1 Supplements

2 Of mice and men – the host response to influenza virus infection

- 3 Heike Kollmus¹, Carolin Pilzner¹, Sarah R. Leist^{1,2}, Mark Heise³, Robert Geffers³, Klaus
- 4 Schughart^{1,4,#}
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9 Fig. S1. Founder contributions in eleven CC strains from this study

Founder contributions for each CC strain as provided by the System Genetics Core facility at
 the University of North Carolina (<u>http://csbio.unc.edu/CCstatus/index.py?run=availableLines</u>);
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Fig. S2. VENN diagram comparing DEGs in mouse founder strains in blood and lungs 16 17 DEGs in lungs and blood were determined between infected and control mouse of C57BL/6J 18 (B6) and 129S1/SvImJ (129) CC founder strains using the data set described by (Leist et al. 19 2016) (GSE74077). 26% of DEGs were shared in the lungs of B6 and 129 strains and 3.8 % 20 in the blood between B6 and 129 strains. However, only 0.1 % were shared when blood of 21 B6 was compared to lung of 129 and 0.3 % when lung of B6 was compared to blood of 129. 22 Thus, lung and blood DEG do not show a strong overlap and, therefore, lung DEGs of mice 23 should not be compared with blood DEGs in humans to evaluate validity of the mouse model. 24

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27 Fig. S3. Expression levels of genes in CC strains over time

Normalized log₂-transformed relative gene expression values of (A) *Ifi27* and (B) *Irf7* in CC mice. Dots represent values from individual mice. Crosses represent mean expression values per group, bars represent +/- 1 SEM (standard error of mean). Mock-infected control mice are designated 'cd3', infected mouse groups are labelled 'd3', 'd5', and 'd8' representing the time points p.i.

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- 35 Supplementary Tables
- 36 **Table S1: Sample list with annotations for CC strains**
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- 40 Table S5: Differentially expressed probesets for comparison of CC infected resistant
- 41 strains to mock controls
- 42 Table S6: Differentially expressed probesets for comparison of CC infected severe
- 43 strains to mock controls
- Table S7: Differentially expressed probesets for comparison of Woods_13 infected
 versus controls
- Table S8: Differentially expressed probesets for comparison of Zhai_15 infected
 versus controls
- Table S9: Differentially expressed probesets for comparison of Tang_17 infected
 versus controls
- 50 Table S10: Differentially expressed probesets for comparison of CC infected severe
- 51 strains to resistant strains
- 52 Table S11: Genes in different groups from VENN diagram in Figure 4A.
- 53 **Table S12: Genes in different groups from VENN diagram in Figure 4B.**

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55 References

- Leist SR, Pilzner C, van den Brand JM, Dengler L, Geffers R, Kuiken T, Balling R, Kollmus
- 57 H, Schughart K (2016) Influenza H3N2 infection of the collaborative cross founder strains
- reveals highly divergent host responses and identifies a unique phenotype in CAST/EiJ mice.
- 59 BMC Genomics 17, 143

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