

1 **Supplementary figure legends**

2 **Supplementary Figure 1. Survival analysis in primary malignant melanoma of the**
3 **esophagus (PMME) and non-esophageal mucosal melanoma (NEMM).** (A) Kaplan–Meier
4 curve of progression free survival (PFS) in patients receiving anti-PD-1 monotherapy. PFS
5 was defined as the time from the start of treatment to progression or last follow-up. (B)
6 Kaplan–Meier curve of overall survival (OS) in patients receiving anti-PD-1 monotherapy.
7 OS was defined as the time from the start of treatment to death or last follow-up.

8 **Supplementary Figure 2. Venn plots showing the number of samples that underwent**
9 **genome and RNA sequencing, and multiplex immunohistochemistry (mIHC) staining.**

10 **Supplementary Figure 3. Genomic differences between primary malignant melanoma of**
11 **the esophagus (PMME) and non-esophageal mucosal melanoma (NEMM).** Differences
12 between the two cohorts in (A) tumor mutational burden (TMB) using mutations (SNVs and
13 indels) per megabase, (B) insertion/deletion (indel) burden, (C) human leukocyte
14 antigen-corrected tumor mutation burden (HLA-TMB), (D) total tumor neoantigen burden
15 (TNB), (E) relative fraction of transversions (Tv), (F) relative fraction of transitions (Ti), (G)
16 relative fraction of C > T Ti, (H) relative fraction of T > G Tv, (I) TMB in samples with and
17 without signature 1, (J) relative fraction of signature 11, (K) relative fraction of signature 19,
18 and (L) relative fraction of signature 1.

19 **Supplementary Figure 4. Proportion of somatic base changes and signature**
20 **contributions in primary malignant melanoma of the esophagus (PMME) and**

1 **non-esophageal mucosal melanoma (NEMM).**

2 **Supplementary Figure 5. The top 20 mutated genes in primary malignant melanoma of**

3 **the esophagus (PMME) and non-esophageal mucosal melanoma (NEMM).**

4 **Supplementary Figure 6. Comparison of the responses and survivals between patients**

5 **with and without mutations in six neurodevelopmental or neurodegenerative**

6 **disease-related genes in three melanoma clinical cohorts including total 238 melanoma**

7 **patients treated with anti-PD-1. (A) Proportion of responders versus non-responders in**

8 **patients with at least one mutation and in patients without mutations in the six genes. (B)**

9 **Proportion of responders versus non-responders in patients with mutant and in patients with**

10 **wild-type *NBPF1*, *DPF1*, *MACF1*, *MAOB*, *MYCBP2*, and *RNF40*. (C–E) Kaplan–Meier**

11 **curves of progression free survival (PFS) in patients with (C) at least one mutation and**

12 **non-mutation in the six genes, (D) mutant and wild-type *NBPF1*, (E) mutant and wild-type**

13 ***MYCBP2*. (F–H) Kaplan–Meier curves of overall survival (OS) in patients with (C) at least**

14 **one mutation and non-mutation in the six genes, (D) mutant and wild-type *NBPF1*, (E)**

15 **mutant and wild-type *MYCBP2*.**