

**Table S4.** List of Significantly Altered Biological Processes in Hypoxia-Selected *Drosophila melanogaster* at Adult Stage

| GOID  | GO Name                                                                                                     | Number Changed | Number Measured | Number in GO | % Changed | % Present | p value |
|-------|-------------------------------------------------------------------------------------------------------------|----------------|-----------------|--------------|-----------|-----------|---------|
| 46683 | response to organophosphorus                                                                                | 1              | 1               | 1            | 100.00    | 100.00    | 0.011   |
| 18130 | heterocycle biosynthetic process                                                                            | 1              | 1               | 1            | 100.00    | 100.00    | 0.017   |
| 19428 | allantoin biosynthetic process                                                                              | 1              | 1               | 1            | 100.00    | 100.00    | 0.017   |
| 255   | allantoin metabolic process                                                                                 | 1              | 1               | 1            | 100.00    | 100.00    | 0.017   |
| 6964  | positive regulation of biosynthetic process of antibacterial peptides active against Gram-negative bacteria | 1              | 1               | 1            | 100.00    | 100.00    | 0.019   |
| 2813  | regulation of biosynthetic process of antibacterial peptides active against Gram-negative bacteria          | 1              | 1               | 1            | 100.00    | 100.00    | 0.019   |
| 2812  | biosynthetic process of antibacterial peptides active against Gram-negative bacteria                        | 1              | 1               | 1            | 100.00    | 100.00    | 0.019   |
| 30104 | water homeostasis                                                                                           | 1              | 1               | 1            | 100.00    | 100.00    | 0.019   |
| 7000  | nucleolus organization and biogenesis                                                                       | 1              | 1               | 1            | 100.00    | 100.00    | 0.020   |
| 35160 | maintenance of epithelial integrity\, open tracheal system                                                  | 1              | 1               | 2            | 100.00    | 50.00     | 0.020   |
| 51295 | establishment of meiotic spindle localization                                                               | 1              | 1               | 1            | 100.00    | 100.00    | 0.020   |
| 35080 | heat shock-mediated polytene chromosome puffing                                                             | 1              | 1               | 1            | 100.00    | 100.00    | 0.020   |
| 35079 | polytene chromosome puffing                                                                                 | 1              | 1               | 1            | 100.00    | 100.00    | 0.020   |
| 46958 | nonassociative learning                                                                                     | 1              | 1               | 1            | 100.00    | 100.00    | 0.022   |
| 7029  | endoplasmic reticulum organization and biogenesis                                                           | 1              | 1               | 1            | 100.00    | 100.00    | 0.023   |
| 9229  | thiamin diphosphate biosynthetic process                                                                    | 1              | 1               | 1            | 100.00    | 100.00    | 0.025   |
| 42724 | thiamin and derivative biosynthetic process                                                                 | 1              | 1               | 1            | 100.00    | 100.00    | 0.025   |
| 6772  | thiamin metabolic process                                                                                   | 1              | 1               | 1            | 100.00    | 100.00    | 0.025   |
| 42357 | thiamin diphosphate metabolic process                                                                       | 1              | 1               | 1            | 100.00    | 100.00    | 0.025   |
| 42723 | thiamin and derivative metabolic process                                                                    | 1              | 1               | 1            | 100.00    | 100.00    | 0.025   |
| 6961  | antibacterial humoral response                                                                              | 9              | 13              | 19           | 69.23     | 68.42     | 0.000   |
| 6805  | xenobiotic metabolic process                                                                                | 3              | 5               | 5            | 60.00     | 100.00    | 0.000   |
| 9410  | response to xenobiotic stimulus                                                                             | 3              | 5               | 5            | 60.00     | 100.00    | 0.000   |
| 19835 | cytolysis                                                                                                   | 4              | 7               | 9            | 57.14     | 77.78     | 0.000   |
| 19732 | antifungal humoral response                                                                                 | 5              | 9               | 9            | 55.56     | 100.00    | 0.000   |
| 50829 | defense response to Gram-negative bacterium                                                                 | 5              | 10              | 14           | 50.00     | 71.43     | 0.000   |

|       |                                                                   |    |    |    |       |        |       |
|-------|-------------------------------------------------------------------|----|----|----|-------|--------|-------|
| 6966  | antifungal humoral response                                       | 4  | 8  | 8  | 50.00 | 100.00 | 0.000 |
| 9405  | pathogenesis                                                      | 2  | 4  | 4  | 50.00 | 100.00 | 0.004 |
| 44403 | symbiosis\, encompassing mutualism through parasitism             | 2  | 4  | 4  | 50.00 | 100.00 | 0.004 |
| 44419 | interspecies interaction between organisms                        | 2  | 4  | 4  | 50.00 | 100.00 | 0.004 |
| 46680 | response to DDT                                                   | 1  | 2  | 2  | 50.00 | 100.00 | 0.026 |
| 18987 | osmoregulation                                                    | 1  | 2  | 2  | 50.00 | 100.00 | 0.030 |
| 8627  | induction of apoptosis by ionic changes                           | 1  | 2  | 2  | 50.00 | 100.00 | 0.033 |
| 48132 | female germ-line stem cell division                               | 1  | 2  | 2  | 50.00 | 100.00 | 0.034 |
| 46131 | pyrimidine ribonucleoside metabolic process                       | 1  | 2  | 2  | 50.00 | 100.00 | 0.036 |
| 46087 | cytidine metabolic process                                        | 1  | 2  | 2  | 50.00 | 100.00 | 0.036 |
| 9303  | rRNA transcription                                                | 1  | 2  | 2  | 50.00 | 100.00 | 0.037 |
| 8306  | associative learning                                              | 1  | 2  | 2  | 50.00 | 100.00 | 0.037 |
| 42742 | defense response to bacterium                                     | 17 | 36 | 45 | 47.22 | 80.00  | 0.000 |
| 9617  | response to bacterium                                             | 17 | 37 | 47 | 45.95 | 78.72  | 0.000 |
| 50830 | defense response to Gram-positive bacterium                       | 5  | 11 | 16 | 45.45 | 68.75  | 0.000 |
| 6967  | positive regulation of antifungal peptide biosynthetic process    | 3  | 7  | 7  | 42.86 | 100.00 | 0.000 |
| 2810  | regulation of antifungal peptide biosynthetic process             | 3  | 7  | 7  | 42.86 | 100.00 | 0.000 |
| 2783  | antifungal peptide biosynthetic process                           | 3  | 7  | 7  | 42.86 | 100.00 | 0.000 |
| 2781  | antifungal peptide production                                     | 3  | 7  | 7  | 42.86 | 100.00 | 0.000 |
| 50832 | defense response to fungus                                        | 5  | 12 | 12 | 41.67 | 100.00 | 0.000 |
| 19730 | antimicrobial humoral response                                    | 13 | 32 | 41 | 40.63 | 78.05  | 0.000 |
| 16998 | cell wall catabolic process                                       | 4  | 10 | 12 | 40.00 | 83.33  | 0.000 |
| 9620  | response to fungus                                                | 5  | 13 | 13 | 38.46 | 100.00 | 0.000 |
| 6959  | humoral immune response                                           | 13 | 35 | 45 | 37.14 | 77.78  | 0.000 |
| 19731 | antibacterial humoral response                                    | 5  | 14 | 18 | 35.71 | 77.78  | 0.000 |
| 51707 | response to other organism                                        | 17 | 48 | 58 | 35.42 | 82.76  | 0.000 |
| 6963  | positive regulation of antibacterial peptide biosynthetic process | 4  | 12 | 13 | 33.33 | 92.31  | 0.000 |
| 2808  | regulation of antibacterial peptide biosynthetic process          | 4  | 12 | 13 | 33.33 | 92.31  | 0.000 |
| 2780  | antibacterial peptide biosynthetic process                        | 4  | 12 | 13 | 33.33 | 92.31  | 0.000 |
| 2778  | antibacterial peptide production                                  | 4  | 12 | 13 | 33.33 | 92.31  | 0.000 |
| 17085 | response to insecticide                                           | 1  | 3  | 3  | 33.33 | 100.00 | 0.044 |

|       |                                                                   |    |    |    |       |        |       |
|-------|-------------------------------------------------------------------|----|----|----|-------|--------|-------|
| 42423 | catecholamine biosynthetic process                                | 1  | 3  | 3  | 33.33 | 100.00 | 0.053 |
| 8624  | induction of apoptosis by extracellular signals                   | 1  | 3  | 3  | 33.33 | 100.00 | 0.056 |
| 6596  | polyamine biosynthetic process                                    | 1  | 3  | 3  | 33.33 | 100.00 | 0.059 |
| 6685  | sphingomyelin catabolic process                                   | 1  | 3  | 3  | 33.33 | 100.00 | 0.061 |
| 9395  | phospholipid catabolic process                                    | 1  | 3  | 3  | 33.33 | 100.00 | 0.061 |
| 51227 | mitotic spindle assembly                                          | 1  | 3  | 3  | 33.33 | 100.00 | 0.067 |
| 45087 | innate immune response                                            | 12 | 40 | 54 | 30.00 | 74.07  | 0.000 |
| 2807  | positive regulation of antimicrobial peptide biosynthetic process | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 43043 | peptide biosynthetic process                                      | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 2805  | regulation of antimicrobial peptide biosynthetic process          | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 2440  | production of molecular mediator of immune response               | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 2775  | antimicrobial peptide production                                  | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 2777  | antimicrobial peptide biosynthetic process                        | 5  | 17 | 18 | 29.41 | 94.44  | 0.000 |
| 2252  | immune effector process                                           | 5  | 18 | 22 | 27.78 | 81.82  | 0.000 |
| 6952  | defense response                                                  | 19 | 69 | 87 | 27.54 | 79.31  | 0.000 |
| 6960  | antimicrobial humoral response                                    | 1  | 4  | 4  | 25.00 | 100.00 | 0.058 |
| 6835  | dicarboxylic acid transport                                       | 1  | 4  | 4  | 25.00 | 100.00 | 0.063 |
| 30723 | ovarian fusome organization and biogenesis                        | 1  | 4  | 5  | 25.00 | 80.00  | 0.069 |
| 6213  | pyrimidine nucleoside metabolic process                           | 1  | 4  | 4  | 25.00 | 100.00 | 0.071 |
| 7352  | zygotic determination of dorsal/ventral axis                      | 1  | 4  | 4  | 25.00 | 100.00 | 0.071 |
| 6826  | iron ion transport                                                | 1  | 4  | 4  | 25.00 | 100.00 | 0.074 |
| 6684  | sphingomyelin metabolic process                                   | 1  | 4  | 4  | 25.00 | 100.00 | 0.078 |
| 42045 | epithelial fluid transport                                        | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 22401 | adaptation of signaling pathway                                   | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 16062 | adaptation of rhodopsin mediated signaling                        | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 42044 | fluid transport                                                   | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 46466 | membrane lipid catabolic process                                  | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 30149 | sphingolipid catabolic process                                    | 1  | 4  | 4  | 25.00 | 100.00 | 0.079 |
| 6595  | polyamine metabolic process                                       | 1  | 4  | 4  | 25.00 | 100.00 | 0.081 |
| 6144  | purine base metabolic process                                     | 1  | 4  | 5  | 25.00 | 80.00  | 0.087 |
| 9951  | polarity specification of dorsal/ventral axis                     | 1  | 4  | 5  | 25.00 | 80.00  | 0.093 |

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|-------|----------------------------------------------------------------------------|----|-----|-----|-------|--------|-------|
| 65001 | specification of axis polarity                                             | 1  | 4   | 5   | 25.00 | 80.00  | 0.093 |
| 9949  | polarity specification of anterior/posterior axis                          | 1  | 4   | 5   | 25.00 | 80.00  | 0.093 |
| 9607  | response to biotic stimulus                                                | 18 | 80  | 96  | 22.50 | 83.33  | 0.000 |
| 6955  | immune response                                                            | 14 | 66  | 83  | 21.21 | 79.52  | 0.000 |
| 6518  | peptide metabolic process                                                  | 5  | 24  | 25  | 20.83 | 96.00  | 0.000 |
| 30037 | actin filament reorganization during cell cycle                            | 1  | 5   | 5   | 20.00 | 100.00 | 0.093 |
| 42401 | biogenic amine biosynthetic process                                        | 2  | 11  | 11  | 18.18 | 100.00 | 0.020 |
| 7311  | maternal determination of dorsal/ventral axis\, oocyte\, germ-line encoded | 1  | 6   | 6   | 16.67 | 100.00 | 0.098 |
| 42398 | amino acid derivative biosynthetic process                                 | 2  | 13  | 13  | 15.38 | 100.00 | 0.024 |
| 2376  | immune system process                                                      | 15 | 104 | 123 | 14.42 | 84.55  | 0.000 |
| 6997  | nuclear organization and biogenesis                                        | 2  | 16  | 16  | 12.50 | 100.00 | 0.040 |
| 6917  | induction of apoptosis                                                     | 2  | 16  | 16  | 12.50 | 100.00 | 0.042 |
| 8063  | Toll signaling pathway                                                     | 3  | 25  | 28  | 12.00 | 89.29  | 0.004 |
| 6633  | fatty acid biosynthetic process                                            | 2  | 17  | 19  | 11.76 | 89.47  | 0.044 |
| 46394 | carboxylic acid biosynthetic process                                       | 2  | 18  | 20  | 11.11 | 90.00  | 0.047 |
| 16053 | organic acid biosynthetic process                                          | 2  | 18  | 20  | 11.11 | 90.00  | 0.047 |
| 7317  | regulation of pole plasm oskar mRNA localization                           | 2  | 18  | 18  | 11.11 | 100.00 | 0.049 |
| 9116  | nucleoside metabolic process                                               | 2  | 19  | 20  | 10.53 | 95.00  | 0.045 |
| 43065 | positive regulation of apoptosis                                           | 2  | 19  | 19  | 10.53 | 100.00 | 0.054 |
| 51704 | multi-organism process                                                     | 4  | 42  | 47  | 9.52  | 89.36  | 0.009 |
| 48878 | chemical homeostasis                                                       | 2  | 21  | 21  | 9.52  | 100.00 | 0.054 |
| 30706 | oocyte differentiation (sensu Insecta)                                     | 2  | 22  | 23  | 9.09  | 95.65  | 0.076 |
| 12502 | induction of programmed cell death                                         | 2  | 22  | 22  | 9.09  | 100.00 | 0.076 |
| 6030  | chitin metabolic process                                                   | 8  | 90  | 109 | 8.89  | 82.57  | 0.000 |
| 6044  | N-acetylglucosamine metabolic process                                      | 8  | 95  | 114 | 8.42  | 83.33  | 0.002 |
| 6040  | amino sugar metabolic process                                              | 8  | 95  | 114 | 8.42  | 83.33  | 0.002 |
| 6041  | glucosamine metabolic process                                              | 8  | 95  | 114 | 8.42  | 83.33  | 0.002 |
| 6631  | fatty acid metabolic process                                               | 3  | 36  | 38  | 8.33  | 94.74  | 0.025 |
| 6576  | biogenic amine metabolic process                                           | 2  | 24  | 26  | 8.33  | 92.31  | 0.065 |
| 5976  | polysaccharide metabolic process                                           | 8  | 102 | 122 | 7.84  | 83.61  | 0.002 |

|       |                                           |    |     |     |      |       |       |
|-------|-------------------------------------------|----|-----|-----|------|-------|-------|
| 44264 | cellular polysaccharide metabolic process | 8  | 102 | 122 | 7.84 | 83.61 | 0.002 |
| 6575  | amino acid derivative metabolic process   | 2  | 27  | 29  | 7.41 | 93.10 | 0.083 |
| 8298  | intracellular mRNA localization           | 3  | 41  | 42  | 7.32 | 97.62 | 0.043 |
| 7293  | egg chamber formation (sensu Insecta)     | 3  | 42  | 46  | 7.14 | 91.30 | 0.046 |
| 32787 | monocarboxylic acid metabolic process     | 3  | 45  | 48  | 6.67 | 93.75 | 0.047 |
| 9950  | dorsal/ventral axis specification         | 3  | 46  | 48  | 6.52 | 95.83 | 0.064 |
| 9994  | oocyte differentiation                    | 5  | 79  | 83  | 6.33 | 95.18 | 0.020 |
| 6403  | RNA localization                          | 3  | 55  | 59  | 5.45 | 93.22 | 0.088 |
| 50896 | response to stimulus                      | 26 | 518 | 584 | 5.02 | 88.70 | 0.000 |
| 8219  | cell death                                | 7  | 143 | 155 | 4.90 | 92.26 | 0.019 |
| 16265 | death                                     | 7  | 144 | 156 | 4.86 | 92.31 | 0.021 |
| 5975  | carbohydrate metabolic process            | 15 | 317 | 349 | 4.73 | 90.83 | 0.002 |
| 9308  | amine metabolic process                   | 11 | 237 | 270 | 4.64 | 87.78 | 0.008 |
| 6807  | nitrogen compound metabolic process       | 11 | 243 | 279 | 4.53 | 87.10 | 0.008 |
| 44249 | cellular biosynthetic process             | 14 | 317 | 342 | 4.42 | 92.69 | 0.006 |
| 6629  | lipid metabolic process                   | 8  | 189 | 206 | 4.23 | 91.75 | 0.030 |
| 44262 | cellular carbohydrate metabolic process   | 9  | 213 | 240 | 4.23 | 88.75 | 0.031 |
| 9056  | catabolic process                         | 11 | 267 | 282 | 4.12 | 94.68 | 0.014 |
| 42221 | response to chemical stimulus             | 6  | 147 | 161 | 4.08 | 91.30 | 0.058 |
| 9798  | axis specification                        | 5  | 126 | 133 | 3.97 | 94.74 | 0.090 |