

## SUPPLEMENTARY TABLE

Supplementary Table 1. Role of studied genes in determining the stress response.

| Target gene   | Characteristics   | Effects   |
|---|---|---|
| Catalase ( <i>Cat</i> )                                     | Enzymes catalyzes the decomposition of hydrogen peroxide in cells [1].  | Is involved in response to photooxidative [2], endoplasmic reticulum [3], oxidative stresses [4] and to hydrogen peroxide stimulus [5]. Overexpression of human catalase, which targets mitochondria, increases life span in <i>Mus musculus</i> by about 20% [6].  |
| frataxin ( <i>fh</i> )                                      | Protein essential for iron-sulfur clusters synthesis, which are necessary for the production of ATP by the respiratory chain, as well as in other biological processes such as steroidogenesis [7–9].   | Is involve in response to oxidative stress [7], to hydrogen peroxide stimulus [10], to iron ion homeostasis [9] and to the hypoxia-induced response [11]. Overexpression of frataxin in mitochondria increases the antioxidant capacity, resistance to oxidative stress, and life span in <i>Drosophila melanogaster</i> females [12].  |
| Growth arrest and DNA damage-inducible 45 ( <i>Gadd45</i> ) | Participates in the regulation of the cell cycle and oviposition; required to activate MAPKKK, JNK activity [8, 13].  | Is involved in response to oxidative, thermal and genotoxic stresses [14, 15]. Overexpression of the <i>D-Gadd45</i> gene in the nervous system leads to a significant increase in the life span in <i>Drosophila melanogaster</i> [16].  |
| Heat shock protein 68 ( <i>Hsp68</i> )                      | Protein necessary for response to temperature or stressing cell stimuli [17].   | Is involved to starvation stimulus [18]. Overexpression in somatic cells led to an increase in the average life span of <i>Drosophila melanogaster</i> by 20% [18, 19].   |
| Heat shock protein 83 ( <i>Hsp83</i> )                      | Protein necessary for response to temperature or stressing cell stimuli [17] orthologous to human HSP90 gene ( <a href="https://www.ncbi.nlm.nih.gov/gene/38389">https://www.ncbi.nlm.nih.gov/gene/38389</a> ).   | Is involved in response to heat, oxidative stresses and ionizing radiation [20–22], also in regulation of circadian sleep/wake cycle [23].  |
| Ku80 ( <i>Ku80</i> )  | Ku70/Ku80 heterodimer, or Ku, is the central component of the nonhomologous end joining (NHEJ) pathway of double strand break repair [24]. Orthologous to human XRCC5 gene ( <a href="https://www.ncbi.nlm.nih.gov/gene/7520">https://www.ncbi.nlm.nih.gov/gene/7520</a> ). | Is involved in gamma radiation and X-ray responses [8, 25]. Deletion of Ku80 leads to signs of premature aging such as osteopenia, atrophic skin, hepatocellular degeneration, and age-related mortality in <i>Mus musculus</i> [26]. Also, <i>Mus musculus</i> showed a decrease in life span by 40% [27].   |
| Peroxiredoxin V ( <i>PrxV</i> )                             | Encodes an atypical member of the thiol-specific peroxidase family, which form intramolecular disulfide bonds during the catalytic cycle [28].  | Is involved in response to oxidative stress, cell redox homeostasis and hydrogen peroxide catabolic process [8, 29]. Overexpression of PrxV caused an increase in the average and median life span in <i>Drosophila melanogaster</i> under normal conditions. Against the dPrxV mutants (- / -) were more susceptible to oxidative stress, had a higher incidence of apoptosis, and a shorter average life span [30]. |

1. Chelikani P, Fita I, Loewen PC. Diversity of structures and properties among catalases. *Cell Mol Life Sci.* 2004; 61:192–208.  
<https://doi.org/10.1007/s00018-003-3206-5>  
PMID:[14745498](https://pubmed.ncbi.nlm.nih.gov/14745498/)
2. Orlandi VT, Martegani E, Bolognese F. Catalase a is involved in the response to photooxidative stress in *Pseudomonas aeruginosa*. *Photodiagnosis Photodyn Ther.* 2018; 22:233–40.  
<https://doi.org/10.1016/j.pdpdt.2018.04.016>  
PMID:[29709605](https://pubmed.ncbi.nlm.nih.gov/29709605/)
3. Wang L, Zeng X, Ryoo HD, Jasper H. Integration of UPRER and oxidative stress signaling in the control of intestinal stem cell proliferation. *PLoS Genet.* 2014; 10:e1004568.  
<https://doi.org/10.1371/journal.pgen.1004568>  
PMID:[25166757](https://pubmed.ncbi.nlm.nih.gov/25166757/)
4. Ershova OA, Bairova TA, Kolesnikov SI, Kalyuzhnaya OV, Darenskaya MA, Kolesnikova LI. Oxidative stress and catalase gene. *Bull Exp Biol Med.* 2016; 161:400–03.  
<https://doi.org/10.1007/s10517-016-3424-0>  
PMID:[27496033](https://pubmed.ncbi.nlm.nih.gov/27496033/)
5. Sun J, Tower J. FLP recombinase-mediated induction of Cu/Zn-superoxide dismutase transgene expression can extend the life span of adult *Drosophila melanogaster* flies. *Mol Cell Biol.* 1999; 19:216–28.  
<https://doi.org/10.1128/mcb.19.1.216> PMID:[9858546](https://pubmed.ncbi.nlm.nih.gov/9858546/)
6. Schriener SE, Linford NJ, Martin GM, Treuting P, Ogburn CE, Emond M, Coskun PE, Ladiges W, Wolf N, Van Remmen H, Wallace DC, Rabinovitch PS. Extension of murine life span by overexpression of catalase targeted to mitochondria. *Science.* 2005; 308:1909–11.  
<https://doi.org/10.1126/science.1106653>  
PMID:[15879174](https://pubmed.ncbi.nlm.nih.gov/15879174/)
7. Navarro JA, Ohmann E, Sanchez D, Botella JA, Liebisch G, Moltó MD, Ganfornina MD, Schmitz G, Schneuwly S. Altered lipid metabolism in a *Drosophila* model of Friedreich's ataxia. *Hum Mol Genet.* 2010; 19:2828–40.  
<https://doi.org/10.1093/hmg/ddq183>  
PMID:[20460268](https://pubmed.ncbi.nlm.nih.gov/20460268/)
8. Gaudet P, Livstone MS, Lewis SE, Thomas PD. Phylogenetic-based propagation of functional annotations within the gene ontology consortium. *Brief Bioinform.* 2011; 12:449–62.  
<https://doi.org/10.1093/bib/bbr042> PMID:[21873635](https://pubmed.ncbi.nlm.nih.gov/21873635/)
9. Navarro JA, Botella JA, Metzendorf C, Lind MI, Schneuwly S. Mitoferrin modulates iron toxicity in a *Drosophila* model of Friedreich's ataxia. *Free Radic Biol Med.* 2015; 85:71–82.  
<https://doi.org/10.1016/j.freeradbiomed.2015.03.014>  
PMID:[25841783](https://pubmed.ncbi.nlm.nih.gov/25841783/)
10. Anderson PR, Kirby K, Orr WC, Hilliker AJ, Phillips JP. Hydrogen peroxide scavenging rescues frataxin deficiency in a *Drosophila* model of Friedreich's ataxia. *Proc Natl Acad Sci USA.* 2008; 105:611–16.  
<https://doi.org/10.1073/pnas.0709691105>  
PMID:[18184803](https://pubmed.ncbi.nlm.nih.gov/18184803/)
11. Guccini I, Serio D, Condò I, Rufini A, Tomassini B, Mangiola A, Maira G, Anile C, Fina D, Pallone F, Mongiardi MP, Levi A, Ventura N, et al. Frataxin participates to the hypoxia-induced response in tumors. *Cell Death Dis.* 2011; 2:e123.  
<https://doi.org/10.1038/cddis.2011.5>  
PMID:[21368894](https://pubmed.ncbi.nlm.nih.gov/21368894/)
12. Runko AP, Griswold AJ, Min KT. Overexpression of frataxin in the mitochondria increases resistance to oxidative stress and extends lifespan in *Drosophila*. *FEBS Lett.* 2008; 582:715–19.  
<https://doi.org/10.1016/j.febslet.2008.01.046>  
PMID:[18258192](https://pubmed.ncbi.nlm.nih.gov/18258192/)
13. Peretz G, Bakhrat A, Abdu U. Expression of the *Drosophila melanogaster* GADD45 homolog (CG11086) affects egg asymmetric development that is mediated by the c-Jun N-terminal kinase pathway. *Genetics.* 2007; 177:1691–702.  
<https://doi.org/10.1534/genetics.107.079517>  
PMID:[18039880](https://pubmed.ncbi.nlm.nih.gov/18039880/)
14. Liebermann DA, Hoffman B. Gadd45 in the response of hematopoietic cells to genotoxic stress. *Blood Cells Mol Dis.* 2007; 39:329–35.  
<https://doi.org/10.1016/j.bcmd.2007.06.006>  
PMID:[17659913](https://pubmed.ncbi.nlm.nih.gov/17659913/)
15. Moskalev A, Plyusnina E, Shaposhnikov M, Shilova L, Kazachenok A, Zhavoronkov A. The role of D-GADD45 in oxidative, thermal and genotoxic stress resistance. *Cell Cycle.* 2012; 11:4222–41.  
<https://doi.org/10.4161/cc.22545>  
PMID:[23095639](https://pubmed.ncbi.nlm.nih.gov/23095639/)
16. Plyusnina EN, Shaposhnikov MV, Moskalev AA. Increase of *Drosophila melanogaster* lifespan due to D-GADD45 overexpression in the nervous system. *Biogerontology.* 2011; 12:211–26.  
<https://doi.org/10.1007/s10522-010-9311-6>  
PMID:[21153055](https://pubmed.ncbi.nlm.nih.gov/21153055/)
17. De Maio A. Heat shock proteins: facts, thoughts, and dreams. *Shock.* 1999; 11:1–12.  
<https://doi.org/10.1097/00024382-199901000-00001>  
PMID:[9921710](https://pubmed.ncbi.nlm.nih.gov/9921710/)
18. Biteau B, Karpac J, Supoyo S, Degennaro M, Lehmann R, Jasper H. Lifespan extension by preserving

- proliferative homeostasis in drosophila. *PLoS Genet.* 2010; 6:e1001159.  
<https://doi.org/10.1371/journal.pgen.1001159>  
PMID:[20976250](https://pubmed.ncbi.nlm.nih.gov/20976250/)
19. Wang MC, Bohmann D, Jasper H. JNK signaling confers tolerance to oxidative stress and extends lifespan in drosophila. *Dev Cell.* 2003; 5:811–16.  
[https://doi.org/10.1016/s1534-5807\(03\)00323-x](https://doi.org/10.1016/s1534-5807(03)00323-x)  
PMID:[14602080](https://pubmed.ncbi.nlm.nih.gov/14602080/)
  20. Neal SJ, Karunanithi S, Best A, So AK, Tanguay RM, Atwood HL, Westwood JT. Thermoprotection of synaptic transmission in a drosophila heat shock factor mutant is accompanied by increased expression of Hsp83 and DnaJ-1. *Physiol Genomics.* 2006; 25:493–501.  
<https://doi.org/10.1152/physiolgenomics.00195.2005>  
PMID:[16595740](https://pubmed.ncbi.nlm.nih.gov/16595740/)
  21. Landis G, Shen J, Tower J. Gene expression changes in response to aging compared to heat stress, oxidative stress and ionizing radiation in drosophila melanogaster. *Aging (Albany NY).* 2012; 4:768–89.  
<https://doi.org/10.18632/aging.100499>  
PMID:[23211361](https://pubmed.ncbi.nlm.nih.gov/23211361/)
  22. Singh MP, Reddy MM, Mathur N, Saxena DK, Chowdhuri DK. Induction of hsp70, hsp60, hsp83 and hsp26 and oxidative stress markers in benzene, toluene and xylene exposed *Drosophila melanogaster*: role of ROS generation. *Toxicol Appl Pharmacol.* 2009; 235:226–43.  
<https://doi.org/10.1016/j.taap.2008.12.002>  
PMID:[19118569](https://pubmed.ncbi.nlm.nih.gov/19118569/)
  23. Shaw PJ, Franken P. Perchance to dream: solving the mystery of sleep through genetic analysis. *J Neurobiol.* 2003; 54:179–202.  
<https://doi.org/10.1002/neu.10167> PMID:[12486704](https://pubmed.ncbi.nlm.nih.gov/12486704/)
  24. Postow L, Ghenoiu C, Woo EM, Krutchinsky AN, Chait BT, Funabiki H. Ku80 removal from DNA through double strand break-induced ubiquitylation. *J Cell Biol.* 2008; 182:467–79.  
<https://doi.org/10.1083/jcb.200802146>  
PMID:[18678709](https://pubmed.ncbi.nlm.nih.gov/18678709/)
  25. Zhang C, Hong Z, Ma W, Ma D, Qian Y, Xie W, Tie F, Fang M. *Drosophila* UTX coordinates with p53 to regulate ku80 expression in response to DNA damage. *PLoS One.* 2013; 8:e78652.  
<https://doi.org/10.1371/journal.pone.0078652>  
PMID:[24265704](https://pubmed.ncbi.nlm.nih.gov/24265704/)
  26. Vogel H, Lim DS, Karsenty G, Finegold M, Hasty P. Deletion of Ku86 causes early onset of senescence in mice. *Proc Natl Acad Sci USA.* 1999; 96:10770–75.  
<https://doi.org/10.1073/pnas.96.19.10770>  
PMID:[10485901](https://pubmed.ncbi.nlm.nih.gov/10485901/)
  27. Holcomb VB, Rodier F, Choi Y, Busuttill RA, Vogel H, Vijg J, Campisi J, Hasty P. Ku80 deletion suppresses spontaneous tumors and induces a p53-mediated DNA damage response. *Cancer Res.* 2008; 68:9497–502.  
<https://doi.org/10.1158/0008-5472.CAN-08-2085>  
PMID:[19010925](https://pubmed.ncbi.nlm.nih.gov/19010925/)
  28. Knoop B, Goemaere J, Van der Eecken V, Declercq JP. Peroxiredoxin 5: structure, mechanism, and function of the mammalian atypical 2-Cys peroxiredoxin. *Antioxid Redox Signal.* 2011; 15:817–29.  
<https://doi.org/10.1089/ars.2010.3584>  
PMID:[20977338](https://pubmed.ncbi.nlm.nih.gov/20977338/)
  29. Poole LB, Hall A, Nelson KJ. Overview of peroxiredoxins in oxidant defense and redox regulation. *Curr Protoc Toxicol.* 2011; Unit7.9.  
<https://doi.org/10.1002/0471140856.tx0709s49>  
PMID:[21818754](https://pubmed.ncbi.nlm.nih.gov/21818754/)
  30. Radyuk SN, Michalak K, Klichko VI, Benes J, Rebrin I, Sohal RS, Orr WC. Peroxiredoxin 5 confers protection against oxidative stress and apoptosis and also promotes longevity in drosophila. *Biochem J.* 2009; 419:437–45.  
<https://doi.org/10.1042/BJ20082003>  
PMID:[19128239](https://pubmed.ncbi.nlm.nih.gov/19128239/)