**Supplemental Figure and Table Legends**

**Figure S1:** Principal Component Analysis of the full dataset (48 samples): Munich, Germany (M9 and M12; purple); Nicosia, Cyprus (C2; teal); Kuala Lumpur, Malaysia (KL; green) and Siavonga, Zambia (ZI; orange). Filled (closed) symbols represent stress samples; empty (open) symbols represent control samples. The sample indicated by the dashed outline was identified as outlier and removed from subsequent analyses.

**Figure S2:** MSB-induced $\log_2$ fold-change (stress/control) of candidate oxidative stress-susceptible genes identified in a genome-wide association study of Weber et al. (2012). Asterisk indicates the adjusted *P*-value from a Wald test as applied in DESeq2. **P* < 0.05.

**Figure S3:** MSB-induced $\log_2$ fold-change (stress/control) in the epoxide hydrolase gene family. Asterisk indicates the adjusted *P*-value from a Wald test as applied in DESeq2. **P* < 0.05.

**Figure S4:** Comparisons of $\log_2$ fold-change (stress/control) under oxidative stress (orange) and cold shock (von Heckel et al. 2016) (purple) of genes reported to have significant genotype-by-environment interaction by von Heckel et al. (2016). Asterisk indicates the adjusted *P*-value from a Wald test as applied in DESeq2. **P* < 0.05.

**Figure S5:** Comparisons of $\log_2$ fold-change (stress/control) in under oxidative stress (orange) and cold shock (von Heckel et al. 2016) (purple) of (A) viable and (B) not viable/malformed candidate genes identified by von Heckel et al. (2016) using RNAi knockdown. Asterisk indicates the adjusted *P*-value from a Wald test as applied in DESeq2. **P* < 0.05.

**Figure S6A**: The 10 reactome pathways that show the highest enrichment for genes under oxidative stress from the WGCNA's turquoise module are shown.

**FigureS6B:** The eight reactome pathways that show the highest enrichment for genes under oxidative stress from the WGCNA's blue module are shown.

**Figure S7A**: The 10 reactome pathways that show the highest enrichment for genes under oxidative stress in the deletion background relative to non-deletion from the WGCNA's turquoise module are shown.

**FigureS7B**: The eight reactome pathways that show the highest enrichment for genes under oxidative stress in the deletion background relative to non-deletion from the WGCNA's blue module are shown.

**Table S1:** Differentially expressed genes induced by MSB (up-regulated)

**Table S2:** Differentially expressed genes induced by MSB (down-regulated)

**Table S3:** Gene ontology enrichment terms summarized by REVIGO for the group of up-regulated genes in stress versus control comparisons.

**Table S4:** Gene ontology enrichment terms summarized by REVIGO for the group of down-regulated genes in stress versus control comparisons.

**Table S5.** Comparison of variation between deletion and non-deletion nearly isogenic lines and isofemale lines from Munich, Germany (M12 and M9), Nicosia, Cyprus (C2) and Kuala Lumpur, Malaysia (KL) in terms of sequence divergence in SNPs/Kb and expression divergence represented as percentage of differentially expressed (% DE) genes at a false discovery rate of 5%.

**Table S6:** Number of differentially expressed genes (p.adj < 0.05) in pairwise comparisons of deletion and non-deletion lines under both treatments from Munich, Germany (M12 and M9), Nicosia, Cyprus (C2) and Kuala Lumpur, Malaysia (KL).

**Table S7:** $Log_2$ fold-change (stress/control) of up- and down-regulated target genes of miRNAs with predicted binding sites within the *MtnA* 3' UTR deletion region (*miR-284-3p*, *miR-956-3p*, *miR-9c-5p* and *bantam-3p*) and their associated p.adj values (DESeq2) (version 1.28.1) (Love et al. 2014). Target genes that are down-regulated in both deletion and non-deletion lines are also indicated in the table. These 203 genes were then evaluated for functional association using FlyMine (Lyne et al. 2007) and the resulting ontology terms sorted by p-value (according to Holm-Bonferroni test-correction) are included below.