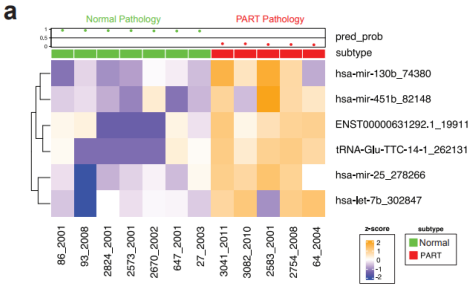
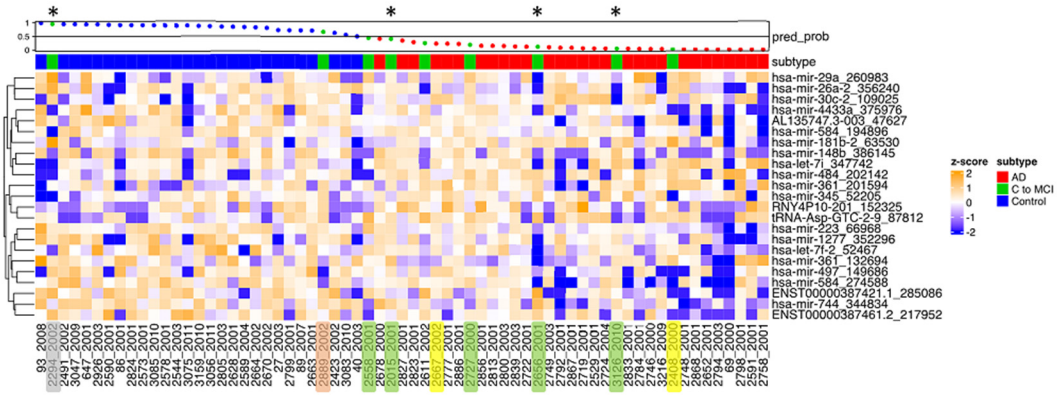


b

Initial clinical DX	Disease progression	Sample number	Years to disease progression (mean ± SD)	Post mortem DX available (n=)	Years to post-mortem DX (mean ± SD)	Primary post mortem DX (*mean Braak score, if available*)
Control	none	46	-	17	10.96 ± 5.27	Normal n=7 (*1.4*), PART n=5 (*3*), AD n=5 (*3*)
	→ MCI	9	5.22 ± 3.19	4	9.18 ± 5.86	AD n=4 (*4.3*)
	→ AD	6	6.17 ± 4.22	3	8.05 ± 2.16	AD n=3 (*6*)
MCI	none	13	-	3	9.47 ± 3.19	AD n=3 (*3.7*)
	→ AD	8	1.88 ± 0.99	4	8.24 ± 1.57	AD n=2 (*6*), DLB n=1 (*1*), PART n=1 (*3*)
	→ DLB	3	5.67 ± 4.73	2	5.69 ± 0.65	AD and DLB n=2 (*1*)
AD	none	32	-	23	8.12 ± 5.03	AD, n=20 (*5.8*), DLB n=1 (*1*), FTD-TDP n=1 (*0*), vascular dementia n=1 (*1*)

Supplementary Figure S1. ELNET modeling to distinguish between different groups based on post mortem pathology findings. (**a**) ELNET model comparing control individuals with normal pathology vs. control individuals with PART pathology using 6 exRNAs can distinguish between groups with 100% accuracy. (**b**) Overview of the new sample groups after model-based trimming, and exclusion of participants with non-AD pathology. Waterfall plot across the top of the heatmap demonstrates ELNET model confidence in assigning groups (0 to 1, with 0.5 being no confidence in assignment), with dots colored to the diagnosis group.



Supplementary Figure S2. ELNET model distinguishing control and AD participants predicts con-version in the control group. The ELNET model between control and AD groups is used to exam-ine the C to MCI converters. Two converters are identified as AD by both the control vs. MCI and control vs. AD models (highlighted yellow), while four are identified by the AD model exclusively (highlighted green). One participant is not marked as disease associated by either MCI or AD model (highlighted gray), while another is only categorized in the disease group by the MCI model (highlighted orange). Asterisks indicate a confirmed post-mortem AD diagnosis at autopsy and waterfall plot across the top of the heatmap demonstrates ELNET model confidence in assign-ing groups (0 to 1, with 0.5 being no confidence in assignment), with dots colored to the diagnosis group.