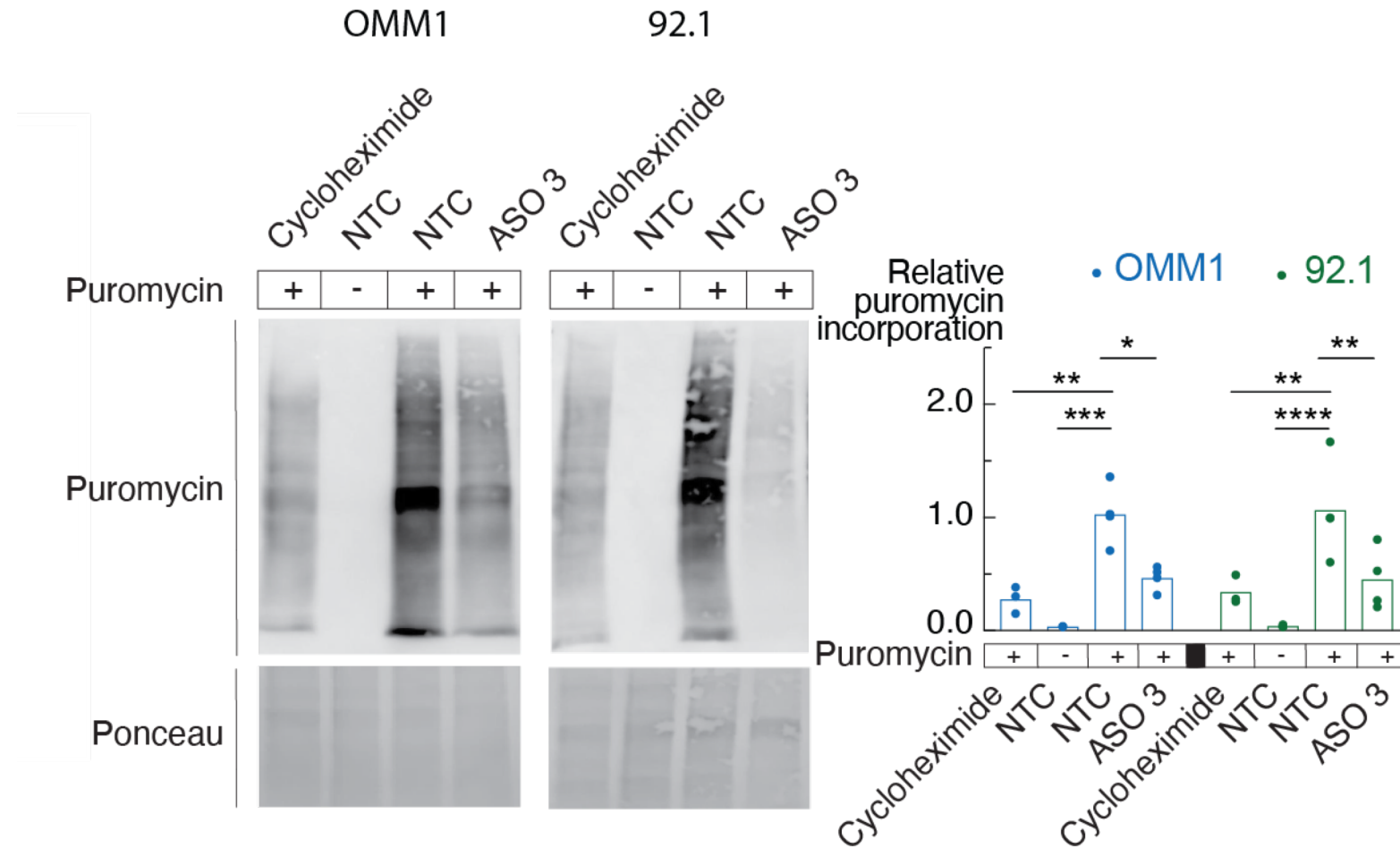
# Reduced tumor growth upon SAMMSON inhibition



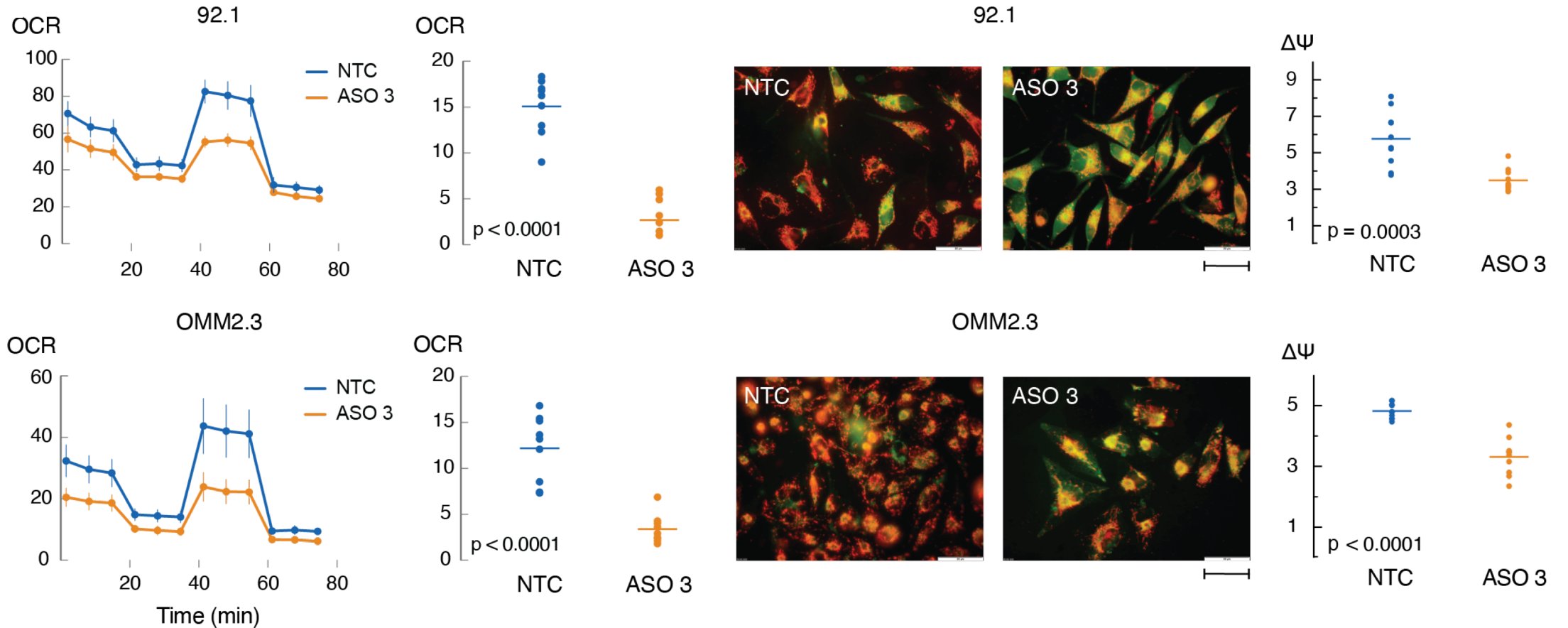
# Mitochondrial proteins involved in translation as SAMMSON interaction partners



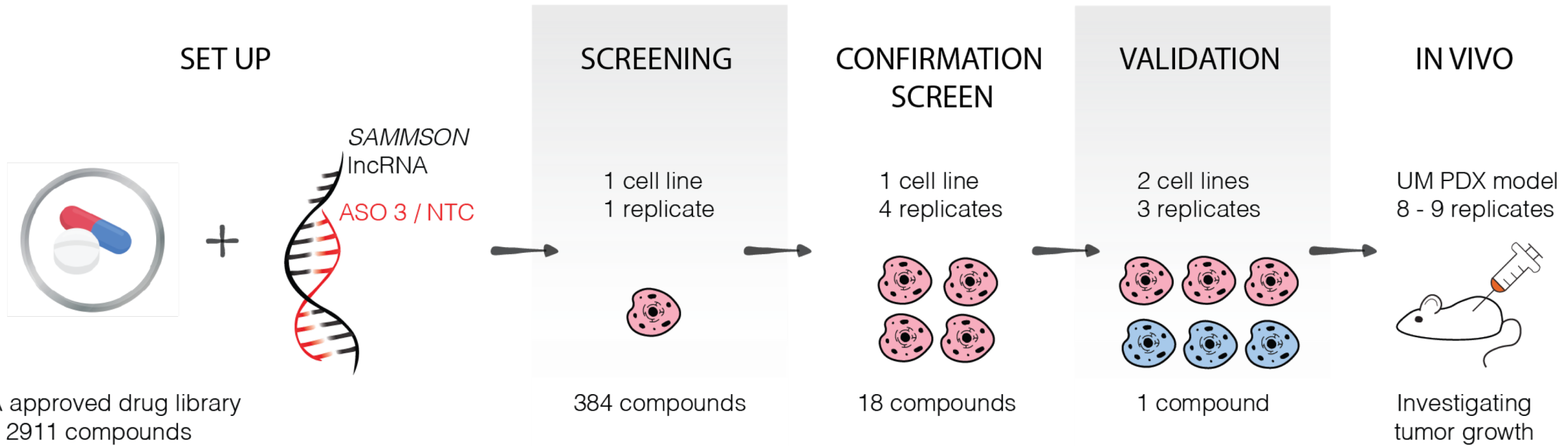
# SAMMSON knock down affects translation



# And consequently impacts mitochondrial function



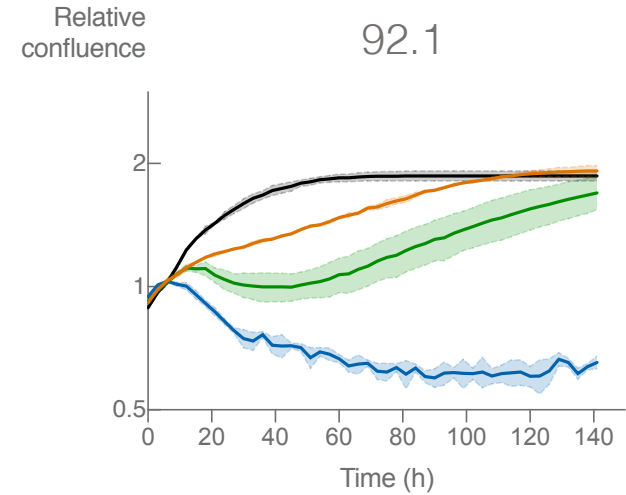
# Drug screen to identify synergistic compounds



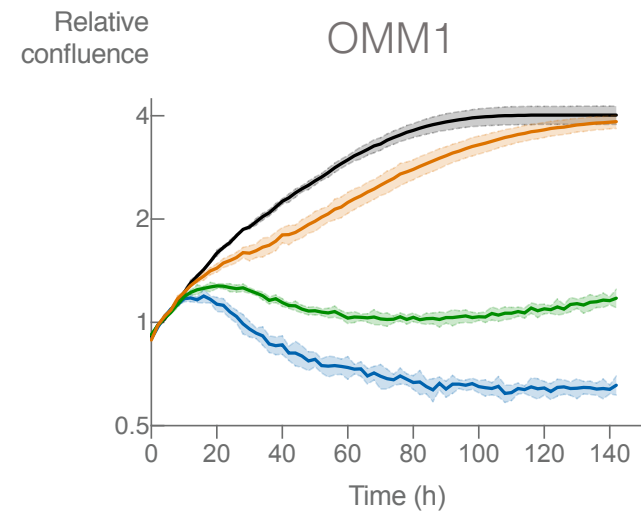


# mTOR inhibitor GDC-0349

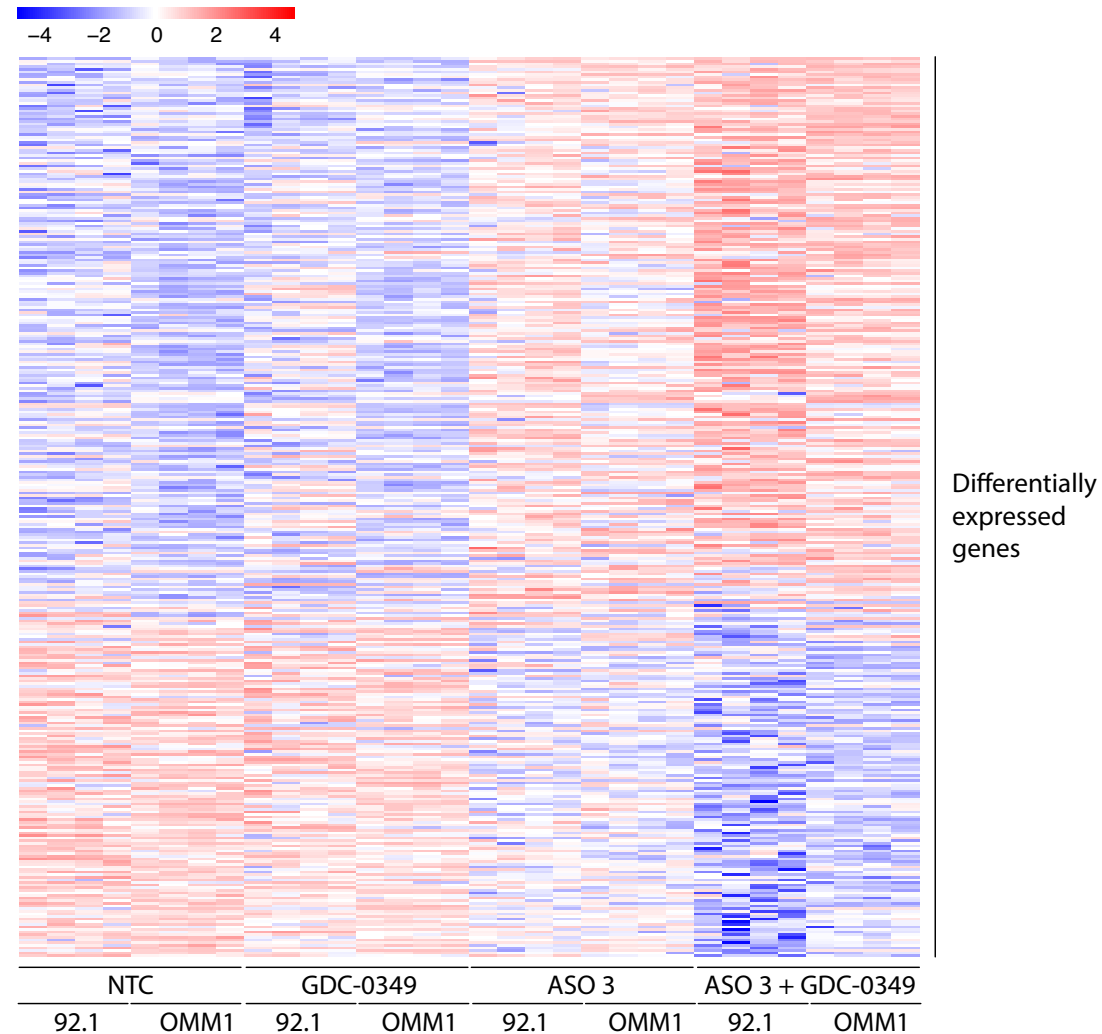
% Viability	92.1					OMM1				
	GDC-0349 ( $\mu\text{M}$ )					GDC-0349 ( $\mu\text{M}$ )				
	0	0.625	1.25	2.5	5	0	0.625	1.25	2.5	5
ASO 3 (nM) 0	100	50	33	19	11	100	60	40	27	13
ASO 3 (nM) 50	54	8	4	3	3	40	8	5	2	1



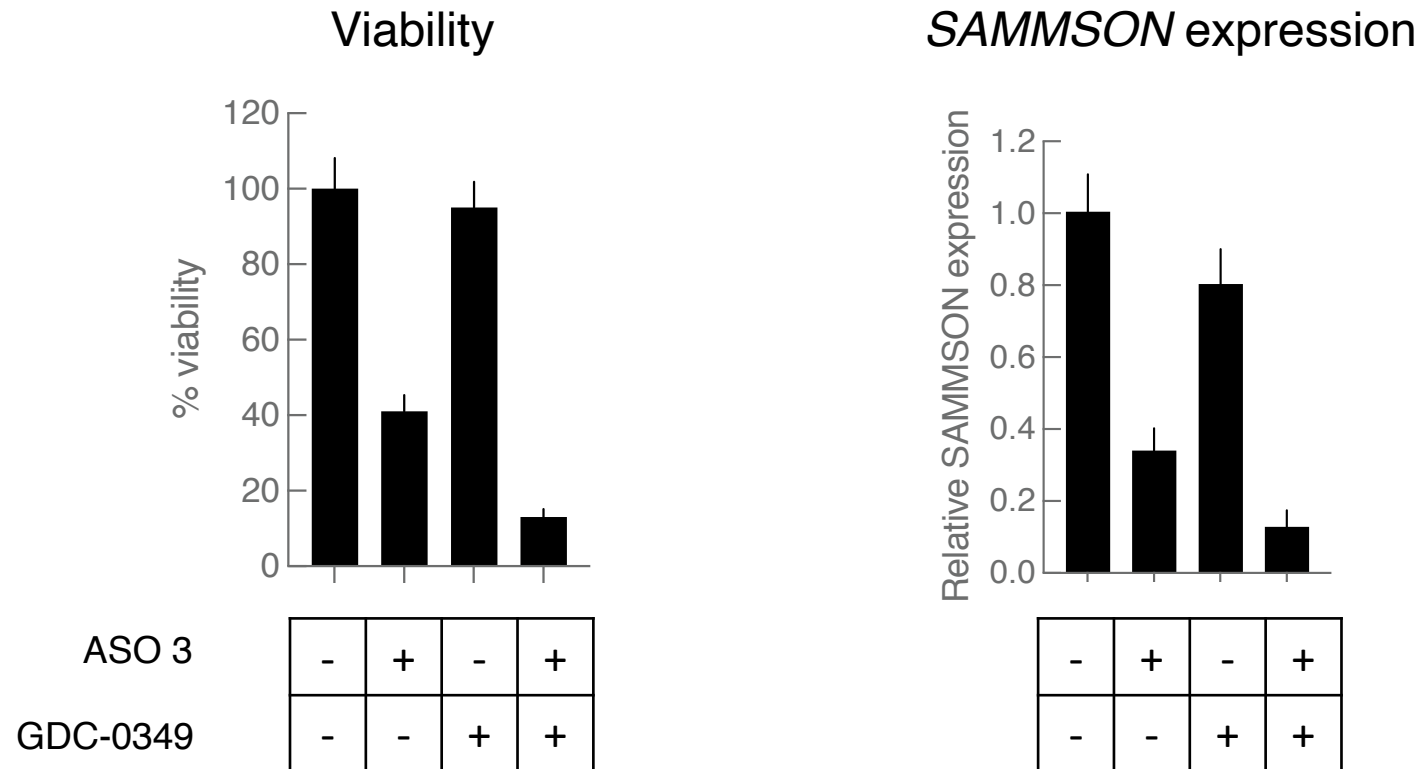
- GDC-0349 0,625  $\mu\text{M}$
- ASO 3 50 nM
- NTC 50 nM
- ASO 3 50 nM + GDC-0349 0,625  $\mu\text{M}$



# Gene expression changes induced by SAMMSON knock down enhanced in the combined treatment



# Combination with mTORi improves SAMMSON knock down



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# **A novel and translational role for autophagy in antisense oligonucleotide trafficking and activity**

**Joseph Ochaba, Andrew F. Powers, Kaitlyn A. Tremble, Sarah Greenlee, Noah M. Post, John E. Matson, A. Robert MacLeod, Shuling Guo and Mariam Aghajan\***

# Conclusions

- SAMMSON inhibition
  - translation and mitochondrial function
  - Promising therapeutic strategy
- Combination with GDC-0349
  - increased SAMMSON knock down

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