Supporting method

Table S1: Inclusion and exclusion criteria of selecting AD patients and normal controls.

	Inclusion criteria	Exclusion criteria
AD patients	Malaysia citizen	Patients under palliative care for other diseases
	65 years old and above	Diagnosed with vascular dementia; Lewy Body dementia; Parkinson's disease dementia; Frontotemporal dementia; Creutzfeldt-Jakob disease; Wernicke-Korsakoff syndrome; Normal pressure hydrocephalus; Huntington's disease; Down-syndrome dementia.
	Symptoms of memory deterioration worsened with time	
	Symptoms of losing the ability to perform daily function	
	Diagnosed with AD for more than 2 months	
	Mini-Mental State Examination (MMSE) $\leqslant$ 24	
Normal controls	Malaysia citizen	Patients under palliative care for other diseases
	65 years old and above	Diagnosed with AD/ any other type of dementia
	Does not show symptoms of memory deterioration which have worsened with time	Diagnosed with a known significant (in the view of the investigator) concurrent medical disease
	Does not show symptoms of losing the ability to perform daily function	
	Mini-Mental State Examination (MMSE) $\geqslant$ 25	

Table S2: Subject details and their corresponding ID used in this study.

Sample ID	Patient/ Control	Gender	Age*	Ethnicity	Cognitive score
AD1	Patient	Male	84	Malay	$\leqslant$ 24
AD2	Patient	Male	75	Malay	$\leqslant$ 24
AD3	Patient	Female	75	Chinese	$\leqslant$ 24
AD4	Patient	Female	74	Chinese	$\leqslant$ 24
AD5	Patient	Female	75	Chinese	$\leqslant$ 24
AD6	Patient	Male	70	Chinese	$\leqslant$ 24
AD7	Patient	Male	75	Chinese	$\leqslant$ 24
AD8	Patient	Female	86	Malay	$\leqslant$ 24
Ctrl1	Control	Female	78	Malay	$\geqslant$ 25
Ctrl2	Control	Male	74	Malay	$\geqslant$ 25
Ctrl3	Control	Male	73	Chinese	$\geqslant$ 25
Ctrl4	Control	Female	84	Chinese	$\geqslant$ 25

Noted: *Age of subjects at the year of recruitment.

Sample preparation

1. Prepare 750µl RiboExTM LS in a 1.5ml microcentrifuge tube.

2. Add 250µl blood sample to the 1.5ml microcentrifuge tube and vortex vigorously.

3. Incubate 2min at room temperature to allows leukocytes to completely be collapsed.

4. Add 0.2ml of chloroform. Shake vigorously for 15sec and let it stand for 2min at room temperature.

5. Centrifuge at 12,000 x g for 15min at 4°C. The mixture will be separated into three phases; a lower layer, an interphase, and a colorless upper aqueous layer. The upper aqueous volume is about 450µl.

6. Transfer the aqueous phase (approximately 450ul) to a EzPureTM filter. Small amount of DNA and other blood contaminants are eliminated by EzPureTM filter.

7. Centrifuge at ≥ 10,000 x g for 30sec at room temperature.

8. Add 2 volume (~900µl) of buffer RB1 to the collection tube including passed-through and mix well by pipetting.

9. Transfer up to 700µl of the mixture to a mini spin column.

10. Centrifuge at ≥ 10,000 x g for 30sec at room temperature. Discard the passed-through and reinsert the mini spin column back into the same tube.

11. Repeat step 9 ~ 10 using the remainder of the sample.

12. Add 500µl of buffer RBW to the mini spin column.

13. Centrifuge at ≥ 10,000 x g for 30sec at room temperature. Discard the passed-through and reinsert the mini spin column back into the same tube.

14. Add 500µl of buffer RNW to the mini spin column.

15. Centrifuge at ≥ 10,000 x g for 30sec at room temperature. Discard the passed-through and reinsert the mini spin column back into the same tube.

16. Centrifuge at ≥ 10,000 x g for an additional 1min at room temperature to remove residual wash buffer. Transfer the mini spin column to a new 1.5ml microcentrifuge tube.

17. Add 30µl of RNase-free water to the center of the membrane in the mini spin column and incubate for 3 min.

18. Centrifuge at ≥ 10,000 x g for 1min at room temperature.

19. Measure quantity and purity using Nanodrop.

Kits information

1) RNA extraction kit: GeneAll HybridRTM Blood RNA Kit (Catalogue No. 305-101)
2) Library prep kit: NEXTflex Illumina Small RNA Sequencing Kit v3 (Catalogue No. NOVA-5132-06)