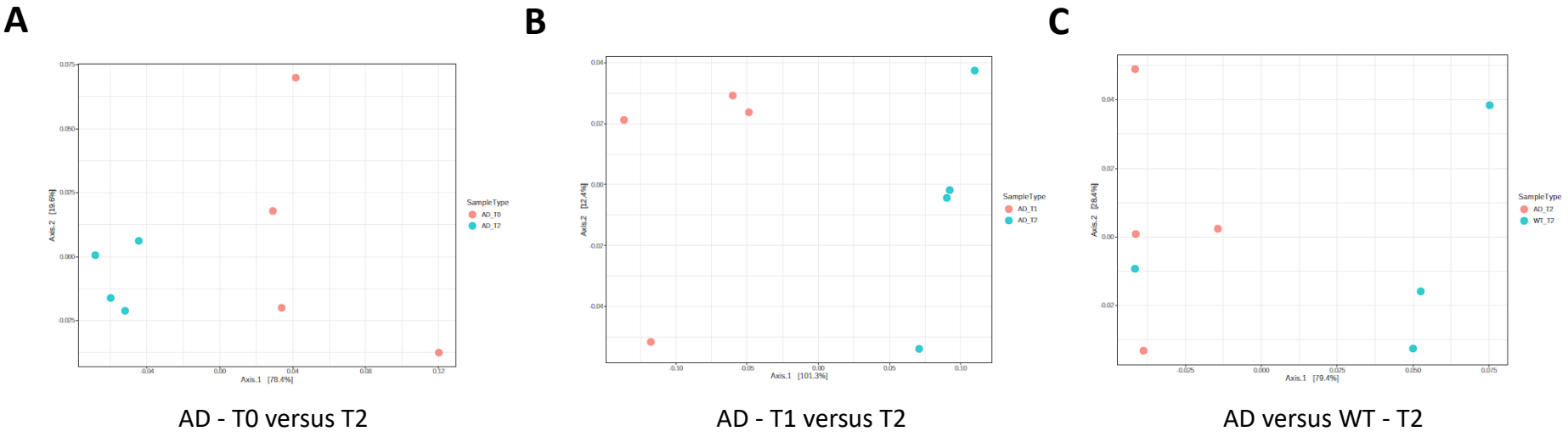
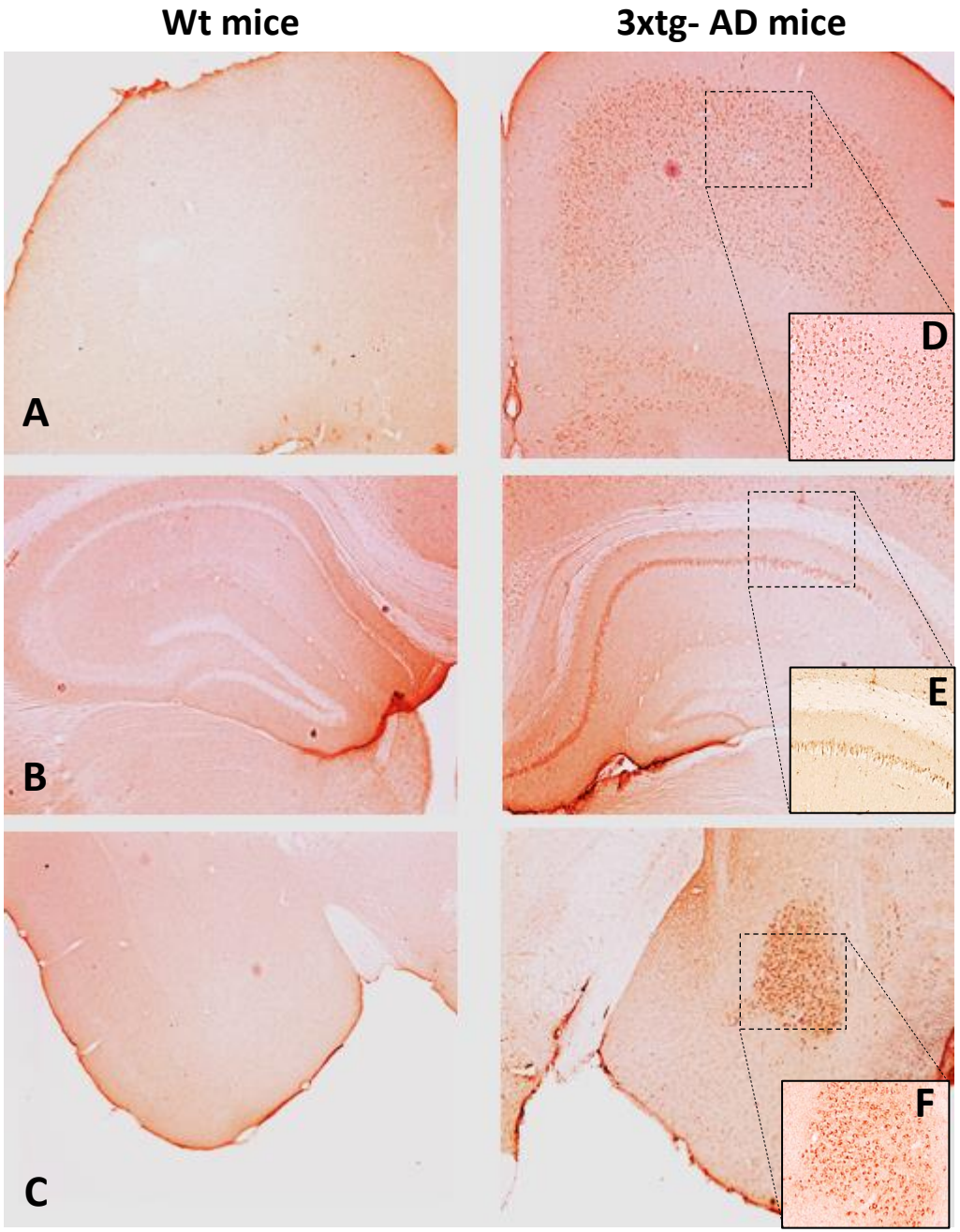


SUPPLEMENTARY FIGURE 1: AD progression drives global perturbations in microbiota. Differences at the genus taxonomic rank in mice stool microbiota between T2 and T0 time points (A), for AD samples; between T1 and T2 time points (B), for AD samples and between WT samples and AD samples at T2 time point (C). Plots show beta diversity values in a PCA diagram.



SUPPLEMENTARY FIGURE 2. Aβ immunoreactivity in 3xTg-AD (left figure) mice compared to wild type mice (right figure).
Low-magnification view of prefrontal cortex (A), hippocampus (B) , basolateral amygdala (C) from 8 months old mice following staining with 6E10 -specific antibody.
Higher-magnification views of section (D-E) showing intraneuronal Aβ immunoreactivity.
Original magnifications: 5 (A,B,C), 20 (D, E, F).
Images were acquired using a Neurolucida microscope**.**

Method.

For immunohistochemical studies, mice were anesthetized with isoflurane and transcardially perfused with paraformaldehyde (4% in 0.1 M phosphate buffer, pH 7.4). Sections from the Prefrontal cortex, hippocampus and basolateral amygdala (35 µm thick) were coronally cut on a microtome. Free-floating sections were incubated overnight with Aβ primary antibodies (anti-β-Amyloid, 6E10 **,** 1:1000, Biolegend).

After washing, sections were incubated in proper biotinylated secondary antibodies. For visualization, the avidin–peroxidase protocol (ABC, Vector Laboratories, UK) was applied, using DAB (Sigma-Aldrich, Milan, Italy) as chromogen. After washing, the sections were mounted on slides, air-dried, dehydrated in ascending concentrations of ethanol, and cleared with xylene.

Table 1. Main molecule modulated at six months. Name, HMDB id, fold change, p-value and relative classes are listed.

	Name	*HMDB ID*	*FC*	*p value*	*Class*
UNTARGETED AQUEOUS PHASE	Benzyl alcohol	HMDB0003119	0.814	0.0054	Benzene and substituted derivatives
	L-Serine	HMDB00187	0.400	0.0138	Amino Acids
	L-Aspartic acid	HMDB00191	0.613	0.0148	Amino Acids
	L-Threonine	HMDB00167	0.639	0.0162	Benzene and substituted derivatives
	3-3-Hydroxyphenylpropanoic acid	HMDB0124925	0.260	0.0171	Phenylpropanoic acids
	Phloretic acid	HMDB02199	0.053	0.0216	Benzene and substituted derivatives
	L-Valine	HMDB00883	0.411	0.0335	Amino Acids
	DL-Phenylalanine	HMDB00159	0.502	0.0347	Amino Acids
	Cyclohexanone, 3,3,5-trimethyl-	HMDB0031195	0.862	0.0353	Organooxygen compounds
	L-Isoleucine	HMDB00172	0.638	0.0427	Amino Acids
UNTARGETED ORGANIC PHASE	Hydrocinnamic acid	HMDB0000764	8.114	0.0002	Phenylpropanoic acids
	Benzeneethanol, 4-hydroxy-	HMDB0004284	2.921	0.0122	Phenols
	Benzeneacetic acid	HMDB0000209	1.869	0.0151	Benzene and substituted derivatives
	Octadecanoic acid	HMDB00827	0.769	0.0228	Fatty Acyls
	3-Phenylpropanol	HMDB0033962	1.993	0.0232	Benzene and substituted derivatives
	Levulinic acid	HMDB0000720	3.607	0.0413	Keto acids and derivatives
	Decanoic acid	HMDB00511	1.583	0.0447	Fatty Acyls
	Hexadecanoic acid	HMDB00220	0.839	0.0461	Fatty Acyls
SCFAs	Butanoic acid	HMDB00039	1.782	0.0048	Fatty Acyls
	Acetic acid	HMDB00042	1.591	0.0213	Carboxylic acids and derivatives