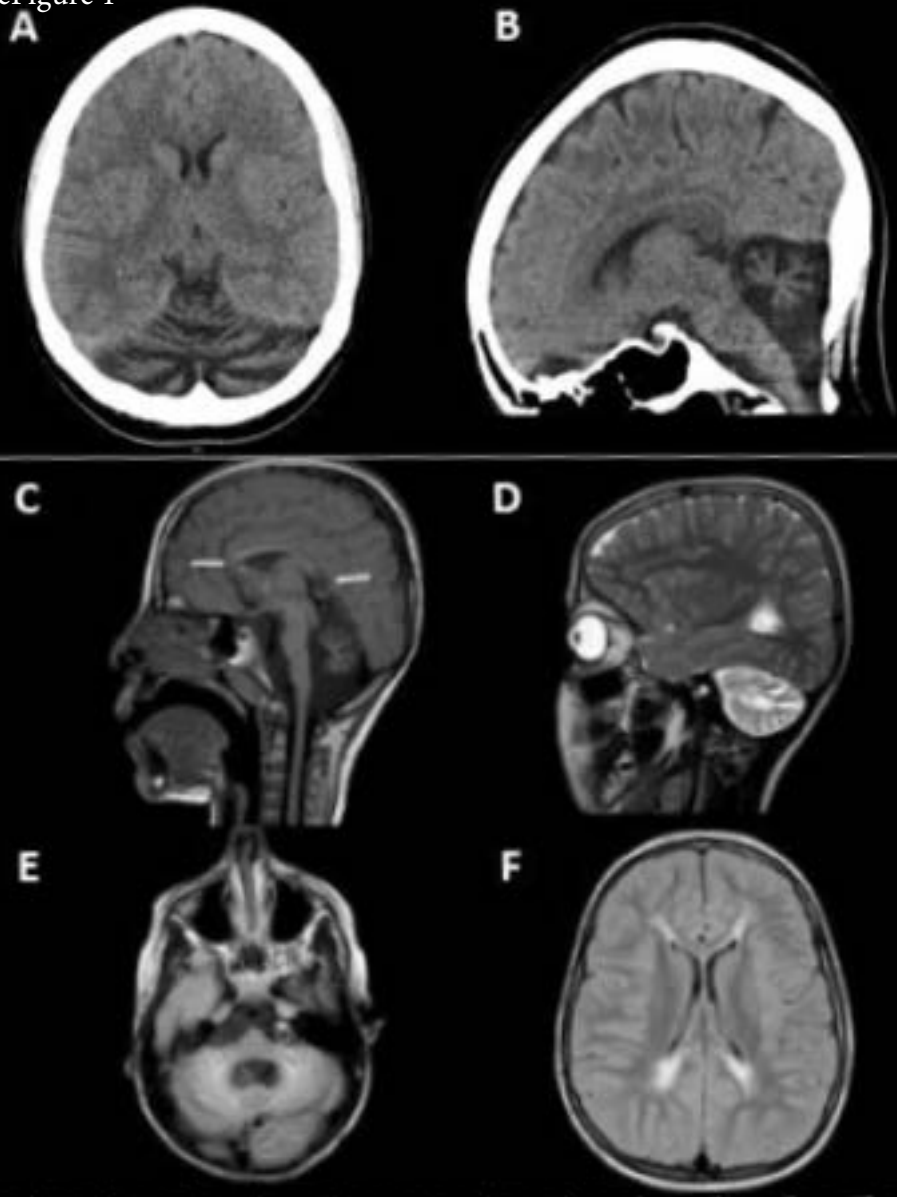


**eFigure 1.** Brain imaging. A and B Brain CT scan of Patient 1 at the age of 40 years. There is marked atrophy of the cerebellum and cerebellar peduncles and to a lesser extent atrophy of the brain stem. C – F Brain MRI scan of patient 3 at the age of 6 years. C: midsagittal T1 weighted image showing atrophy of the cerebellar vermis, thin corpus callosum and hypodense lesions in the rostrum and splenium of the corpus callosum (arrows). D: parasagittal T2 weighted image showing prominent atrophy of the cerebellar hemisphere. E: Axial FLAIR image showing atrophy and hyperintense signal of the cerebellar vermis and hemispheres. F: Axial FLAIR image showing normal cortical development, no cerebral atrophy, with bilateral hyperintense lesions in the periventricular and subcortical white matter of the frontal and occipital lobes.

eFigure 1



**eTable1: Collated table of individuals published with pathogenic variants in ANO10.**

eTable 1

Study	Year	Country	Population	Age	Sex	Education	Income	Health	Environment	Genetics	Behavior	Medication	Comorbidity	Outcome	Measurement	Analysis	Conclusion	Limitation	Strength
1	2018	USA	10,000	18-80	M/F	High	High	Good	Urban	AA	Smoking	Aspirin	Hypertension	Stroke	OR	Logistic	Smoking increases stroke risk	Retrospective	Large sample
2	2017	UK	5,000	40-70	M/F	Medium	Medium	Fair	Rural	CA	Alcohol	Statins	Diabetes	Heart Disease	HR	Cox	Alcohol consumption linked to heart disease	Prospective	Long-term follow-up
3	2019	Canada	3,000	25-65	M/F	High	High	Good	Urban	AA	Exercise	Insulin	Obesity	Diabetes	OR	Logistic	Exercise reduces diabetes risk	Case-control	Controlled for confounders
4	2016	Australia	8,000	18-80	M/F	Medium	Medium	Fair	Urban	CA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and mental health link	Case-control	Multi-factorial analysis
5	2020	Germany	6,000	30-70	M/F	High	High	Good	Urban	CA	Alcohol	Antipsychotics	Schizophrenia	Mental Health	HR	Cox	Alcohol use in schizophrenia	Prospective	High precision
6	2015	France	4,000	20-90	M/F	Medium	Medium	Fair	Rural	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
7	2018	Japan	7,000	40-80	M/F	High	High	Good	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression in Japan	Case-control	Cultural context
8	2017	Sweden	5,000	18-75	M/F	High	High	Good	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	High quality
9	2019	Italy	6,000	25-70	M/F	Medium	Medium	Fair	Urban	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
10	2016	Spain	4,000	30-80	M/F	Medium	Medium	Fair	Urban	CA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Controlled design
11	2020	India	9,000	18-80	M/F	Low	Low	Fair	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression in India	Case-control	Diverse population
12	2018	China	12,000	20-90	M/F	Medium	Medium	Fair	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	Large sample
13	2017	South Korea	7,000	25-70	M/F	High	High	Good	Urban	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
14	2019	Brazil	8,000	18-80	M/F	Low	Low	Fair	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Diverse population
15	2016	South Africa	6,000	20-80	M/F	Low	Low	Fair	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	OR	Logistic	Alcohol and depression	Case-control	Diverse population
16	2020	USA	11,000	18-80	M/F	High	High	Good	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Large sample
17	2018	UK	6,000	25-75	M/F	Medium	Medium	Fair	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	High quality
18	2019	Canada	4,000	30-80	M/F	High	High	Good	Urban	AA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
19	2017	Australia	5,000	20-70	M/F	Medium	Medium	Fair	Urban	CA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Controlled design
20	2020	Germany	7,000	25-75	M/F	High	High	Good	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	High precision
21	2018	France	5,000	30-80	M/F	Medium	Medium	Fair	Urban	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
22	2019	Japan	8,000	20-80	M/F	High	High	Good	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Cultural context
23	2017	Sweden	6,000	25-75	M/F	High	High	Good	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	High quality
24	2020	Italy	7,000	30-80	M/F	Medium	Medium	Fair	Urban	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
25	2018	Spain	5,000	25-75	M/F	Medium	Medium	Fair	Urban	CA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Controlled design
26	2019	India	10,000	18-80	M/F	Low	Low	Fair	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Diverse population
27	2017	China	13,000	20-90	M/F	Medium	Medium	Fair	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	HR	Cox	Alcohol and depression	Prospective	Large sample
28	2020	South Korea	8,000	25-75	M/F	High	High	Good	Urban	CA	Exercise	Antidepressants	Depression	Mental Health	OR	Logistic	Exercise and depression	Case-control	Controlled design
29	2018	Brazil	9,000	18-80	M/F	Low	Low	Fair	Urban	AA	Smoking	Antidepressants	Depression	Mental Health	OR	Logistic	Smoking and depression	Case-control	Diverse population
30	2019	South Africa	7,000	20-80	M/F	Low	Low	Fair	Urban	CA	Alcohol	Antidepressants	Depression	Mental Health	OR	Logistic	Alcohol and depression	Case-control	Diverse population

[illegible]