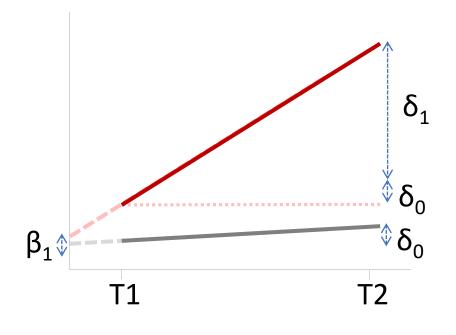
	Analysis	Annotation	Expression
1.		Reference genome	RNA-Seq reads (WT = 29 , TG = 30)
2.		Iso-Seq defined transcriptome $(n = 12)$	RNA-Seq reads (WT = 29 , TG = 30)
3.		Iso-Seq defined transcriptome $(n = 12)$	Iso-Seq reads $(WT = 6, TG = 6)$



Inference from regression coefficients

 $\beta_{\,\scriptscriptstyle 1}:$ WT vs TG at T1 δ_0 : WT over time δ_1 : WT vs TG over time

Model	β_1 CasevsControl	δ ₀ Time	δ_1 TimexCase	Condition	Effects
1	✓	X	X		Genotype
2	✓	✓	X		Genotype + Age
3	X	√	X		Age
4	X	√	✓		Interaction
5	✓	X	√		Interaction
6	X	X	✓		Interaction
7	✓	√	√		Interaction

	Differential Gene Expression	Differential Isoform Usage	Major isoform switching	Condition		
1	✓	√	✓	Gene Counts Soform Counts	/T TG	
2	✓	✓	X	Gene Counts Soform Counts	VT TG	
3	X	√	✓	Gene form	VT TG	
4	X	√	X	form	VT TG	

Isoform	Associated Gene	Structural Category	Associated Transcript	Length	FL Sample 1	FL Sample 2
PB.1.1	Gene 1	FSM	ENMUST1	3000	10	10
PB.1.2	Gene 1	ISM	ENMUST1	1500	100	90
PB.1.3	Gene 1	ISM	ENMUST2	2400	20	20
PB.1.4	Gene 1	ISM	ENMUST3	2900	5	4
PB.1.5	Gene 1	ISM	ENMUST3	2190	5	2
PB.1.6	Gene 1	ISM	ENMUST4	1250	1	0



Isoform	Associated Gene	Structural Category	Associated Transcript	Length	FL Sample 1	FL Sample 2
PB.1.1	Gene 1	FSM	ENMUST1	3000	110	100
PB.1.3	Gene 1	ISM	ENMUST2	2400	20	20
PB.1.4	Gene 1	ISM	ENMUST3	2900	10	6

Lipid Homeostasis

Apoe, Abca7, Abca1

Immune Response

Trem2, Cd33, Ptk2b

Bin1

Rhbdf2

Synaptic Signalling

Trpa1, Vgf

Endocytosis

Clu

Picalm, Sorl1

EWAS

Ank1

Pathology

Amyloid : App
Tau : Mant Eyn

FTD: Fus

TDP-43 : Tardbp

Tau : Mapt, Fyn α-synuclein : Snca

