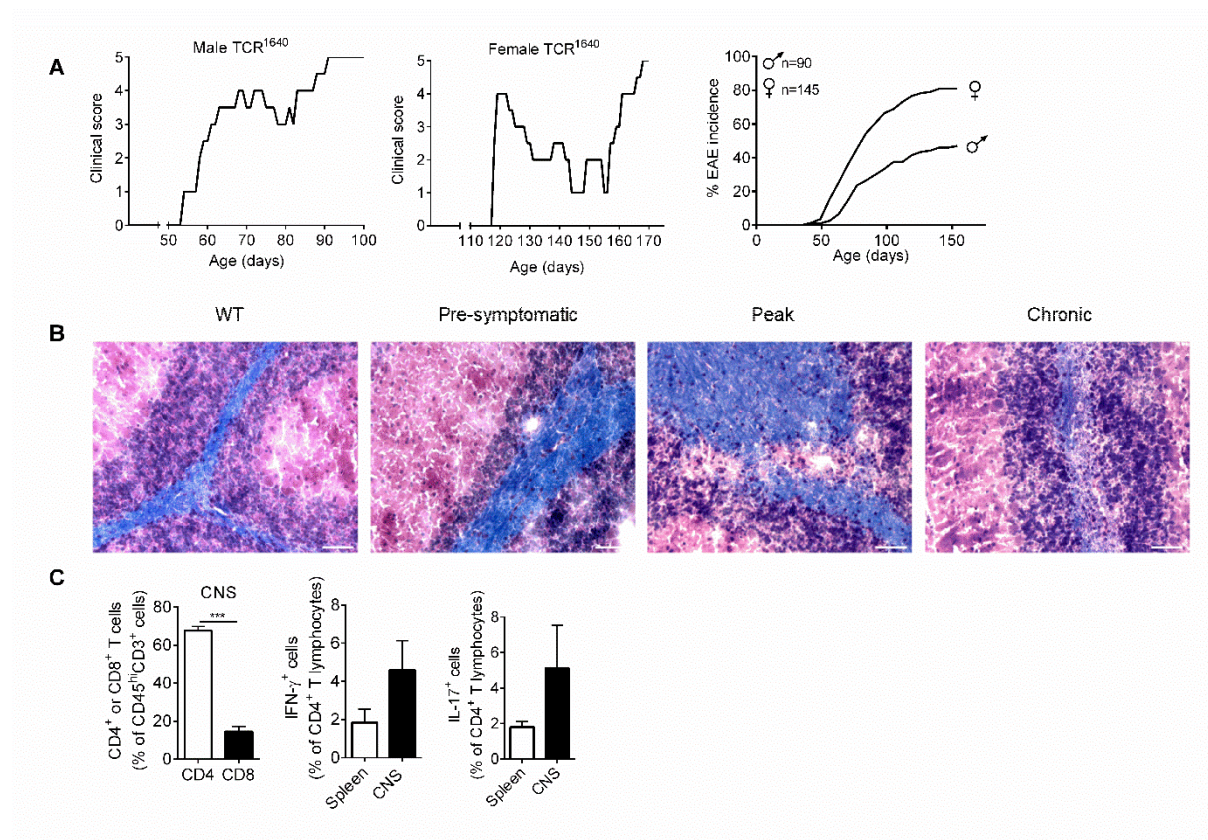
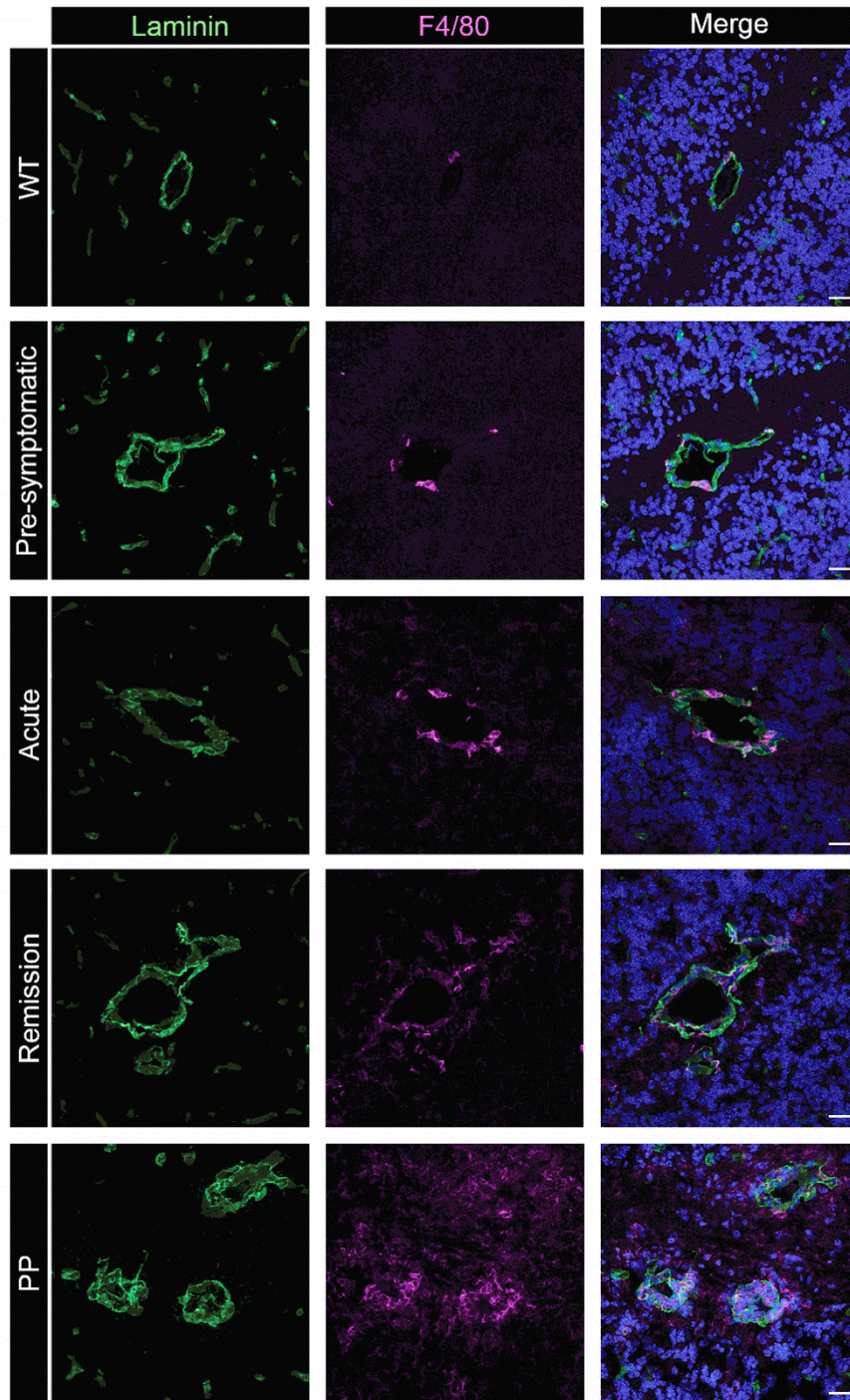


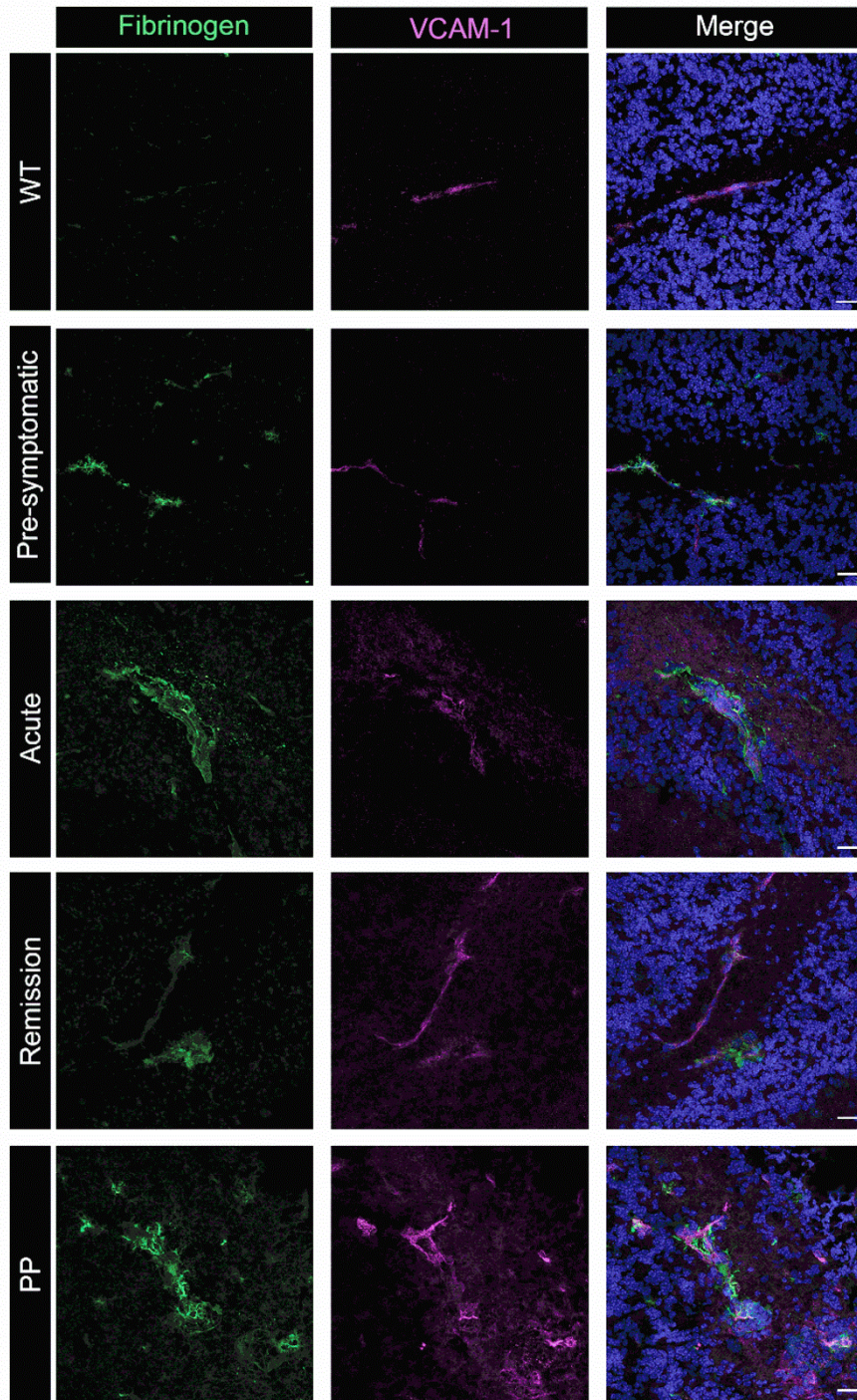
SUPPLEMENTAL TABLES FIGURES AND FIGURE LEGENDS



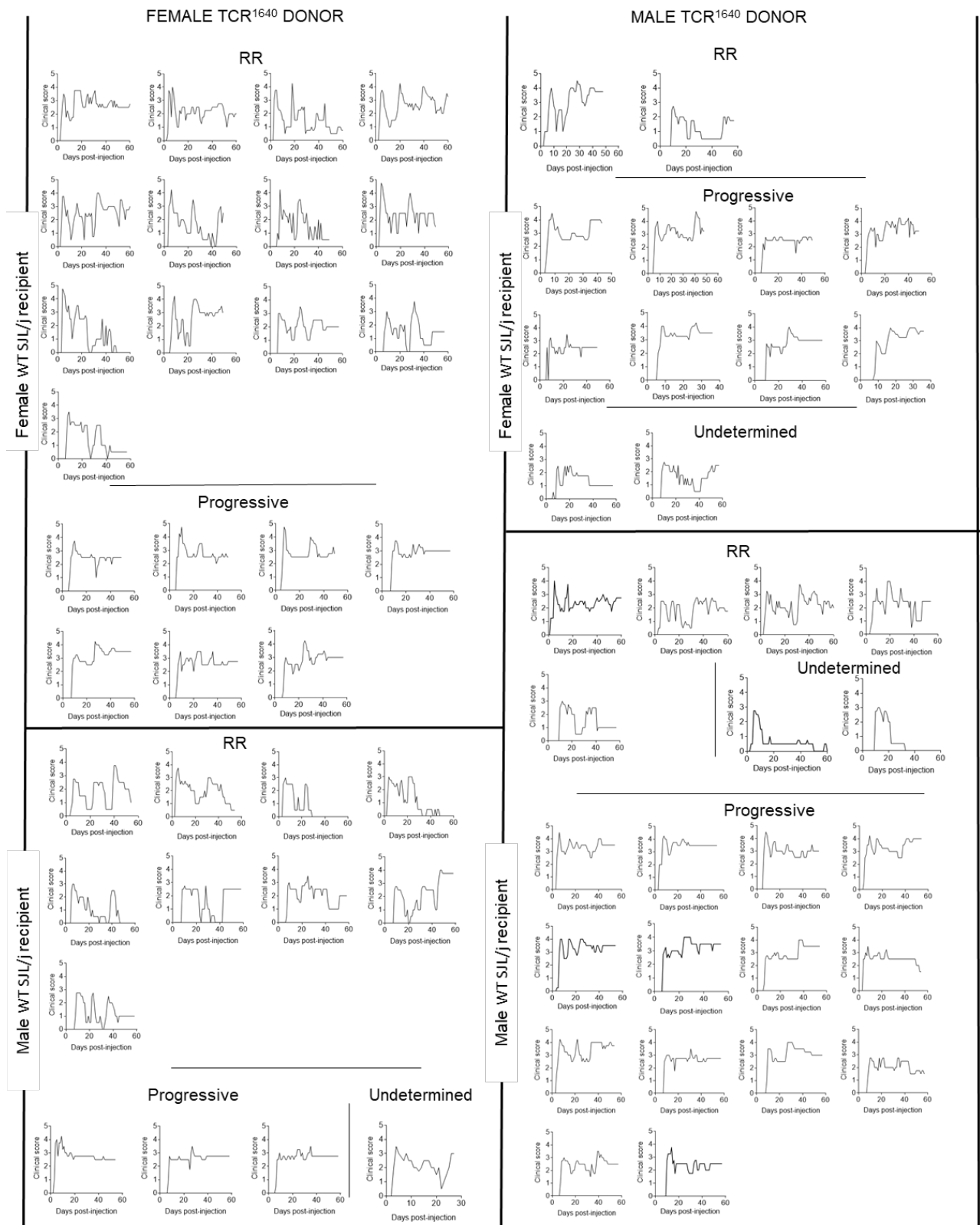
Supplemental Figure 1. Characterization and validation of the TCR¹⁶⁴⁰ mouse model. (A) A total of 90 male mice were followed up and an average of 40% developed a primary progressive EAE disease. A representative example is shown here (left graph). A total of 146 female mice were followed up and 80% of the females developed a RR form of the EAE disease. A representative example is shown here (middle graph). Incidence of EAE disease in female and male TCR¹⁶⁴⁰ mice (right graph). (B) Luxol fast blue staining combined with hematoxylin and eosin to analyze demyelination and immune cell infiltration in SJL/j wild-type mice and TCR¹⁶⁴⁰ mouse at pre-symptomatic, peak and chronic phase of the disease. (C) Cellular infiltrates into the central nervous system (CNS) of sick (score ≥ 3) TCR¹⁶⁴⁰ mice undergoing spontaneous EAE are composed of CD4⁺ T lymphocytes that have a T_{H1}/T_{H17} cytokine expression. Data are representative of at least 3 sick TCR¹⁶⁴⁰ mice, analyzed in 3 independent experiments. Data are represented as mean \pm SEM and an one-side unpaired t-test was used with *** p<0.001. Scale bar: 100 μ m. A p-value less than 0,05 was considered significant.



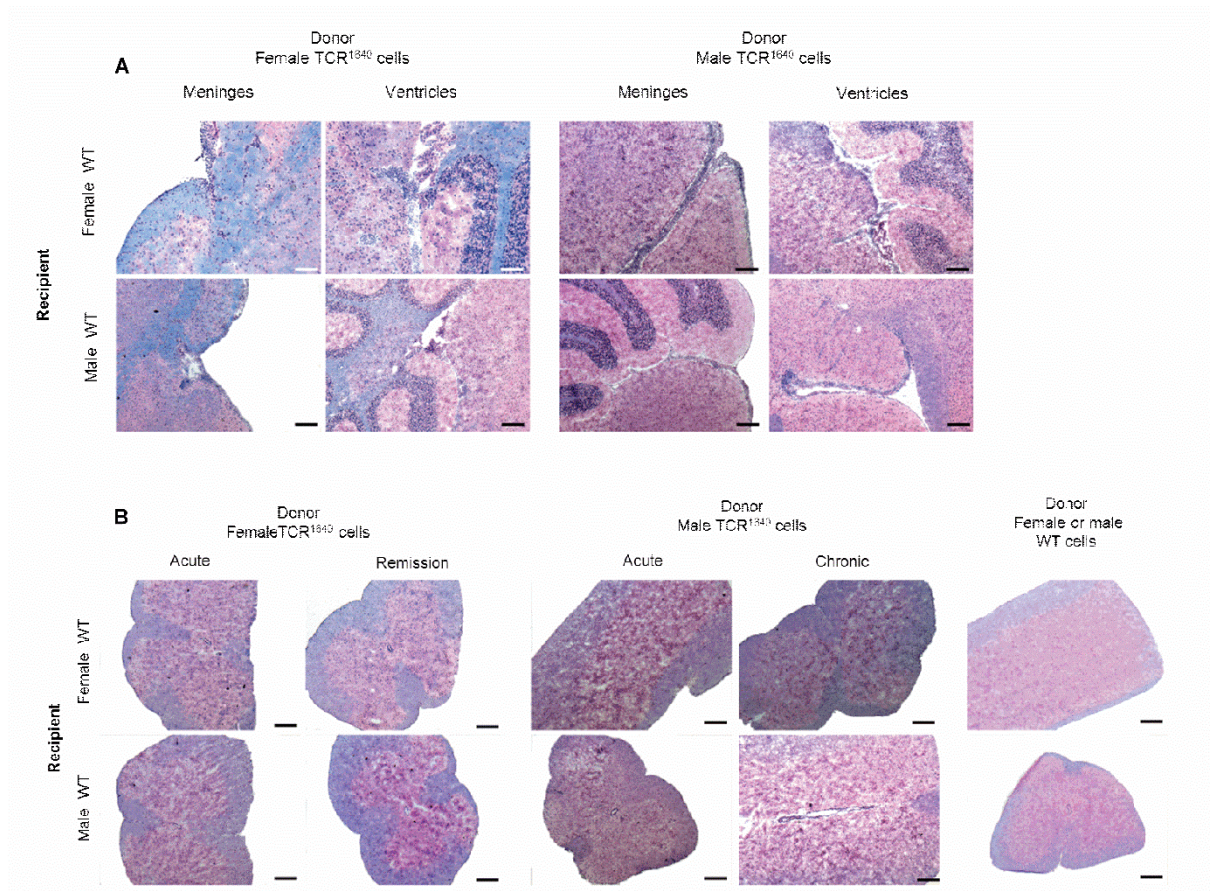
Supplemental Figure 2. Analysis of the blood-brain barrier integrity at different disease phases in TCR^{1640} mice. BBB integrity was measured by immunofluorescent staining for infiltrating macrophages ($F4/80^+$) and activation of the basal membrane (laminin staining) in TCR^{1640} mice at different disease phases: pre-symptomatic (age day 30-40), acute disease (score ≥ 3), remissions (recovery of score with $\Delta 2$) and primary progressive disease. Data are representative of at least 3 independent experiments with at least 3 TCR^{1640} mice at the different disease phases. Scale bar: 100 μm



Supplemental Figure 3. Analysis of the blood-brain barrier integrity at different disease phases in TCR^{1640} mice. BBB integrity was measured by immunofluorescent staining for extravasation of blood proteins into the parenchyma (fibrinogen) and activation of adhesion molecules on the BBB (VCAM-1) in TCR^{1640} mice at different disease phases: pre-symptomatic (age day 30-40), acute disease (score ≥ 3), remissions (recovery of score with $\Delta 2$) and primary progressive disease. Data are representative of at least 3 independent experiments with at least 3 TCR^{1640} mice at the different disease phases. Scale bar: 100 μm



Supplemental Figure 4. Graphs of EAE disease course (progressive, relapsing-remitting (RR) or undetermined) after injection of male or female transgenic TCR¹⁶⁴⁰ cells into male or female WT SJL/j recipient followed for 60 days.



Supplemental Figure 5. Histological analysis of meninges, ventricles and spinal cord of SJL/j female and male recipients after adoptive transfer. After injection of female TCR¹⁶⁴⁰ immune cells, recipients were sacrificed at acute disease (first peak, score ≥ 3) and during remission (clinical score of $\Delta \geq 2$). After injection of male TCR¹⁶⁴⁰ immune cells, recipients were sacrificed at acute disease (score ≥ 3) and during chronic disease (clinical score ≥ 3 for more than 20 days). Histological analysis was performed using luxol fast blue for myelin and counterstained by hematoxylin and eosin for cellular infiltrates. **(A)** Representative image of histological analysis of meninges and ventricles of SJL/j female and male recipients after adoptive transfer. **(B)** Representative image of histological analysis of spinal cord of SJL/j female and male recipients after adoptive transfer. Histological analysis of spinal cord of SJL/j female and male mice after injection with SJL/j immune cells were performed as a control (right panel). Data are representative of 3 or more independent experiments with three mice per group. White scale bar: 100 μm ; Black scale bar : scale 250 μm .

Supplemental table 1: mRNA expression levels (Normalized log2(exp) by sample)

GENE	WT_M1	WT_M2	WT_F1	WT_F2	TCR_F1	TCR_F2	TCR_M1	TCR_M2
EXOSC9	9,276	9,198	9,107	9,032	8,497	8,508	7,533	7,474
GUF1	8,917	8,860	9,147	9,042	8,612	8,483	7,414	7,286
HSP90B1	9,187	9,137	8,746	8,637	8,023	7,996	7,604	7,581
AMZ2	8,862	8,840	8,885	8,793	8,091	8,174	7,375	7,268
CRYBG3	9,038	9,014	8,957	8,871	8,568	8,461	8,060	7,950
RCCD1	8,979	8,873	8,730	8,698	8,363	8,322	7,982	7,911
CDK4	9,184	9,114	9,050	9,014	8,706	8,653	8,272	8,241
AP3M1	9,884	9,798	9,654	9,608	8,387	8,411	7,773	7,607
ARHGEF12	9,047	9,015	9,136	9,060	10,149	10,039	9,639	9,524
ECHDC1	9,210	9,215	9,295	9,277	9,657	9,572	8,909	8,857
PMEL	8,392	8,372	8,395	8,330	9,658	9,579	9,051	9,032
GDI2	7,747	7,752	7,629	7,628	8,332	8,180	7,221	7,148
SRPK2	7,690	7,691	7,683	7,607	8,352	8,354	6,963	6,941
GBP2	7,662	7,574	7,469	7,386	8,096	8,036	7,195	7,135
CCDC66	7,717	7,583	7,595	7,498	8,076	7,939	6,790	6,802
SNHG14	8,259	8,170	8,200	8,158	8,667	8,574	7,492	7,454
CTLA4	8,338	8,298	8,032	8,033	7,333	7,314	7,014	6,940
LCORL	7,935	7,905	7,825	7,671	7,220	7,148	6,609	6,492
IL17F	8,812	8,789	8,579	8,588	7,517	7,495	7,226	7,026
DEGS2	7,628	7,409	7,729	7,627	9,105	9,030	8,145	8,098
RPS11	7,327	7,270	6,952	6,967	9,012	8,915	8,667	8,597
SYN3	10,034	9,933	9,593	9,548	5,045	4,887	4,638	4,213
FKBP3	7,183	7,270	7,155	7,045	7,647	7,549	6,632	6,630
HDGFL3	7,381	7,303	7,024	6,963	7,580	7,395	6,576	6,450
CCDC39	6,638	6,603	6,810	6,720	7,258	7,310	5,985	5,961
DGAT1	7,432	7,322	7,217	7,237	6,695	6,611	6,013	6,061
LILR4B	7,211	7,191	6,807	6,814	6,164	6,158	5,770	5,419
CDC73	7,631	7,480	7,752	7,687	6,557	6,529	5,358	5,255
PLEK	6,497	6,440	6,137	6,270	4,976	5,053	4,087	4,183
SELL	5,050	4,815	4,574	4,417	7,335	7,288	6,773	6,652
DAGLB	10,310	10,230	10,265	10,189	9,881	9,802	9,455	9,385
METTL23	10,182	10,085	10,045	9,951	9,680	9,665	9,389	9,300
ULK4	10,047	9,981	9,955	9,832	10,221	10,140	9,383	9,298
ACAT3	10,813	10,792	10,706	10,679	10,279	10,226	9,781	9,720
BYSL	10,683	10,595	10,443	10,414	10,204	10,123	9,955	9,867
PHYKPL	11,937	11,867	11,931	11,857	11,269	11,205	10,895	10,844
TMCC1	11,573	11,509	11,433	11,386	11,080	11,026	10,652	10,584