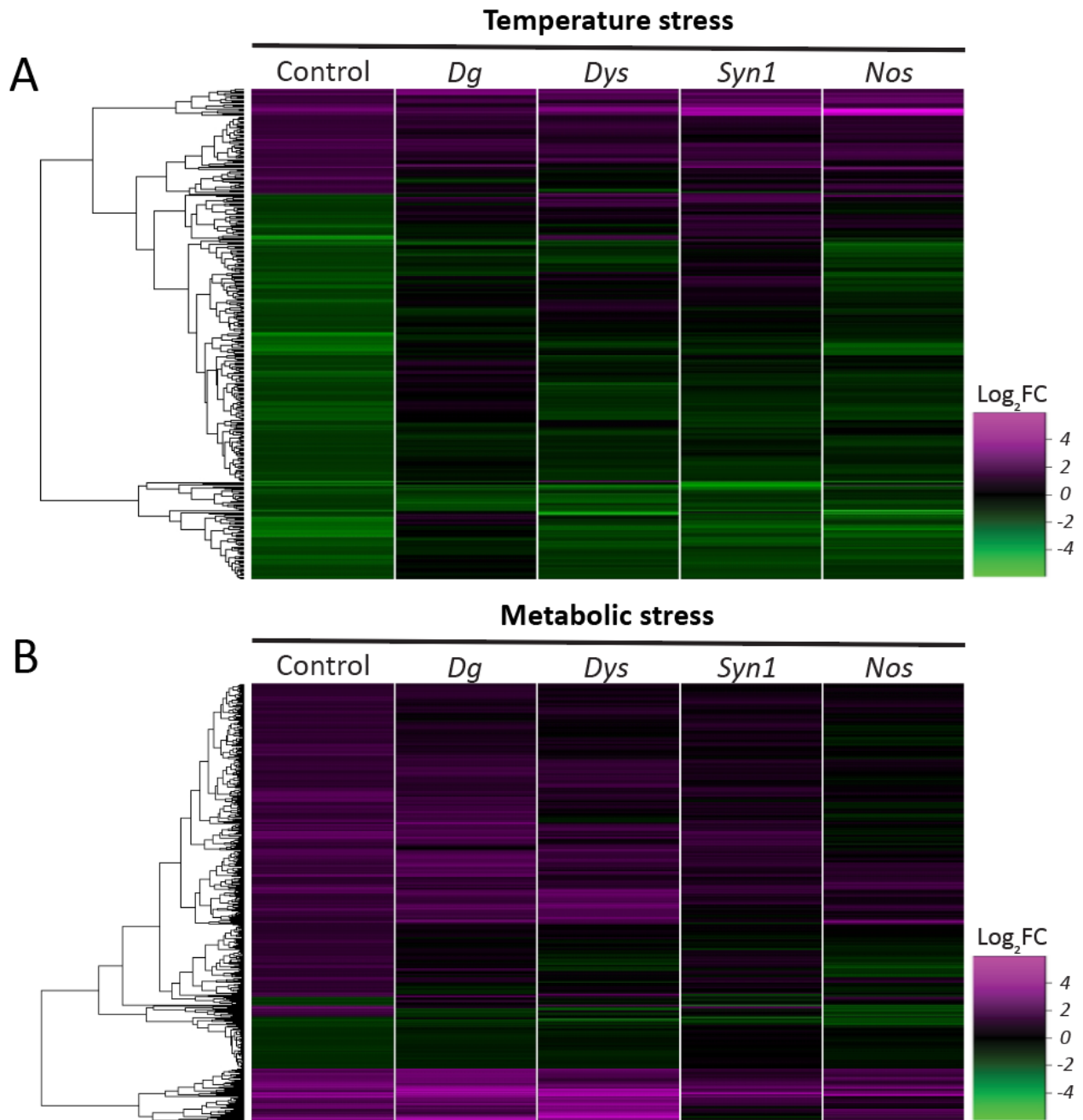


### Fig. S1. Generation of new *Syntrophin1* deficiency, $\Delta$ *Syn1*

A. Deficiency was generated using Flp-mediated recombination between two FRT-containing transposons flanking the *Syn1* gene (*PBac{WH}CG14565<sup>05859</sup>* and *P{XP}CG7370<sup>d06092</sup>*; see Materials and Methods).

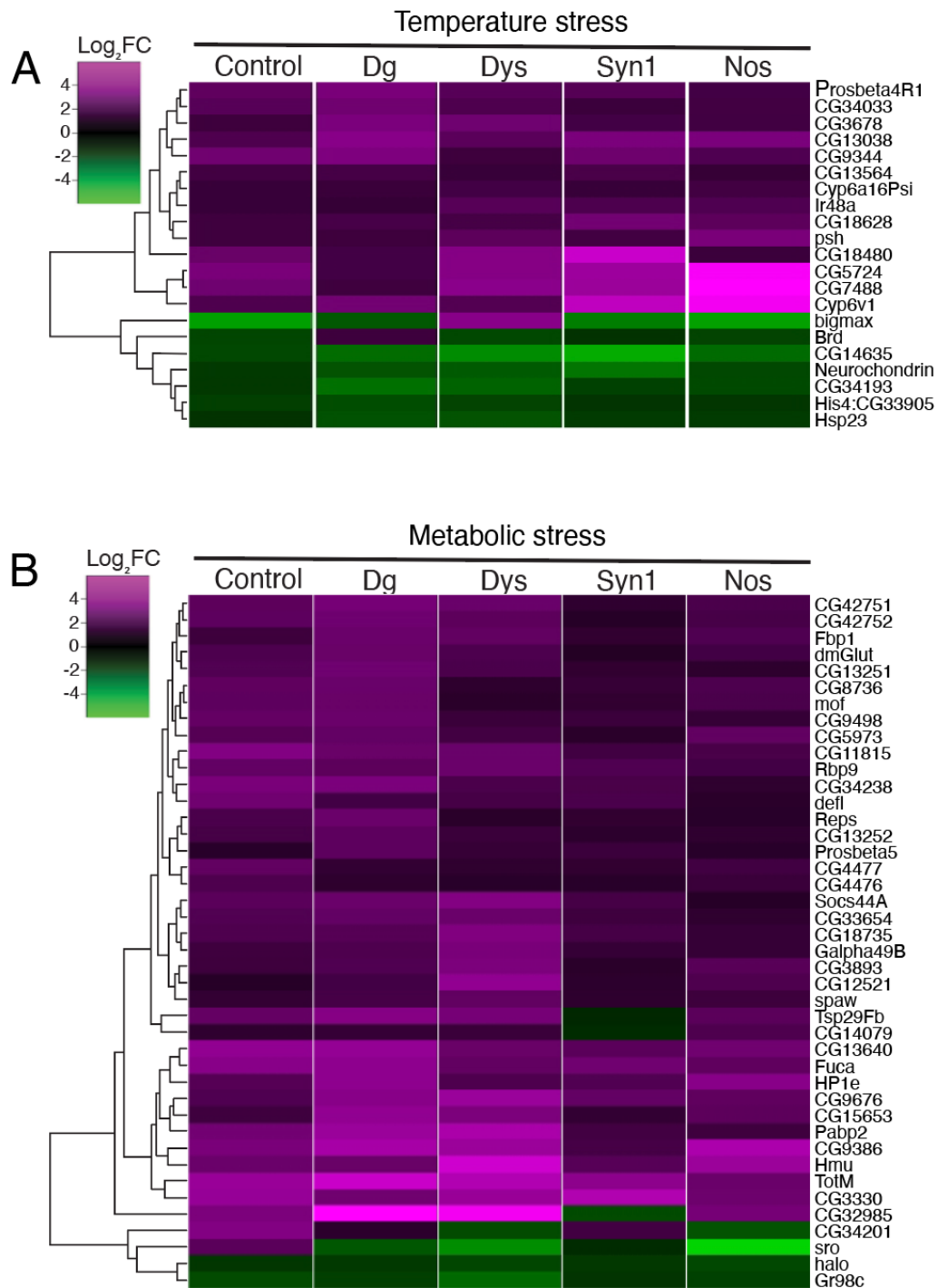
B-B'. PCR confirmation of new  $\Delta$ *Syn1* alleles. (B) Primers specific for the endogenous *Syn1* gene result in PCR amplification in the parental strains *PBac{WH}CG14565<sup>05859</sup>* and *P{XP}CG7370<sup>d06092</sup>*, but no bands are present in lanes representing *Syn1* deletions. (B') Primers that recognize residual transposon fragments flanking the new deficiency positively detect the presence of the deficiency in flies with deletion alleles, but not in parental flies.

C. RT-qPCR confirms the absence of RNA from *Syn1* deletion mutants, while it is readily detected in control flies (Oregon-R-C).



**Fig. S2. All genes dysregulated by temperature and metabolic stress (related to Figure 2)**

A-B. Heat maps with all genes dysregulated in control flies by temperature stress (A; 357 genes) and metabolic stress (B; 483 genes), also showing the expression level of these genes in the four DGC mutants.



**Fig. S3. DGC-independent genes are regulated by stress irrespective of presence of a functional DGC (related to Figures 3 and 4)**

A-B. Heat maps showing all genes that are dysregulated by temperature stress (A; 21 genes) or metabolic stress (B; 42 genes) in all genotypes, including controls, indicating a DGC-independent stress-response mechanism. Of these genes, 90% of temperature-responsive genes and 88% of metabolic-responsive genes are dysregulated similarly (up- or downregulated) in all genotypes.

**Table S1. Log2-FC values for all comparisons**

[Click here to download Table S1](#)

**Table S2. 46 genes dysregulated in all 4 DGC mutants: Dg Dys Syn1 & Nos**

[Click here to download Table S2](#)

**Table S3. 71 genes dysregulated in 3 mutant genotypes: Dg, Dys, & Syn1 (when Nos is excluded)**

[Click here to download Table S3](#)

**Table S4. 357 genes dysregulated by temperature stress (77 upregulated and 280 downregulated)**

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**Table S5. 483 genes dysregulated by metabolic stress (416 upregulated and 67 downregulated)**

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**Table S6. 59 genes dysregulated by both temperature stress and metabolic stress**

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**Table S7. DGC-dependent and DGC-prevented temperature-response genes**

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**Table S8. DGC-dependent and DGC-prevented metabolic-response genes**

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**Table S9. DGC-independent temperature-response genes**

[Click here to download Table S9](#)

**Table S10. DGC-independent metabolic stress-response genes**

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