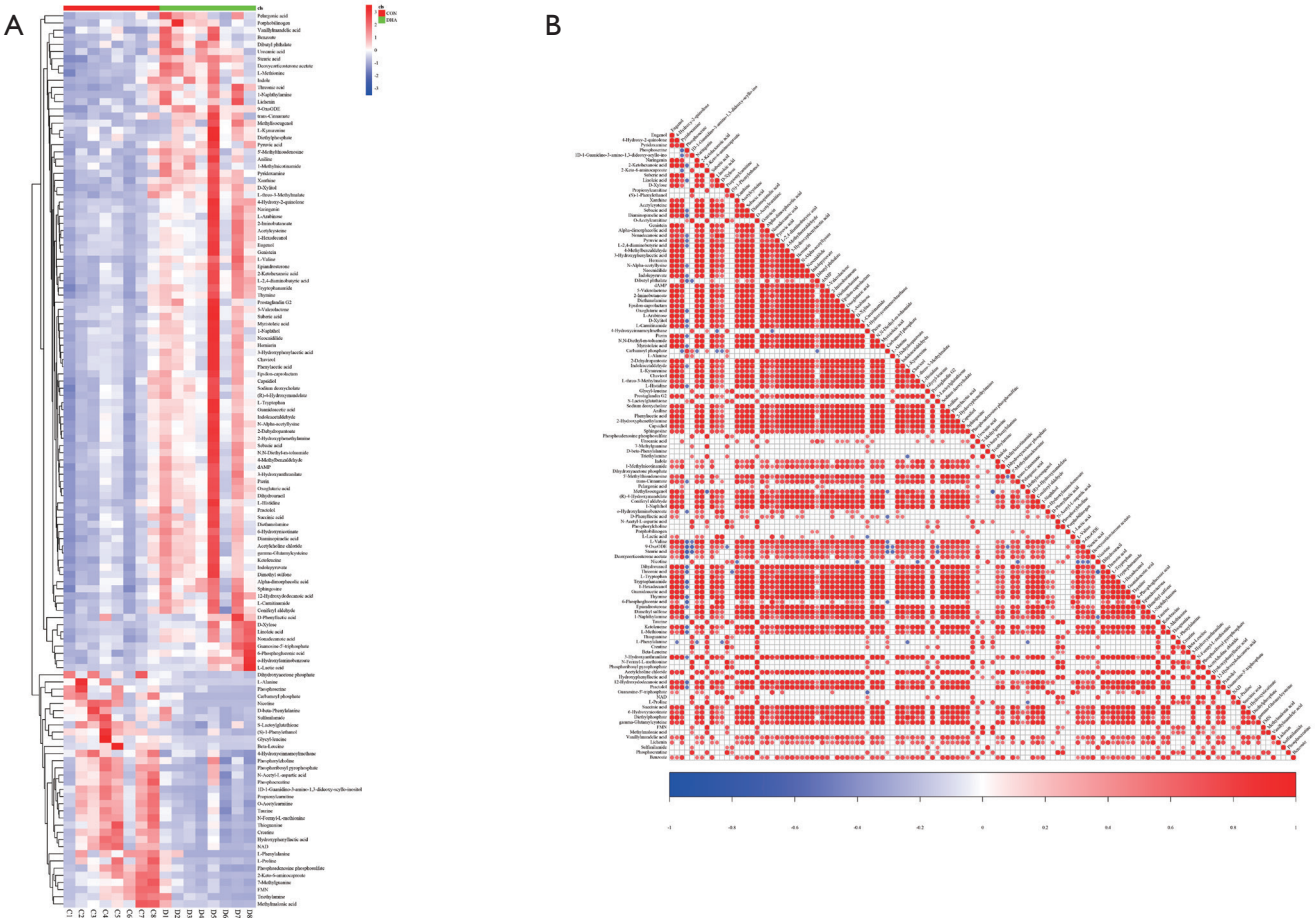


**Figure S1** Comparison of metabolome between DHA group and control group. (A) Heat map showing significantly changed metabolites in the control and DHA administration groups. (B) Differential metabolite-associated heat map of significantly altered metabolites arranged according to direction of change by DHA in SH-SY5Y cells. DHA, dihydroartemisinin; cls, cluster.


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**Table S1** The list of 125 metabolites that changed significantly after cells were treated with DHA

| Metabolite | Variable importance in the project | Fold change control/DHA | P value | False discovery rate |
|---|---|---|---|---|
| 1-Naphthylamine | 1.6 | 0.18 | 0.00538 | 0.0416 |
| L-lactic acid | 1.3 | 0.20 | 0.00094 | 0.0284 |
| D-dylose | 1.5 | 0.23 | 0.00195 | 0.0370 |
| L-kynurenine | 1.3 | 0.26 | 0.00741 | 0.0549 |
| 9-OxoODE | 1.9 | 0.28 | 0.00094 | 0.0284 |
| Dibutyl phthalate | 1.7 | 0.30 | 0.00388 | 0.0432 |
| 6-Phosphogluconic acid | 1.5 | 0.30 | 0.00388 | 0.0357 |
| Methyl isoeugenol | 1.5 | 0.32 | 0.03132 | 0.1202 |
| Pelargonic acid | 1.4 | 0.33 | 0.03132 | 0.1202 |
| Linoleic acid | 1.8 | 0.33 | 0.00136 | 0.0349 |
| 4-Hydroxy-2-quinolone | 1.6 | 0.33 | 0.00094 | 0.0349 |
| Naringenin | 1.5 | 0.33 | 0.00094 | 0.0349 |
| L-valine | 1.9 | 0.34 | 0.00094 | 0.0284 |
| Stearic acid | 2.0 | 0.35 | 0.00195 | 0.0284 |
| Eugenol | 1.5 | 0.35 | 0.00094 | 0.0349 |
| 2-Iminobutanoate | 1.4 | 0.35 | 0.00538 | 0.0489 |
| Deoxycorticosterone acetate | 1.7 | 0.36 | 0.00195 | 0.0284 |
| Indole | 1.3 | 0.36 | 0.02395 | 0.1005 |
| L-threo-3-methylmalate | 1.4 | 0.36 | 0.01008 | 0.0642 |
| Xanthine | 1.8 | 0.36 | 0.00276 | 0.0401 |
| Urocanic acid | 1.6 | 0.36 | 0.01813 | 0.0855 |
| Threonic acid | 1.7 | 0.38 | 0.00276 | 0.0314 |
| Diethylphosphate | 1.2 | 0.38 | 0.01359 | 0.0654 |
| 5-Valerolactone | 1.4 | 0.38 | 0.00538 | 0.0489 |
| Suberic acid | 1.4 | 0.39 | 0.00136 | 0.0349 |
| D-phenyllactic acid | 1.1 | 0.39 | 0.04057 | 0.1405 |
| Guanosine-5'-triphosphate | 1.3 | 0.40 | 0.01008 | 0.0566 |
| Benzoate | 1.2 | 0.40 | 0.04057 | 0.1263 |
| L-arabinose | 1.5 | 0.41 | 0.00538 | 0.0489 |
| Aniline | 1.5 | 0.41 | 0.01359 | 0.0735 |
| Myristoleic acid | 1.5 | 0.41 | 0.00538 | 0.0489 |
| 12-Hydroxydodecanoic acid | 1.6 | 0.41 | 0.01008 | 0.0566 |
| Nonadecanoic acid | 1.8 | 0.41 | 0.00276 | 0.0401 |
| 3-Hydroxyphenylacetic acid | 1.5 | 0.41 | 0.00388 | 0.0432 |
| Genistein | 1.4 | 0.42 | 0.00276 | 0.0401 |
| Trans-cinnamate | 1.3 | 0.42 | 0.03132 | 0.1202 |
| Pyruvic acid | 1.6 | 0.42 | 0.00388 | 0.0432 |
| o-Hydroxylaminobenzoate | 1.3 | 0.42 | 0.04057 | 0.1405 |
| 1-Hexadecanol | 1.5 | 0.43 | 0.00276 | 0.0314 |
| Acetylcysteine | 1.6 | 0.43 | 0.00276 | 0.0401 |
| Practolol | 1.4 | 0.43 | 0.01008 | 0.0566 |
| 2-Ketohexanoic acid | 1.7 | 0.44 | 0.00136 | 0.0349 |
| Chavicol | 1.4 | 0.44 | 0.01008 | 0.0642 |
| Herniarin | 1.4 | 0.44 | 0.00388 | 0.0432 |
| Tryptophanamide | 1.7 | 0.45 | 0.00276 | 0.0314 |
| Dihydrouracil | 1.7 | 0.45 | 0.00276 | 0.0314 |
| Epiandrosterone | 1.6 | 0.45 | 0.00388 | 0.0357 |
| Indolepyruvate | 1.6 | 0.46 | 0.00388 | 0.0432 |
| L-carnitinamide | 1.7 | 0.46 | 0.00538 | 0.0489 |
| Vanillylmandelic acid | 1.4 | 0.46 | 0.01813 | 0.0779 |
| Alpha-dimorphecolic acid | 1.7 | 0.46 | 0.00276 | 0.0401 |
| Phenylacetic acid | 1.4 | 0.47 | 0.01359 | 0.0735 |
| 1-Methylnicotinamide | 1.4 | 0.47 | 0.02395 | 0.1005 |
| 5'-Methylthioadenosine | 1.4 | 0.47 | 0.02395 | 0.1005 |
| Sebacic acid | 1.6 | 0.47 | 0.00276 | 0.0401 |
| Thymine | 1.7 | 0.48 | 0.00388 | 0.0357 |
| 4-Methylbenzaldehyde | 1.5 | 0.48 | 0.00388 | 0.0432 |
| Prostaglandin G2 | 1.4 | 0.48 | 0.01008 | 0.0642 |
| Pyridoxamine | 1.9 | 0.49 | 0.00094 | 0.0349 |
| Pterin | 1.6 | 0.49 | 0.00538 | 0.0489 |
| D-xylitol | 1.8 | 0.50 | 0.00538 | 0.0489 |
| Diaminopimelic acid | 1.7 | 0.50 | 0.00276 | 0.0401 |
| 3-Hydroxyanthranilate | 1.5 | 0.50 | 0.00741 | 0.0480 |
| 1-Naphthol | 1.2 | 0.50 | 0.04057 | 0.1405 |
| Diethanolamine | 1.6 | 0.50 | 0.00538 | 0.0489 |
| Oxoglutaric acid | 1.7 | 0.50 | 0.00538 | 0.0489 |

**Table S1** (*continued*)


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**Table S1** (*continued*)

| Metabolite | Variable importance in the project | Fold change control/DHA | P value | False discovery rate |
|---|---|---|---|---|
| Ketoleucine | 1.6 | 0.51 | 0.00538 | 0.0416 |
| L-tryptophan | 1.5 | 0.51 | 0.00276 | 0.0314 |
| Neocnidilide | 1.4 | 0.51 | 0.00388 | 0.0432 |
| L-2,4-diaminobutyric acid | 1.6 | 0.51 | 0.00388 | 0.0432 |
| Gamma-glutamylcysteine | 1.4 | 0.52 | 0.01359 | 0.0654 |
| Epsilon-caprolactam | 1.3 | 0.52 | 0.00538 | 0.0489 |
| L-methionine | 1.6 | 0.52 | 0.00538 | 0.0416 |
| N-alpha-acetyllysine | 1.6 | 0.53 | 0.00388 | 0.0432 |
| Dimethyl sulfone | 1.5 | 0.53 | 0.00538 | 0.0416 |
| N,N-Diethyl-m-toluamide | 1.4 | 0.53 | 0.00538 | 0.0489 |
| 6-Hydroxynicotinate | 1.5 | 0.53 | 0.01359 | 0.0654 |
| Porphobilinogen | 1.2 | 0.53 | 0.04057 | 0.1405 |
| 2-Dehydropantoate | 1.5 | 0.53 | 0.00741 | 0.0549 |
| dAMP | 1.6 | 0.53 | 0.00388 | 0.0432 |
| Acetylcholine chloride | 1.4 | 0.53 | 0.01008 | 0.0566 |
| Guanidoacetic acid | 1.5 | 0.54 | 0.00388 | 0.0357 |
| Lichenin | 1.3 | 0.54 | 0.03132 | 0.1072 |
| L-Histidine | 1.5 | 0.54 | 0.01008 | 0.0642 |
| Sodium deoxycholate | 1.5 | 0.55 | 0.01008 | 0.0642 |
| Coniferyl aldehyde | 1.4 | 0.57 | 0.03132 | 0.1202 |
| Succinic acid | 1.3 | 0.58 | 0.01359 | 0.0654 |
| 2-Hydroxyphenethylamine | 1.4 | 0.58 | 0.01359 | 0.0735 |
| Capsidiol | 1.4 | 0.58 | 0.01359 | 0.0735 |
| Sphingosine | 1.7 | 0.58 | 0.01359 | 0.0735 |
| Indoleacetaldehyde | 1.5 | 0.60 | 0.00741 | 0.0549 |
| (R)-4-hydroxymandelate | 1.3 | 0.61 | 0.03132 | 0.1202 |
| Phosphorylcholine | 1.2 | 1.46 | 0.04057 | 0.1405 |
| N-acetyl-L-aspartic acid | 1.3 | 1.56 | 0.04057 | 0.1405 |
| Phosphocreatine | 1.4 | 1.89 | 0.03132 | 0.1072 |
| Taurine | 1.7 | 2.05 | 0.00538 | 0.0416 |
| S-lactoylglutathione | 1.7 | 2.08 | 0.01008 | 0.0642 |
| Sulfanilamide | 1.0 | 2.15 | 0.03132 | 0.1072 |
| D-beta-phenylalanine | 1.1 | 2.18 | 0.01813 | 0.0855 |
| O-acetylcarnitine | 1.9 | 2.34 | 0.00276 | 0.0401 |
| Phosphoribosyl pyrophosphate | 1.5 | 2.42 | 0.00741 | 0.0480 |
| 4-Hydroxycinnamoylmethane | 1.7 | 2.55 | 0.00538 | 0.0489 |
| N-formyl-L-methionine | 1.7 | 2.59 | 0.00741 | 0.0480 |
| Hydroxyphenyllactic acid | 1.6 | 2.61 | 0.01008 | 0.0566 |
| Triethylamine | 1.2 | 2.66 | 0.02395 | 0.1005 |
| Propionylcarnitine | 1.9 | 2.73 | 0.00195 | 0.0370 |
| 7-Methylguanine | 1.4 | 2.90 | 0.01813 | 0.0855 |
| Creatine | 1.7 | 2.90 | 0.00741 | 0.0480 |
| Phosphoadenosine phosphosulfate | 1.6 | 3.05 | 0.01359 | 0.0735 |
| Methylmalonic acid | 1.1 | 3.16 | 0.01813 | 0.0779 |
| FMN | 1.4 | 3.89 | 0.01359 | 0.0654 |
| 1D-1-guanidino-3-amino-1,3-dideoxy-scyllo-inositol | 2.1 | 4.14 | 0.00094 | 0.0349 |
| Thioguanine | 1.5 | 4.24 | 0.00538 | 0.0416 |
| L-phenylalanine | 1.5 | 4.36 | 0.00596 | 0.0459 |
| NAD | 1.6 | 4.71 | 0.01008 | 0.0566 |
| Dihydroxyacetone phosphate | 1.4 | 5.16 | 0.02395 | 0.1005 |
| (S)-1-phenylethanol | 1.6 | 5.18 | 0.00276 | 0.0401 |
| Beta-leucine | 1.1 | 5.31 | 0.00741 | 0.0480 |
| L-proline | 1.4 | 5.37 | 0.01359 | 0.0654 |
| Carbamoyl phosphate | 1.6 | 7.14 | 0.00596 | 0.0535 |
| Glycyl-leucine | 1.1 | 7.44 | 0.01008 | 0.0642 |
| Phosphoserine | 1.6 | 8.73 | 0.00094 | 0.0349 |
| 2-Keto-6-aminocaproate | 1.8 | 9.01 | 0.00136 | 0.0349 |
| L-alanine | 1.2 | 12.26 | 0.00741 | 0.0549 |
| Nicotine | 1.6 | 12.40 | 0.00212 | 0.0308 |

DHA, dihydroartemisinin.


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