# SUPPLEMENTARY MATERIALS

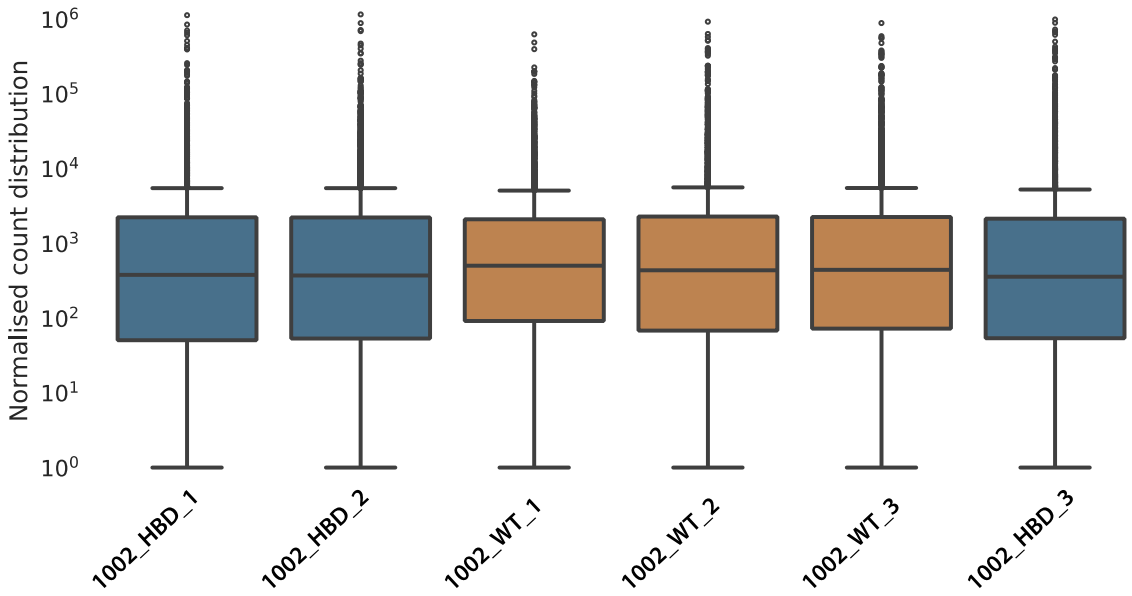


**Figure S1.** Boxplot of raw and normalized data contrasting CB1002 HBD (blue boxes) and CB1002 WT (orange boxes) triplicate samples.

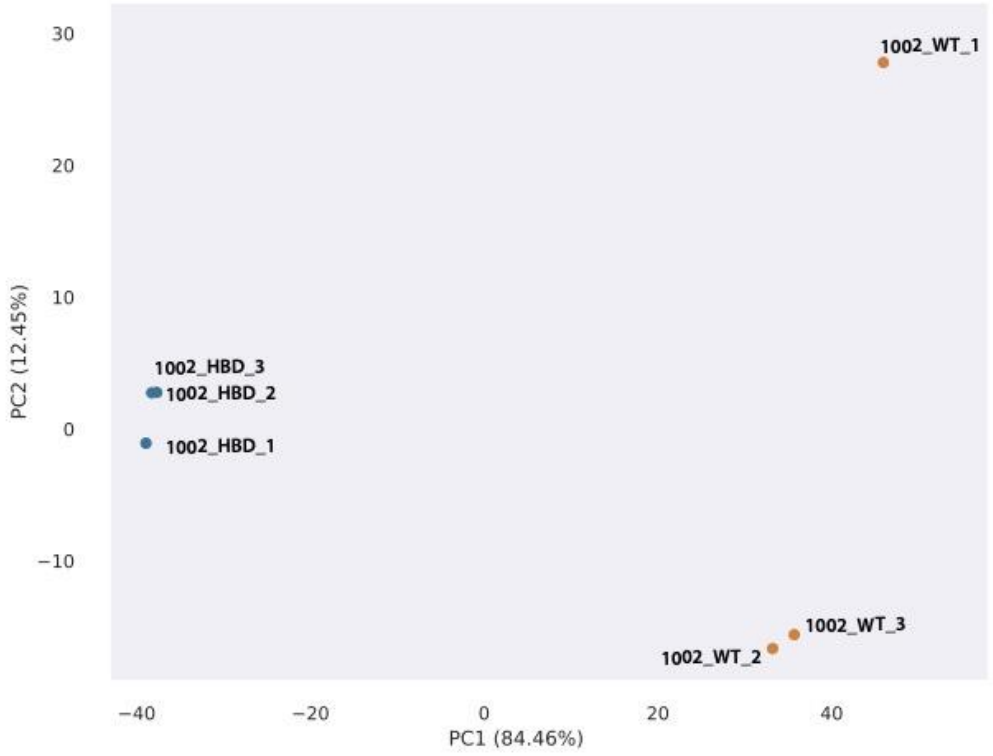


**Figure S2.** Principal component analysis plot showing the clustering of the conditions CB1002 HBD (blue) and CB1002 WT (orange) with 80% of the variance on component 1 showing the differences between the two conditions.

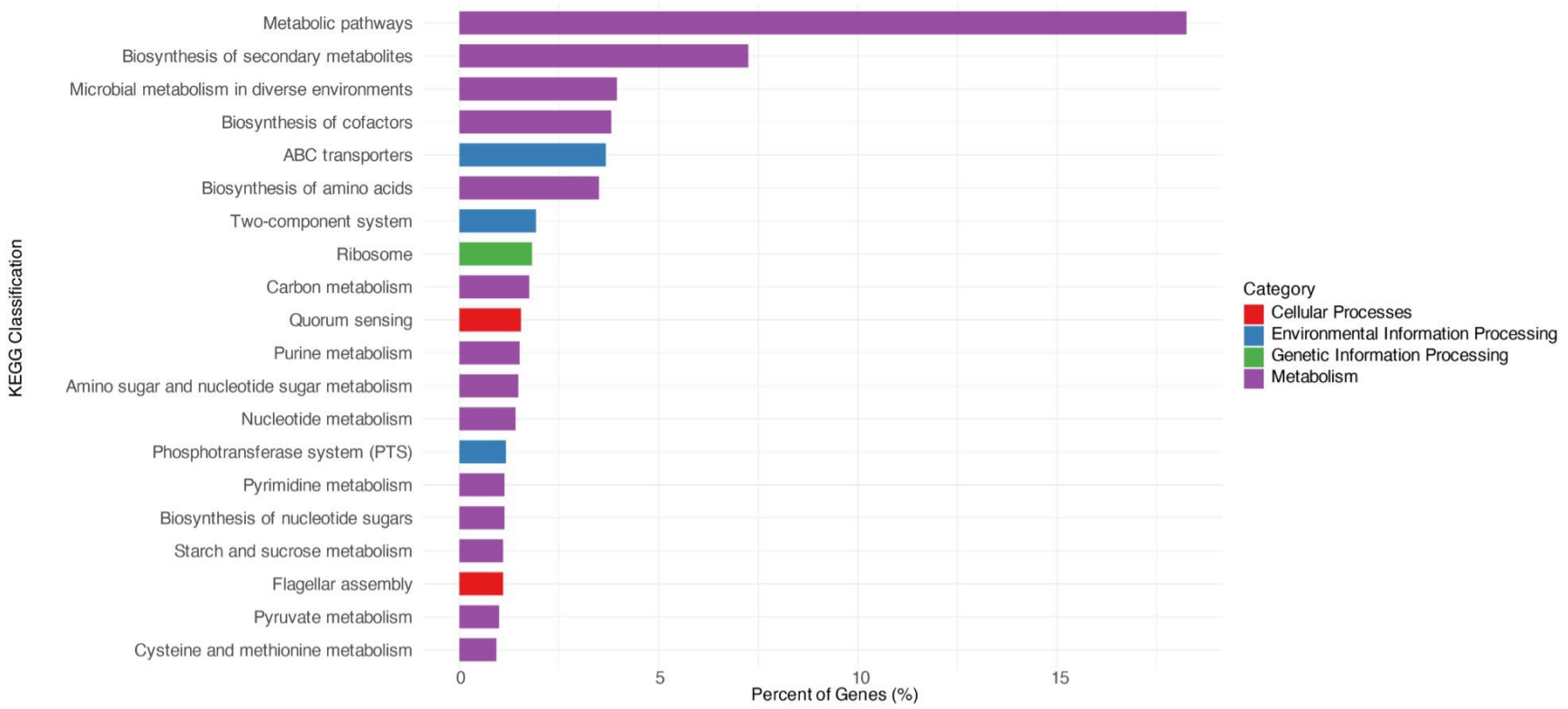


**Figure S3.** Top 20 enriched pathways according to the KEGG analysis, based on differentially expressed genes of CB1002 HBD vs CB1002 WT.

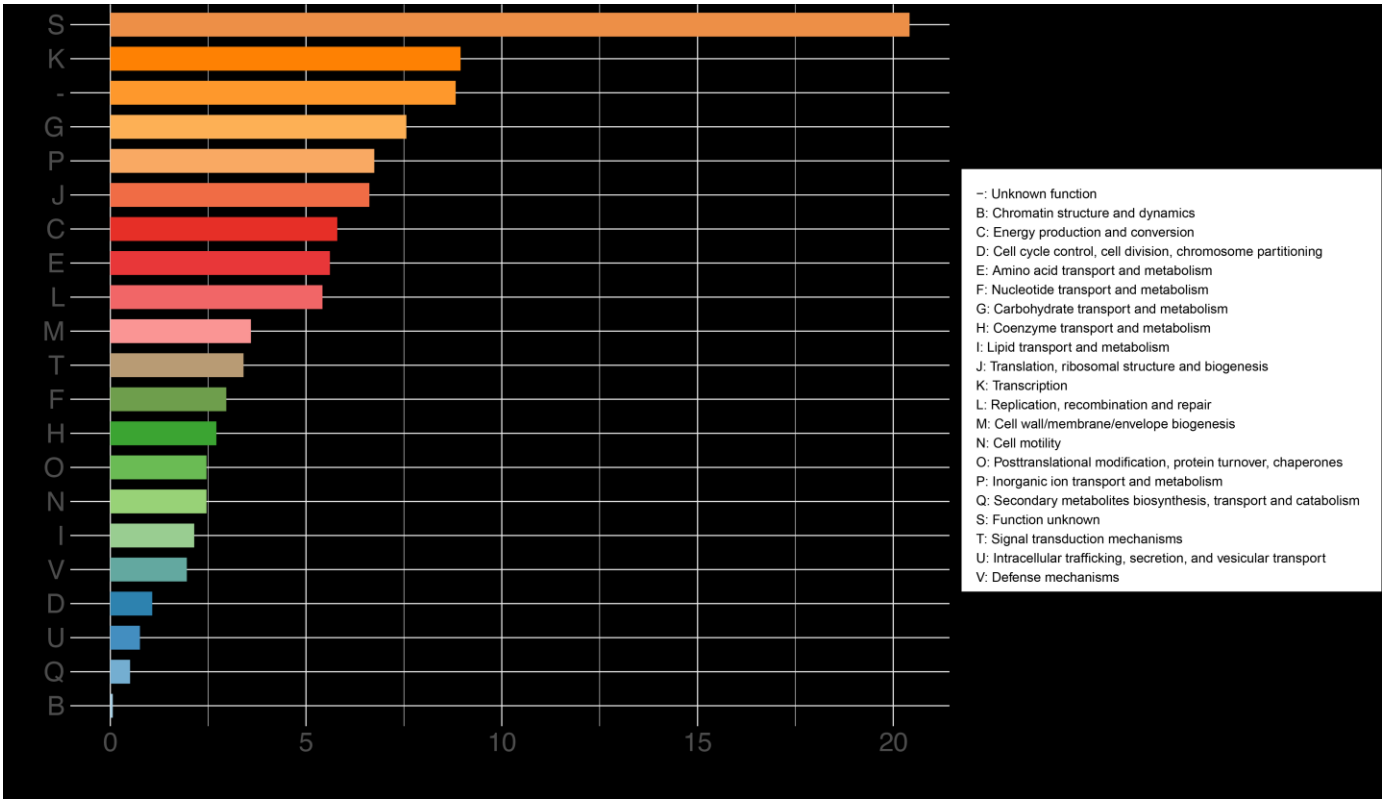


**Figure S4.** Clusters of COG database, based on differentially expressed genes of CB1002 HBD vs CB1002 WT.

| Locus | Gene ID | log2Fold Change | Adjusted *p*-value | KEGG | Function | Class | Category | Subcategory |
|---|---|---|---|---|---|---|---|---|
| CBUT_v1_160022 | *fliM* | -0.12 | 0.75 | K02416 | flagellar motor switch protein | | | |
| CBUT_v1_160023 | *fliN* | -0.08 | 0.84 | K02417 | flagellar motor switch protein | | | |
| CBUT_v1_160024 | *flgM* | -0.26 | 0.45 | K02398 | negative regulator of flagellin synthesis | | | |
| CBUT_v1_160026 | *flgK* | -0.16 | 0.66 | K02396 | flagellar hook-associated protein 1 | | | |
| CBUT_v1_160027 | *flgL* | -0.09 | 0.81 | K02397 | flagellar hook-associated protein 3 | | | |
| CBUT_v1_160032 | *fliS* | 0.04 | 0.9 | K02422 | flagellar secretion chaperone | | | |
| CBUT_v1_160033 | *fliD* | -0.04 | 0.92 | K02407 | flagellar hook-associated protein | | | |
| CBUT_v1_160036 | *fliC* | -0.01 | 0.98 | K02406 | flagellin protein | | | |
| CBUT_v1_160049 | *fliC* | -0.05 | 0.86 | K02406 | flagellin protein | | | |
| CBUT_v1_160050 | *flgB* | 0.09 | 0.68 | K02387 | flagellar basal-body rod protein | | | |
| CBUT_v1_160051 | *flgC* | 0.22 | 0.42 | K02388 | flagellar basal-body rod protein | | | |
| CBUT_v1_160052 | *fliE* | 0.29 | 0.4 | K02408 | flagellar hook-basal body complex protein | | | |
| CBUT_v1_160053 | *flif* | 0.29 | 0.18 | K02409 | flagellar M-ring protein | | | |
| CBUT_v1_160054 | *fliG* | 0.41 | 0.12 | K02410 | flagellar motor switch protein | | | |
| CBUT_v1_160055 | *fliH* | 0.22 | 0.36 | K02411 | flagellar assembly protein | | | |
| CBUT_v1_160056 | *fliI* | 0.3 | 0.2 | K02412 | flagellum-specific ATP synthase | | | |
| CBUT_v1_160057 | *fliJ* | 0.47 | 0.15 | K02413 | flagellar protein | Flagellar assembly | | |
| CBUT_v1_160058 | *fliK* | 0.28 | 0.29 | K02414 | flagellar hook-length control protein | | | |
| CBUT_v1_160059 | *flgD* | 0.12 | 0.7 | K02389 | flagellar basal-body rod modification protein | | | |

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|---|---|---|---|---|---|---|---|
| CBUT_v1_160061 | *flgE* | -0.06 | 0.87 | K02390 | flagellar hook protein | | |
| CBUT_v1_160062 | *flgE* | -0.11 | 0.77 | K02390 | flagellar hook protein | | |
| CBUT_v1_120010 | *motA* | -1.02 | < 0.001 | K02556 | chemotaxis protein | | |
| CBUT_v1_160064 | *motA* | 0.23 | 0.37 | K02556 | chemotaxis protein | | |
| CBUT_v1_120011 | *motB* | -0.86 | < 0.001 | K02557 | chemotaxis protein | | |
| CBUT_v1_160065 | *motB* | 0.15 | 0.63 | K02557 | chemotaxis protein | | |
| CBUT_v1_160066 | *fliL* | 0.17 | 0.48 | K02415 | flagellar protein | | |
| CBUT_v1_160067 | *fliO, fliZ* | 0.04 | 0.91 | K02418 | flagellar protein | | |
| CBUT_v1_160068 | *fliP* | 0.24 | 0.41 | K02419 | flagellar biosynthesis protein | | |
| CBUT_v1_160069 | *fliQ* | 0.26 | 0.41 | K02420 | flagellar biosynthesis protein | | |
| CBUT_v1_160070 | *fliR, flhB* | 0.32 | 0.3 | K13820 | flagellar biosynthesis protein | | |
| CBUT_v1_160071 | *flhA* | 0.37 | 0.19 | K02400 | flagellar biosynthesis protein | | |
| CBUT_v1_160075 | *fliA* | 0.45 | 0.05 | K02405 | RNA polymerase sigma factor | | |
| CBUT_v1_160078 | *flgf* | 0.21 | 0.38 | K02391 | flagellar basal-body rod protein | | |
| CBUT_v1_160079 | *flgG* | 0.17 | 0.46 | K02392 | flagellar basal-body rod protein | | |
| CBUT_v1_150033 | *RpoD* | -0.02 | 0.96 | K03086 | RNA polymerase primary sigma factor | | |
| CBUT_v1_170070 | *RpoN* | -0.32 | 0.32 | K03092 | RNA polymerase primary sigma factor | | |
| CBUT_v1_160014 | *cheW* | -0.19 | 0.55 | K03408 | purine-binding chemotaxis protein | | Cell motility |
| CBUT_v1_160021 | *cheW* | -0.31 | 0.27 | K03408 | purine-binding chemotaxis protein | | |
| CBUT_v1_160015 | *cheD* | 0.21 | 0.41 | K03411 | chemotaxis protein | | |
| CBUT_v1_160016 | *cheB* | 0.32 | 0.25 | K03412 | chemotaxis protein | | |
| CBUT_v1_160017 | *cheR* | 0.3 | 0.29 | K00575 | chemotaxis protein methyltransferase | | |

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|---|---|---|---|---|---|---|---|
| CBUT_v1_160018 | *cheA* | 0.07 | 0.83 | K03407 | sensor kinase | Bacterial chemotaxis | |
| CBUT_v1_160019 | *chec* | 0.01 | 0.98 | K02406 | chemotaxis protein | | |
| CBUT_v1_130478 | *cheY* | -1.59 | < 0.001 | K03413 | chemotaxis protein | | |
| CBUT_v1_160020 | *cheY* | -0.09 | 0.77 | K03413 | chemotaxis protein | | |
| CBUT_v1_190141 | *cheV* | 0.48 | < 0.05 | K03415 | chemotaxis protein | | |
| CBUT_v1_160022 | *fliM* | -0.12 | 0.75 | K02416 | flagellar motor switch protein | | |
| CBUT_v1_160023 | *fliN* | -0.08 | 0.84 | K02417 | flagellar motor switch protein | | |
| CBUT_v1_160054 | *fliG* | 0.41 | 0.12 | K02410 | flagellar motor switch protein | | |
| CBUT_v1_130876 | *mglB* | -0.06 | 0.88 | K10540 | methyl-galactoside transport system substrate-binding protein | | |
| CBUT_v1_190539 | *mglB* | -0.05 | 0.9 | K10540 | methyl-galactoside transport system substrate-binding protein | | |
| CBUT_v1_230011 | *mglB* | -0.31 | 0.5 | K10540 | methyl-galactoside transport system substrate-binding protein | | |
| CBUT_v1_130957 | *rbsB* | -3.59 | < 0.001 | K10439 | ribose transport system substrate-binding protein | | |
| CBUT_v1_180099 | *rbsB* | 0.44 | 0.32 | K10439 | ribose transport system substrate-binding protein | | |
| CBUT_v1_130004 | *mcp* | -0.22 | 0.38 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_130921 | *mcp* | 4.55 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_130962 | *mcp* | 1.07 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_140076 | *mcp* | -3.05 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_180079 | *mcp* | 0.13 | 0.66 | K03406 | methyl-accepting chemotaxis protein | | |

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|---|---|---|---|---|---|---|---|
| CBUT_v1_190458 | *mcp* | -0.93 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_190541 | *mcp* | 2.14 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_230026 | *mcp* | 0.3 | 0.39 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_230060 | *mcp* | -0.48 | 0.24 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_280039 | *mcp* | 3.09 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_290003 | *mcp* | 1.45 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_290084 | *mcp* | -0.32 | 0.2 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_300126 | *mcp* | -2.46 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_300127 | *mcp* | 3.51 | < 0.001 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_300136 | *mcp* | 1.22 | < 0.01 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_300161 | *mcp* | -0.11 | 0.74 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_370011 | *mcp* | 0.2 | 0.53 | K03406 | methyl-accepting chemotaxis protein | | |
| CBUT_v1_120010 | *motA* | -1.02 | < 0.001 | K02556 | chemotaxis protein | | |
| CBUT_v1_160064 | *motA* | 0.23 | 0.37 | K02556 | chemotaxis protein | | |
| CBUT_v1_120011 | *motB* | -0.86 | < 0.001 | K02557 | chemotaxis protein | | |
| CBUT_v1_160065 | *motB* | 0.15 | 0.63 | K02557 | chemotaxis protein | | |
| CBUT_v1_130816 | *aroF, aroG, aroH* | -1 | < 0.01 | K01626 | 3-deoxy-7-phosphoheptulonate synthase | | |
| CBUT_v1_130831 | *trpE* | -0.05 | 0.9 | K01657 | anthranilate synthase component I | | |

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|---|---|---|---|---|---|
| CBUT_v1_130830 | *trpG* | 0.01 | 0.98 | K01658 | anthranilate synthase component II |
| CBUT_v1_190291 | *livF* | 0.09 | 0.82 | K01996 | branched-chain amino acid transport system ATP-binding protein |
| CBUT_v1_190292 | *livG* | 0.08 | 0.84 | K01995 | branched-chain amino acid transport system ATP-binding protein |
| CBUT_v1_190293 | *livM* | 0.2 | 0.63 | K01998 | branched-chain amino acid transport system permease protein |
| CBUT_v1_190294 | *livH* | 0.57 | 0.28 | K01997 | branched-chain amino acid transport system permease protein |
| CBUT_v1_300029 | *ddpD* | -0.12 | 0.75 | K02031 | peptide/nickel transport system ATP-binding protein |
| CBUT_v1_130458 | *ddpB* | 1.52 | < 0.001 | K02033 | peptide/nickel transport system permease protein |
| CBUT_v1_300031 | *ddpB* | -0.55 | 0.16 | K02033 | peptide/nickel transport system permease protein |
| CBUT_v1_130459 | *ddpC* | 1.8 | < 0.001 | K02034 | peptide/nickel transport system permease protein |
| CBUT_v1_300030 | *ddpC* | 0.07 | 0.87 | K02034 | peptide/nickel transport system permease protein |
| CBUT_v1_130460 | *ddpA* | 1.66 | < 0.001 | K02035 | peptide/nickel transport system substrate-binding protein |
| CBUT_v1_300032 | *ddpA* | -0.36 | 0.14 | K02035 | peptide/nickel transport system substrate-binding protein |
| CBUT_v1_130462 | *ddpF* | 1.14 | < 0.01 | K02032 | peptide/nickel transport system ATP-binding protein |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_300028 | *ddpF* | -0.12 | 0.71 | K02032 | peptide/nickel transport system ATP-binding protein | | | |
| CBUT_v1_250091 | *ydcS* | 0.3 | 0.22 | K02055 | putative spermidine/putrescine transport system substrate-binding protein | | | |
| CBUT_v1_170175 | *secA* | 0.12 | 0.62 | K03070 | preprotein translocase subunit | | | |
| CBUT_v1_50033 | *secE* | 0 | 1 | K03073 | preprotein translocase subunit | | | |
| CBUT_v1_170060 | *secG* | -0.64 | < 0.05 | K03075 | preprotein translocase subunit | | | |
| CBUT_v1_50066 | *secY* | -0.08 | 0.85 | K03076 | preprotein translocase subunit | | | |
| CBUT_v1_130312 | *ffh* | 0.8 | < 0.01 | K03106 | signal recognition particle subunit | | | |
| CBUT_v1_130310 | *ftsY* | 0.18 | 0.5 | K03110 | fused signal recognition particle receptor | | | |
| CBUT_v1_190523 | *yajC* | 0.11 | 0.72 | K03210 | preprotein translocase subunit | | | |
| CBUT_v1_380065 | *yidC* | 0.36 | 0.06 | K03217 | YidC/Oxa1 family membrane protein insertase | | | |
| CBUT_v1_130788 | *hfq* | -0.31 | 0.36 | K03666 | host factor-I protein | | | |
| CBUT_v1_280027 | *luxS* | -0.19 | 0.4 | K07173 | S-ribosylhomocysteine lyase | Quorum sensing | | |
| CBUT_v1_170037 | *kdpE* | -0.43 | 0.12 | K07667 | two-component system. OmpR family. KDP operon response regulator | | | |
| CBUT_v1_290131 | *kdpE* | 0.74 | < 0.001 | K07667 | two-component system. OmpR family. KDP operon response regulator | | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_190322 | *spo0A* | -1.79 | < 0.001 | K07699 | two-component system. response regulator. stage 0 sporulation protein A | | | |
| CBUT_v1_130969 | *agrC* | -3.62 | < 0.001 | K07706 | two-component system. LytTR family. sensor histidine kinase | | | |
| CBUT_v1_230080 | *agrC* | -2.56 | < 0.001 | K07706 | two-component system. LytTR family. sensor histidine kinase | | | |
| CBUT_v1_230081 | *agrC* | -2.82 | < 0.001 | K07706 | two-component system. LytTR family. sensor histidine kinase | | | |
| CBUT_v1_130968 | *agrA* | -2.78 | < 0.001 | K07707 | two-component system. LytTR family. response regulator | | | |
| CBUT_v1_130088 | *agrB* | -1.11 | < 0.001 | K07813 | accessory gene regulator B | | | |
| CBUT_v1_130971 | *agrB* | -2.96 | < 0.001 | K07813 | accessory gene regulator B | | | |
| CBUT_v1_190534 | *agrB* | -2.98 | < 0.001 | K07813 | accessory gene regulator B | | | Cellular community |
| CBUT_v1_130541 | *ydcZ* | 1.1 | < 0.01 | K09936 | bacterial transporter family-2 protein | | | |
| CBUT_v1_130542 | *ydcZ* | 1.08 | < 0.01 | K09936 | bacterial transporter family-2 protein | | | |
| CBUT_v1_380028 | *ydcZ* | -0.89 | < 0.05 | K09936 | bacterial transporter family-2 protein | | | |
| CBUT_v1_130453 | *oppF* | -2.94 | < 0.001 | K10823 | oligopeptide transport system ATP-binding protein | | | |
| CBUT_v1_190508 | *crp* | 0.31 | 0.19 | K10914 | CRP/FNR family transcriptional regulator. cyclic AMP receptor protein | | | |
| CBUT_v1_360039 | *crp* | 0.08 | 0.84 | K10914 | CRP/FNR family transcriptional regulator. cyclic AMP receptor protein | | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_130779 | *slo* | -1.11 | < 0.001 | K11031 | thiol-activated cytolysin | | | |
| CBUT_v1_130367 | *ribD* | -0.37 | 0.38 | K11752 | diaminohydroxyphosphoribosylaminopyrimidine deaminase / 5-amino-6-(5-phosphoribosylamino) uracil reductase | | | |
| CBUT_v1_140074 | *ciaH* | 0.22 | 0.24 | K14982 | two-component system. OmpR family. sensor histidine kinase | | | |
| CBUT_v1_140075 | *ciaR* | 0.34 | 0.11 | K14983 | two-component system. OmpR family. response regulator | | | |
| CBUT_v1_130454 | *oppA* | -3.35 | < 0.001 | K15580 | oligopeptide transport system permease protein | | | |
| CBUT_v1_50225 | *oppA* | 0.4 | 0.13 | K15580 | oligopeptide transport system permease protein | | | |
| CBUT_v1_130450 | *oppB* | -3.31 | < 0.001 | K15581 | oligopeptide transport system permease protein | | | |
| CBUT_v1_130451 | *oppC* | -3.29 | < 0.001 | K15582 | oligopeptide transport system permease protein | | | |
| CBUT_v1_130452 | *oppD* | -3.28 | < 0.001 | K15583 | oligopeptide transport system ATP-binding protein | | | |
| CBUT_v1_190068 | *nisK* | 0.34 | 0.22 | K20487 | two-component system. OmpR family. lantibiotic biosynthesis sensor histidine kinase | | | |
| CBUT_v1_190069 | *nisR* | 0.12 | 0.75 | K20488 | two-component system. OmpR family. lantibiotic biosynthesis response regulator | | | |
| CBUT_v1_190070 | *nisG* | -0.14 | 0.71 | K20492 | lantibiotic transport system permease protein | | | |
| CBUT_v1_190071 | *nisE* | 0.12 | 0.76 | K20491 | lantibiotic transport system permease protein | | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_190072 | *nisF* | 0.01 | 0.98 | K20490 | lantibiotic transport system ATP-binding protein | | | |
| CBUT_v1_150042 | *glp* | -3.49 | < 0.001 | K00688 | glycogen phosphorylase | Biofilm formation | | |
| CBUT_v1_50148 | *glp* | -4.07 | < 0.001 | K00688 | glycogen phosphorylase | | | |
| CBUT_v1_90005 | *glgA* | -4.7 | < 0.001 | K00703 | glycogen (starch) synthase | | | |
| CBUT_v1_90001 | *glgD* | -4.13 | < 0.001 | K00975 | Glycogen biosynthesis protein GlgD. glucose-1-phosphate adenylyltransferase family | | | |
| CBUT_v1_90002 | *glgC* | -4.3 | < 0.001 | K00975 | Glycogen biosynthesis protein GlgD. glucose-1-phosphate adenylyltransferase family | | | |
| CBUT_v1_160024 | *flgM* | -0.26 | 0.45 | K02398 | negative regulator of flagellin synthesis | | | |
| CBUT_v1_160075 | *fliA* | 0.45 | 0.05 | K02405 | RNA polymerase sigma factor | | | |
| CBUT_v1_100001 | *crr* | 0.01 | 0.97 | K02777 | sugar PTS system EIIA component | | | |
| CBUT_v1_240087 | *crr* | -4.5 | < 0.001 | K02777 | sugar PTS system EIIA component | | | |
| CBUT_v1_160029 | *csrA* | 0.01 | 0.99 | K03563 | carbon storage regulator | | | |
| CBUT_v1_280027 | *luxS* | -0.19 | 0.4 | K07173 | S-ribosylhomocysteine lyase | | | |
| CBUT_v1_190508 | *crp* | 0.31 | 0.19 | K10914 | CRP/FNR family transcriptional regulator. cyclic AMP receptor protein | | | |
| CBUT_v1_360039 | *crp* | 0.08 | 0.84 | K10914 | CRP/FNR family transcriptional regulator. cyclic AMP receptor protein | | | |
| CBUT_v1_130831 | *trpE* | -0.05 | 0.9 | K01657 | anthranilate synthase component I | | | |

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|---|---|---|---|---|---|---|---|
| CBUT_v1_130830 | *trpG* | 0.01 | 0.98 | K01658 | anthranilate synthase component II | | |
| CBUT_v1_130788 | *hfq* | -0.31 | 0.36 | K03666 | host factor-I protein | | |
| CBUT_v1_170070 | *rpoN* | -0.32 | 0.32 | K03092 | RNA polymerase sigma-54 factor | | |
| CBUT_v1_130972 | *cysE* | 0.14 | 0.72 | K00640 | serine O-acetyltransferase | | |
| CBUT_v1_170082 | *cysE* | 4.83 | < 0.001 | K00640 | serine O-acetyltransferase | | |
| CBUT_v1_170199 | *wecB* | 0.8 | < 0.01 | K01791 | UDP-N-acetylglucosamine 2-epimerase (non-hydrolysing) | | |
| CBUT_v1_170175 | *secA* | 0.12 | 0.62 | K03070 | preprotein translocase subunit | Bacterial secretion system | Environmental information processing | Membrane transport |
| CBUT_v1_190520 | *secD* | -0.22 | 0.5 | K03072 | preprotein translocase subunit | | | |
| CBUT_v1_50033 | *secE* | 0 | 1 | K03073 | preprotein translocase subunit | | | |
| CBUT_v1_190519 | *secF* | -0.11 | 0.74 | K03074 | preprotein translocase subunit | | | |
| CBUT_v1_170060 | *secG* | -0.64 | < 0.05 | K03075 | preprotein translocase subunit | | | |
| CBUT_v1_50066 | *secY* | -0.08 | 0.85 | K03076 | preprotein translocase subunit | | | |
| CBUT_v1_130312 | *ffh* | 0.8 | < 0.01 | K03106 | signal recognition particle subunit | | | |
| CBUT_v1_130310 | *ftsY* | 0.18 | 0.5 | K03110 | fused signal recognition particle receptor | | | |
| CBUT_v1_390001 | *virD* | -0.54 | < 0.05 | K03205 | type IV secretion system protein | | | |
| CBUT_v1_190523 | *yajC* | 0.11 | 0.72 | K03210 | preprotein translocase subunit | | | |
| CBUT_v1_380065 | *yidC* | 0.36 | 0.06 | K03217 | YidC family membrane protein insertase | | | |
| CBUT_v1_130972 | *cysE* | 0.14 | 0.72 | K00640 | serine O-acetyltransferase | Exopolysaccharide biosynthesis | | |
| CBUT_v1_170082 | *cysE* | 4.83 | < 0.001 | K00640 | serine O-acetyltransferase | | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_290175 | *algI* | 0.33 | 0.09 | K19294 | alginate O-acetyltransferase complex protein | | | |
| CBUT_v1_170114 | *tagT, tagU, tagV* | -0.09 | 0.75 | K01005 | polyisoprenyl-teichoic acid--peptidoglycan teichoic acid transferase | Teichoic acid biosynthesis | | |
| CBUT_v1_190462 | *tagT, tagU, tagV* | -0.07 | 0.84 | K01005 | polyisoprenyl-teichoic acid--peptidoglycan teichoic acid transferase | | | |
| CBUT_v1_170008 | *dltC* | -0.48 | 0.12 | K14188 | D-alanine--poly(phosphoribitol) ligase subunit 2 | | | |
| CBUT_v1_170009 | *dltB* | -0.21 | 0.4 | K03739 | membrane protein involved in D-alanine export | | | |
| CBUT_v1_170010 | *dltA* | -0.33 | 0.19 | K03367 | D-alanine--poly(phosphoribitol) ligase subunit 1 | | | |
| CBUT_v1_170012 | *dltD* | -0.48 | 0.09 | K03740 | D-alanine transfer protein | | | |
| CBUT_v1_170209 | *ugtP* | -0.29 | 0.28 | K03429 | processive 1.2-diacylglycerol beta-glucosyltransferase | | | |
| CBUT_v1_130124 | *tagA* | 0.37 | 0.14 | K05946 | N-acetylglucosaminyldiphosphoundecaprenol N-acetyl-beta-D-mannosaminyltransferase | | | |
| CBUT_v1_130136 | *bacA* | 0.22 | 0.49 | K06153 | undecaprenyl-diphosphatase | | | |
| CBUT_v1_130392 | *bacA* | 0.01 | 0.97 | K06153 | undecaprenyl-diphosphatase | | | |
| CBUT_v1_300101 | *licD* | 0.11 | 0.61 | K07271 | lipopolysaccharide cholinephosphotransferase | | | |
| CBUT_v1_130646 | *ltaS* | 0.44 | 0.09 | K19005 | lipoteichoic acid synthase | | | |
| CBUT_v1_190391 | *bcrC* | 0.5 | < 0.01 | K19302 | undecaprenyl-diphosphatase | | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_280016 | *bcrC* | 0.6 | < 0.01 | K19302 | undecaprenyl-diphosphatase | | | |
| CBUT_v1_290152 | *murB* | 0.27 | 0.2 | K00075 | UDP-N-acetylmuramate dehydrogenase | | | |
| CBUT_v1_170187 | *murA* | -1.72 | < 0.001 | K00790 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase | | | |
| CBUT_v1_380025 | *murA* | 0.08 | 0.84 | K00790 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase | | | |
| CBUT_v1_130329 | *uppS* | -0.06 | 0.87 | K00806 | undecaprenyl diphosphate synthase | | | |
| CBUT_v1_250102 | *uppS* | -0.37 | 0.19 | K00806 | undecaprenyl diphosphate synthase | | | |
| CBUT_v1_190372 | *mraY* | 0.29 | 0.17 | K01000 | phospho-N-acetylmuramoyl-pentapeptide-transferase | | | |
| CBUT_v1_170078 | *ddl* | 0.55 | < 0.001 | K01921 | D-alanine-D-alanine ligase | | | |
| CBUT_v1_140033 | *murC* | 0.04 | 0.88 | K01924 | UDP-N-acetylmuramate--alanine ligase | | | |
| CBUT_v1_140002 | *murD* | -0.41 | 0.22 | K01925 | UDP-N-acetylmuramoylalanine--D-glutamate ligase | | Metabolism | Glycan biosynthesis and metabolism |
| CBUT_v1_190374 | *murE* | 0.29 | 0.17 | K01928 | UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2.6-diaminopimelate ligase | | | |
| CBUT_v1_190373 | *murF* | 0.11 | 0.61 | K01929 | UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase | | | |
| CBUT_v1_160005 | *murG* | -0.27 | 0.4 | K02563 | UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase | | | |
| CBUT_v1_290154 | *pbpA* | 0.14 | 0.48 | K05364 | penicillin-binding protein A | | | |

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|---|---|---|---|---|---|---|---|
| CBUT_v1_130043 | *mrcA* | 0.2 | 0.23 | K05366 | penicillin-binding protein 1A | Peptidoglycan biosynthesis | |
| CBUT_v1_170136 | *mdra* | -0.09 | 0.7 | K05515 | penicillin-binding protein 2 | | |
| CBUT_v1_130136 | *bacA* | 0.22 | 0.49 | K06153 | undecaprenyl-diphosphatase | | |
| CBUT_v1_130392 | *bacA* | 0.01 | 0.97 | K06153 | undecaprenyl-diphosphatase | | |
| CBUT_v1_130108 | *gatD* | 0.15 | 0.46 | K07009 | lipid II isoglutaminyl synthase (glutamine-hydrolysing) | | |
| CBUT_v1_130106 | *dacC, dacA, dacD* | 0.34 | 0.16 | K07258 | serine-type D-Ala-D-Ala carboxypeptidase (penicillin-binding protein 5/6) | | |
| CBUT_v1_130544 | *dacC, dacA, dacD* | -0.4 | 0.25 | K07258 | serine-type D-Ala-D-Ala carboxypeptidase (penicillin-binding protein 5/6) | | |
| CBUT_v1_130550 | *dacC, dacA, dacD* | 0.47 | 0.05 | K07258 | serine-type D-Ala-D-Ala carboxypeptidase (penicillin-binding protein 5/6) | | |
| CBUT_v1_170112 | *dacC, dacA, dacD* | -0.53 | < 0.05 | K07258 | serine-type D-Ala-D-Ala carboxypeptidase (penicillin-binding protein 5/6) | | |
| CBUT_v1_190134 | *vanY* | 0.02 | 0.97 | K07260 | zinc D-Ala-D-Ala carboxypeptidase | | |
| CBUT_v1_190375 | *spoVD* | -0.12 | 0.74 | K08384 | stage V sporulation protein D (sporulation-specific penicillin-binding protein) | | |
| CBUT_v1_190376 | *spoVD* | -0.32 | 0.16 | K08384 | stage V sporulation protein D (sporulation-specific penicillin-binding protein) | | |
| CBUT_v1_190391 | *bcrC* | 0.5 | < 0.01 | K19302 | undecaprenyl-diphosphatase | | |

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|---|---|---|---|---|---|---|---|---|
| CBUT_v1_280016 | *bcrC* | 0.6 | < 0.01 | K19302 | undecaprenyl-diphosphatase | | | |
| CBUT_v1_130109 | *murT* | 0.14 | 0.56 | K23393 | lipid II isoglutaminyl synthase (glutamine-hydrolysing) | | | |

**Table S1.** Other differentially expressed genes between CB1002 HBD and CB1002 WT, based on automatic annotation through MaGe MicroScope platform software (v3.17.3).

| In House database annotations | Variable number | Experimental m/z | Experimental RT (min) | Monoisotopic Molecular Weight | Log2 Fold Change | KEGG ID | Class | Sub-class |
|---|---|---|---|---|---|---|---|---|
| *Lactic acid* | M89T227_2 | 89.02423 | 3.78 | 90.03151 | 0.69 | C00256 | Organic Acids and Derivatives | Hydroxy Acids and Derivatives |
| *Phenol* | M95T68 | 95.04905 | 1.14 | 94.04177 | 0.14 | C00146 | Aromatic Homomonocyclic Compounds | Phenols and Derivatives |
| *Oxobutyric acid* | M101T129 | 101.02435 | 2.15 | 102.03163 | 0.34 | C00109 | Organic Acids and Derivatives | Keto-Acids and Derivatives |
| *Nicotinic acid* | M122T144 | 122.02461 | 2.4 | 123.03189 | 0.67 | C00253 | Aromatic Heteromonocyclic Compounds | Pyridines and Derivatives |
| *Benzoic acid* | M123T68_2 | 123.04396 | 1.14 | 122.03668 | 0.14 | C00180 | Aromatic Homomonocyclic Compounds | Benzoic Acid and Derivatives |
| *Leucine* | M132T78_5 | 132.10174 | 1.3 | 131.09446 | 0.14 | C00123/C01933 | Amino Acids Peptides and Analogues | Amino Acids and Derivatives |
| *Hydroxyphenylethanol* | M137T100 | 137.06061 | 1.67 | 138.06789 | 0.74 | C06044 | Aromatic Homomonocyclic Compounds | Phenols and Derivatives |
| *Glutamine* | M145T430 | 145.06174 | 7.17 | 146.06902 | 1.99 | C00819/C00064 | Amino Acids Peptides and Analogues | Amino Acids and Derivatives |
| *N-Acetylserine* | M146T285 | 146.04569 | 4.75 | 147.05297 | 2.53 | C00979/C00979 | Amino Acids. Peptides | Amino Acids and Derivatives |
| *Histidine* | M154T399_1 | 154.06196 | 6.65 | 155.06924 | 0.2 | C00135 | Amino Acids Peptides and Analogues | Amino Acids and Derivatives |
| *Phenyllactic acid* | M165T99 | 165.05537 | 1.66 | 166.06265 | 0.3 | C01479 | Aromatic Homomonocyclic Compounds | Benzyl Alcohols and Derivatives |
| *N-Acetylglutamic acid* | M188T448 | 188.05645 | 7.47 | 189.06373 | 0.43 | C00624/C00624 | Amino Acids Peptides and Analogues | Amino Acids and Derivatives |
| *Indolelactic acid* | M204T146 | 204.06619 | 2.43 | 205.07347 | 0.86 | C02043 | Aromatic Heteropolycyclic Compounds | Indoles |

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|---|---|---|---|---|---|---|---|---|
| *Apigenin flavone* | M271T457 | 271.0597 | 7.62 | 270.05242 | 3.14 | C01477/C06563 | Aromatic Heteropolycyclic Compounds | Flavonoids |
| *Pelargonidin* | M271T386 | 271.06037 | 6.43 | 270.05309 | 1.88 | C05904 | Aromatic Heteropolycyclic Compounds | Flavonoids |
| *Naringenin* | M273T457 | 273.07538 | 7.62 | 272.0681 | 4.15 | C00509 | Aromatic Heteropolycyclic Compounds | Flavonoids |
| *Glycitein* | M285T418 | 285.0756 | 6.96 | 284.06832 | 0.64 | C14536 | Aromatic Heteropolycyclic Compounds | Flavonoids |
| *Hexadecanedioic acid* | M285T78 | 285.20697 | 1.29 | 286.21425 | 1.19 | C19615 | Organic Acids and Derivatives | Carboxylic Acids and Derivatives |
| *Hydroxyoctadecadienoic acid* | M295T76 | 295.22763 | 1.26 | 296.23491 | 1.1 | *NA* | *NA* | *NA* |
| *Isobutyric acid* | M87T141 | 87.04501 | 2.34 | 88.05229 | -4.32 | C02632/C00466 | Organic Acids and Derivatives | Carboxylic Acids and Derivatives |
| *Monomethyl succinate* | M131T133 | 131.03534 | 2.21 | 132.04262 | -0.74 | C08645/C08645 | Organic Acids and Derivatives | Carboxylic Acids and Derivatives |
| *Monomethyl adipate* | M159T92 | 159.06606 | 1.53 | 160.07334 | -4.64 | *NA* | Organic Acids and Derivatives | Carboxylic Acids and Derivatives |
| *N8-Acetylspermidine* | M188T46 | 188.17566 | 0.77 | 187.16838 | -1.47 | C01029 | Organic Acids and Derivatives | Carboxylic Acids and Derivatives |
| *N6-Acetyl-Lysine* | M189T56 | 189.12331 | 0.93 | 188.11603 | -0.47 | C02727 | Amino Acids Peptides and Analogues | Amino Acids and Derivatives |
| *Biopterin* | M238T74 | 238.0935 | 1.23 | 237.08622 | -0.97 | C06313 | Aromatic Heteropolycyclic Compounds | Pteridines and Derivatives |

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|---|---|---|---|---|---|---|---|---|
| *Deoxyadenosine* | M252T83 | 252.10923 | 1.39 | 251.10195 | -0.38 | C00559 | Nucleosides. Nucleotides and Analogues | Purine Nucleosides and Analogues |
| *Cyclic AMP* | M330T59 | 330.05927 | 0.99 | 329.05199 | -0.29 | C00575 | Nucleosides. Nucleotides and Analogues | Purine Nucleotides |
| *Tetrasaccharides* | M665T594 | 665.21316 | 9.89 | 666.22044 | -0.64 | C02052/C01613 | Carbohydrates and Carbohydrate Conjugates | Tetrasaccharides |

**Table S2.** List of 28 significantly differentially identified metabolites from non-targeted metabolomics of CB1002 HBD compared to CB1002 WT from the culture supernatant used for RNA-Seq analysis.