**Supplementary Figure legends**

**Supplementary Figure S1: Representative flow strategies for detection of apoptotic cells.** Tumor cells were gated for GFP positive cell population (middle panel), among which activated caspase-3-positive cells were then gated (right panel).

**Supplementary Figure S2:** **The top 20 candidates with the highest *comboscores* from the ORF screen.**

**Supplementary Figure S3: *MEX3B* expression is higher in non-responders than in responders to anti-PD-1 immunotherapy.** qRT-PCR for *MEX3B* and *GAPDH* was performed on tumor RNA samples from melanoma patients treated with anti-PD-1. Each dot shows the log10 transformed mean relative MEX3B mRNA expression of each patient. The relative MEX3B mRNA expression was compared between non-responders (n=16) and responders (n=11). P=0.08 by Student’s t test.

**Supplementary Figure S4:** **Knockdown of MEX3B increases the susceptibility of tumor cells to T cell-mediated cytotoxicity.** 2549 or 2559 melanoma cells were infected with lentiviral vectors expressing a control shRNA sequence or a shRNA sequence targeting *MEX3B*, and stable cell lines were generated by puromycin selection. (A, B) qRT-PCR validation of *MEX3B* knockdown in 2549 cells (A) or 2559 cells (B). (C, D) 2549 cells (C) or 2559 cells (D) transduced with control shRNA (shControl) or *MEX3B* shRNA (shMEX3B) were incubated with 2549 autologous TILs (C) or 2559 autologous TILs (D) at E:T ratio 3:1 for 3 hours, followed by quantification of apoptosis by flow cytometry analysis of activated caspase-3. Data are represented as mean ± SEM. \*P<0.05, \*\* P<0.01, \*\*\*\*P<0.0001 by Student’s t test.

**Supplementary Figure S5:** **Overexpression of HLA-A2 in 2549 melanoma cells results in similar IFNɣ release in MART-1-specific TILs incubated with melanoma cells overexpressing GFP-MEX3B or GFP control.** GFP-MEX3B-overexpressing or GFP control 2549 cells overexpressing exogenous HLA-A2, were pulsed with MART-1 for 1 hour and incubated with MART-1-specific TILs at different E:T ratios for 24 hours, followed by measurement of IFNɣ levels in supernatants by ELISA. Data are represented as mean ± SEM.

**Supplementary Figure S6:** **Overexpression of MEX3B in 2549 melanoma cells decreases surface HLA-A31 expression.** GFP-MEX3B-overexpressing or GFP control 2549 cells were treated with or without IFNɣ for 24 hours and stained for HLA-A31 followed by flow cytometry analysis. The representative histograms of each cell line and unstained control, as well as their mean fluorescent intensity (MFI) of HLA-A31, are shown.

**Supplementary Figure S7: Overexpression of MEX3B in 2549 melanoma cells does not alter HLA-B or HLA-C expression.** GFP-MEX3B-overexpressing or GFP control 2549 or 2559 cells were treated with or without IFNɣ for 24 hours, and stained for pan-HLA-A, B, C (A), HLA-B (B) or HLA-C (C) followed by flow cytometry analysis. The representative histograms of each cell line and unstained control are shown. Orange: unstained control; Red: GFP control cells; Blue: GFP-MEX3B-overexpressing cells.

**Supplementary Figure S8: Alteration of expression of antigen processing and presentation machinery components upon MEX3B overexpression.** qRT-PCR analysis of HLA-A, B2M, TAP1, TAP2, TAPBP, CALR, CANX, PSMB8 or PSMB9 mRNA expression in GFP-MEX3B-overexpressing or GFP control 2549 (A) or 2559 (B) cells. Data are represented as mean ± SEM.

**Supplementary Figure S9:** **A schematic graph representing transcription factors that may regulate MEX3B expression.** The transcription factors were predicted by a bioinformatic search using Champion ChIP transcription factor search portal (http://www.sabiosciences.com/chipqpcrsearch.php?app=TFBS)

**Supplementary Tables**

**Supplementary Table S1: A list of all the 384 ORFs screened in the kinome library.**

**Supplementary Table S2: Major pathways that involve the top 20 genes with the highest comboscores.** The major pathways involving these high-comboscore genes were identified by Pathway Commons Database. The genes involved in each pathway are listed under the pathway names (on the first row). The high-comboscore candidates from the ORF screen are highlighted in red.