***animal* journal**

**Genome-wide association and pathway analysis of carcass and meat quality traits in Piemontese young bulls.**

S. Pegolo1, A. Cecchinato1, S. Savoia2, L. Di Stasio3, A. Pauciullo3, A. Brugiapaglia3, G. Bittante1 and A. Albera2

1Department of Agronomy, Food, Natural Resources, Animals and Environment (DAFNAE), University of Padua, Viale dell’Università 16, 35020 Legnaro, Padua, Italy

2Associazione Nazionale Allevatori Bovini di Razza Piemontese, Strada Trinità 32/A, 12061 Carrù (CN), Italy

3Department of Agricultural, Forest and Food Science, Università degli studi di Torino, Via L. Da Vinci 44, 10095 Grugliasco (TO), Italy

Short title: Genomic study for meat traits in Piemontese bulls

**Supplementary Table S1.** Complete list of the significant single nucleotide polymorphism (SNPs) obtained after standard genome-wide association (GWAS) analysis in Piemontese beef cattle.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **CHR** | **BP** | ***P*-value** | **LOG** | **effB** | **Trait1** | **MAF** | $$σ\_{SNP}^{2}$$ | $$σ\_{g}^{2}$$ | $$σ\_{g\_{SNP}}^{2}$$ |
| BovineHD2300000877 | 23 | 3907142 | 4.47E-05 | 4.350 | 0.316 | a\* | 0.3568 | 0.0458 | 0.5184 | 8.83 |
| BovineHD2500003345 | 25 | 11960157 | 7.79E-06 | 5.108 | -0.368 | a\* | 0.2699 | 0.0534 | 0.5184 | 10.29 |
| ARS-BFGL-NGS-45457 | 6 | 38715250 | 1.86E-06 | 5.731 | -9.284 | AS | 0.4324 | 42.3079 | 273.8923 | 15.45 |
| MS-rs109570900 | 6 | 38777311 | 3.35E-05 | 4.475 | -8.032 | AS | 0.4620 | 32.0690 | 273.8923 | 11.71 |
| Hapmap49816-BTA-98191 | 6 | 91906227 | 1.78E-05 | 4.751 | -10.840 | AS | 0.1775 | 34.3094 | 273.8923 | 12.53 |
| BovineHD2400005258 | 24 | 19872257 | 4.58E-05 | 4.339 | 0.290 | b\* | 0.3773 | 0.0394 | 0.5880 | 6.70 |
| BovineHD2500003345 | 25 | 11960157 | 3.53E-05 | 4.453 | -0.327 | b\* | 0.2699 | 0.0422 | 0.5880 | 7.17 |
| BovineHD2500003345 | 25 | 11960157 | 1.46E-05 | 4.836 | -0.440 | C\* | 0.2699 | 0.0763 | 0.8440 | 9.04 |
| ARS-BFGL-NGS-76281 | 3 | 31524593 | 3.75E-05 | 4.426 | -0.017 | CDG | 0.3882 | 0.0001 | 0.0040 | 3.56 |
| Hapmap30134-BTC-034283 | 6 | 38464203 | 7.13E-06 | 5.147 | -0.019 | CDG | 0.4810 | 0.0002 | 0.0040 | 4.43 |
| BovineHD0600010655 | 6 | 38538611 | 6.35E-06 | 5.197 | -0.019 | CDG | 0.4869 | 0.0002 | 0.0040 | 4.50 |
| BovineHD0600010657 | 6 | 38541611 | 6.35E-06 | 5.197 | -0.019 | CDG | 0.4869 | 0.0002 | 0.0040 | 4.50 |
| BovineHD0600010666 | 6 | 38574125 | 1.73E-05 | 4.762 | 0.018 | CDG | 0.4814 | 0.0002 | 0.0040 | 4.02 |
| Hapmap26308-BTC-057761 | 6 | 38576012 | 6.37E-09 | 8.196 | 0.025 | CDG | 0.3817 | 0.0003 | 0.0040 | 7.31 |
| BovineHD0600010673 | 6 | 38590515 | 1.30E-05 | 4.886 | 0.018 | CDG | 0.4843 | 0.0002 | 0.0040 | 4.12 |
| MS-rs110839532 | 6 | 38599667 | 1.30E-05 | 4.886 | 0.018 | CDG | 0.4843 | 0.0002 | 0.0040 | 4.12 |
| MS-rs43702361 | 6 | 38599672 | 1.32E-05 | 4.879 | 0.018 | CDG | 0.4835 | 0.0002 | 0.0040 | 4.12 |
| MS-rs109241256 | 6 | 38599864 | 1.12E-05 | 4.952 | 0.018 | CDG | 0.4846 | 0.0002 | 0.0040 | 4.20 |
| MS-rs41255599 | 6 | 38599993 | 1.30E-05 | 4.886 | 0.018 | CDG | 0.4843 | 0.0002 | 0.0040 | 4.12 |
| BovineHD0600010685 | 6 | 38616248 | 1.30E-05 | 4.886 | 0.018 | CDG | 0.4846 | 0.0002 | 0.0040 | 4.12 |
| ARS-BFGL-NGS-45457 | 6 | 38715250 | 2.44E-11 | 10.613 | 0.028 | CDG | 0.4324 | 0.0004 | 0.0040 | 9.61 |
| MS-rs109570900 | 6 | 38777311 | 1.07E-08 | 7.971 | 0.024 | CDG | 0.4620 | 0.0003 | 0.0040 | 7.08 |
| MS-rs110251642 | 6 | 38808241 | 3.34E-08 | 7.476 | 0.023 | CDG | 0.4752 | 0.0003 | 0.0040 | 6.51 |
| BovineHD4100004576 | 6 | 38834676 | 3.19E-08 | 7.496 | 0.023 | CDG | 0.4766 | 0.0003 | 0.0040 | 6.52 |
| BovineHD0600010755 | 6 | 38866381 | 5.33E-08 | 7.273 | 0.022 | CDG | 0.4781 | 0.0003 | 0.0040 | 6.26 |
| Hapmap31285-BTC-041097 | 6 | 38869785 | 3.34E-08 | 7.476 | 0.023 | CDG | 0.4752 | 0.0003 | 0.0040 | 6.51 |
| Hapmap33628-BTC-041023 | 6 | 38939012 | 1.23E-08 | 7.909 | 0.024 | CDG | 0.4583 | 0.0003 | 0.0040 | 7.07 |
| BovineHD0600010795 | 6 | 39185743 | 1.22E-06 | 5.915 | 0.020 | CDG | 0.4931 | 0.0002 | 0.0040 | 5.07 |
| BovineHD4100004612 | 6 | 39340446 | 2.11E-06 | 5.676 | -0.020 | CDG | 0.4145 | 0.0002 | 0.0040 | 5.04 |
| Hapmap31044-BTC-071337 | 6 | 39346170 | 1.10E-06 | 5.960 | -0.021 | CDG | 0.4142 | 0.0002 | 0.0040 | 5.31 |
| BovineHD0600010842 | 6 | 39441548 | 3.66E-06 | 5.437 | -0.020 | CDG | 0.3630 | 0.0002 | 0.0040 | 4.66 |
| BovineHD0600008146 | 6 | 29225507 | 4.04E-05 | 4.394 | 0.629 | CL | 0.2617 | 0.1531 | 0.7387 | 20.72 |
| ARS-BFGL-NGS-70946 | 10 | 14574453 | 4.15E-05 | 4.382 | -0.552 | CL | 0.4237 | 0.1489 | 0.7387 | 20.16 |
| Hapmap30134-BTC-034283 | 6 | 38464203 | 2.82E-06 | 5.550 | -8.421 | CW | 0.4810 | 35.4019 | 639.2217 | 5.54 |
| BovineHD0600010655 | 6 | 38538611 | 2.18E-06 | 5.662 | -8.516 | CW | 0.4869 | 36.2401 | 639.2217 | 5.67 |
| BovineHD0600010657 | 6 | 38541611 | 2.18E-06 | 5.662 | -8.516 | CW | 0.4869 | 36.2401 | 639.2217 | 5.67 |
| BovineHD0600010666 | 6 | 38574125 | 2.14E-05 | 4.670 | 7.593 | CW | 0.4814 | 28.7844 | 639.2217 | 4.50 |
| Hapmap26308-BTC-057761 | 6 | 38576012 | 4.81E-07 | 6.318 | 9.212 | CW | 0.3817 | 40.0582 | 639.2217 | 6.27 |
| BovineHD0600010673 | 6 | 38590515 | 3.25E-05 | 4.488 | 7.408 | CW | 0.4843 | 27.4132 | 639.2217 | 4.29 |
| MS-rs110839532 | 6 | 38599667 | 3.25E-05 | 4.488 | 7.408 | CW | 0.4843 | 27.4132 | 639.2217 | 4.29 |
| MS-rs43702361 | 6 | 38599672 | 3.29E-05 | 4.483 | 7.408 | CW | 0.4835 | 27.4122 | 639.2217 | 4.29 |
| MS-rs109241256 | 6 | 38599864 | 2.79E-05 | 4.554 | 7.478 | CW | 0.4846 | 27.9328 | 639.2217 | 4.37 |
| MS-rs41255599 | 6 | 38599993 | 3.25E-05 | 4.488 | 7.408 | CW | 0.4843 | 27.4132 | 639.2217 | 4.29 |
| BovineHD0600010685 | 6 | 38616248 | 3.25E-05 | 4.488 | 7.408 | CW | 0.4846 | 27.4144 | 639.2217 | 4.29 |
| ARS-BFGL-NGS-45457 | 6 | 38715250 | 8.32E-08 | 7.080 | 9.611 | CW | 0.4324 | 45.3451 | 639.2217 | 7.09 |
| MS-rs109570900 | 6 | 38777311 | 5.55E-06 | 5.256 | 8.113 | CW | 0.4620 | 32.7199 | 639.2217 | 5.12 |
| MS-rs110251642 | 6 | 38808241 | 5.98E-06 | 5.223 | 8.018 | CW | 0.4752 | 32.0629 | 639.2217 | 5.02 |
| BovineHD4100004576 | 6 | 38834676 | 7.97E-06 | 5.098 | 7.901 | CW | 0.4766 | 31.1429 | 639.2217 | 4.87 |
| BovineHD0600010755 | 6 | 38866381 | 7.71E-06 | 5.113 | 7.885 | CW | 0.4781 | 31.0245 | 639.2217 | 4.85 |
| Hapmap31285-BTC-041097 | 6 | 38869785 | 5.98E-06 | 5.223 | 8.018 | CW | 0.4752 | 32.0629 | 639.2217 | 5.02 |
| Hapmap33628-BTC-041023 | 6 | 38939012 | 3.92E-06 | 5.407 | 8.279 | CW | 0.4583 | 34.0334 | 639.2217 | 5.32 |
| BovineHD0600011056 | 6 | 40563707 | 4.55E-05 | 4.342 | -10.471 | CW | 0.1410 | 26.5563 | 639.2217 | 4.15 |
| ARS-BFGL-NGS-4893 | 19 | 6895198 | 3.07E-05 | 4.513 | 7.536 | CW | 0.4284 | 27.8162 | 639.2217 | 4.35 |
| BovineHD0900013319 | 9 | 48330996 | 1.54E-05 | 4.811 | 0.209 | PL | 0.4288 | 0.0215 | 0.1644 | 13.06 |
| BovineHD0400032408 | 4 | 1.13E+08 | 3.34E-05 | 4.476 | -0.378 | H\* | 0.4573 | 0.0709 | 1.0140 | 6.99 |
| BovineHD2500003345 | 25 | 11960157 | 3.13E-05 | 4.504 | -0.417 | H\* | 0.2699 | 0.0686 | 1.0140 | 6.77 |
| BovineHD2300001826 | 23 | 7245409 | 3.56E-05 | 4.448 | 0.608 | L\* | 0.3692 | 0.1720 | 3.6370 | 4.73 |
| ARS-BFGL-NGS-114722 | 8 | 28464160 | 2.02E-05 | 4.695 | 0.011 | pH | 0.1939 | 0.0000 | 0.0002 | 22.78 |
| BTA-76623-no-rs | 6 | 71154473 | 9.69E-06 | 5.014 | -0.433 | EUS | 0.1194 | 0.0395 | 0.4135 | 9.55 |
| ARS-BFGL-NGS-116123 | 11 | 94686959 | 4.83E-05 | 4.316 | 0.263 | EUS | 0.3240 | 0.0303 | 0.4135 | 7.33 |

SNP: single nucleotide polymorphism; CHR: chromosome; BP: SNP location in bp; LOG: -log10(*P*-value); effB: SNP effect; MAF: minor allele frequency; $σ\_{SNP}^{2}$: variance explained by the SNP, calculated as *2pqa2,* where *p* is the frequency of one allele, *q = 1-p* is the frequency of the second allele, and *a* is the estimated additive genomic effect; $σ\_{g}^{2}$: additive genomic variance; $σ\_{g\_{SNP}}^{2}:$proportion of genomic variance explained by each SNP, calculated as $σ\_{g\_{SNP}}^{2}=\frac{σ\_{SNP}^{2}}{σ\_{g}^{2}}×100$.

1Trait: AS: age at slaughtering; CW: carcass weight; CDG: carcass daily gain, carcass; EUS: carcass conformation according to the EU linear grading system (Commission of the European Communities 1982). The six main grades (S, E, U, R, O, P from best to worst) were furtherly subdivided in + or – subclasses and then converted into numerical scores (EUS) ranging from 18 (S+ class) to 1 (P- class); PL: purge loss; CL: cooking loss; L\*: lightness; a\*: redness; b\*: yellowness; C\*: chroma; H\*: hue

**Supplementary Table S2.** Significantly enriched gene ontology (GO) terms and Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathways for carcass and meat quality traits in Piemontese beef cattle.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **Term** | **Nr. Genes** | **% AG** | **FDR** | **Associated Genes Found** |
| ***1a\**** |   |   |   |   |   |
| KEGG:04728 | dopaminergic synapse | 12 | 21.1 | 0.042 | [AKT3, CACNA1B, CACNA1D, CAMK2D, GNG3, GRIA2, ITPR1, ITPR2, ITPR3, MAPK10, PLCB1, PRKCG] |
| GO\_MF:0005262 | calcium channel activity | 14 | 25.0 | 0.014 | [CACNA1B, CACNA1D, CACNG5, CACNG7, FAM155A, ITPR1, ITPR2, ITPR3, ORAI3, SLC24A4, TPCN2, TRPC3, TRPM8, TRPV5] |
| GO\_MF:0022890 | inorganic cation transmembrane transporter activity | 32 | 13.9 | 0.029 | [ATP5G3, CACNA1B, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, GRIA2, ITPR1, ITPR2, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, ORAI3, SLC12A6, SLC20A2, SLC24A4, SLC30A3, SLC36A1, SLC5A1, SLC6A11, SLC9A1, SLC9A8, SLC9B2, TPCN2, TRPC3, TRPM8, TRPV5] |
| GO\_BP:0098662 | inorganic cation transmembrane transport | 33 | 12.5 | 0.047 | [ATP5G3, CACNA1B, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, ITPR1, ITPR2, ITPR3, KCND2, KCNIP4, KCNK3, KEL, LOC534223, NDUFA4L2, NEDD4L, ORAI3, SLC12A6, SLC20A2, SLC24A4, SLC30A3, SLC36A1, SLC9A1, SLC9A8, SLC9B2, STIM1, TESC, TPCN2, TRPC3, TRPM8, TRPV5] |
| ***1b\**** |   |   |  |  |   |
| GO\_MF:0005262 | calcium channel activity | 13 | 23.2 | 0.021 | [CACNA1D, CACNB3, CACNG7, FAM155A, ITGAV, ITPR3, ORAI3, PKD2, SLC24A4, TPCN2, TRPC3, TRPM8, TRPV5] |
| GO\_BP:0034030 | ribonucleoside bisphosphate biosynthetic process | 5 | 71.4 | 0.019 | [ACAT1, ACOT7, PANK2, PAPSS1, PPCDC] |
| GO\_BP:0034033 | purine nucleoside bisphosphate biosynthetic process | 5 | 71.4 | 0.019 | [ACAT1, ACOT7, PANK2, PAPSS1, PPCDC] |
| ***1C\**** |  |  |  |  |  |
| KEGG:04713 | circadian entrainment | 10 | 21.7 | 0.043 | [CACNA1D, CAMK2D, GNAI1, GRIA1, GRIA2, ITPR1, ITPR3, PLCB1, PRKCG, PRKG1] |
| KEGG:04730 | long-term depression | 8 | 27.6 | 0.048 | [GNAI1, GRIA1, GRIA2, ITPR1, ITPR3, PLCB1, PRKCG, PRKG1] |
| GO\_MF:0005262 | calcium channel activity | 12 | 21.4 | 0.035 | [CACNA1D, CACNG5, CACNG7, FAM155A, ITGAV, ITPR1, ITPR3, ORAI3, SLC24A4, TPCN2, TRPC3, TRPV6] |
| GO\_MF:0008324 | cation transmembrane transporter activity | 36 | 12.9 | 0.013 | [ATP5G3, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, GRIA1, GRIA2, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, ORAI3, SCN2A, SLC12A6, SLC1A4, SLC20A2, SLC24A4, SLC28A1, SLC30A3, SLC30A4, SLC36A1, SLC39A11, SLC5A1, SLC6A11, SLC6A16, SLC9A8, SLC9B2, TPCN2, TRPC3, TRPV6] |
| GO\_BP:0015671 | oxygen transport | 4 | 57.1 | 0.047 | [HBA, HBM, HBQ1, HBZ] |
| GO\_BP:0015672 | monovalent inorganic cation transport | 23 | 12.6 | 0.049 | [ATP5G3, CACNA1D, CNGA3, COMMD9, COX7A2L, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, NEDD4L, NKAIN2, NNT, SCN2A, SLC12A6, SLC20A2, SLC24A4, SLC36A1, SLC5A1, SLC9A8, SLC9B2, TESC, TSC1] |
| GO\_MF:0022890 | inorganic cation transmembrane transporter activity | 34 | 14.8 | 0.002 | [ATP5G3, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, GRIA1, GRIA2, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, ORAI3, SCN2A, SLC12A6, SLC20A2, SLC24A4, SLC28A1, SLC30A3, SLC36A1, SLC39A11, SLC5A1, SLC6A11, SLC6A16, SLC9A8, SLC9B2, TPCN2, TRPC3, TRPV6] |
| GO\_MF:0046873 | metal ion transmembrane transporter activity | 28 | 13.5 | 0.030 | [CACNA1D, CACNG5, CACNG7, CNGA3, FAM155A, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, ORAI3, SCN2A, SLC12A6, SLC20A2, SLC24A4, SLC28A1, SLC30A3, SLC39A11, SLC5A1, SLC6A11, SLC6A16, SLC9A8, SLC9B2, TPCN2, TRPC3, TRPV6] |
| GO\_BP:0098655 | cation transmembrane transport | 34 | 11.0 | 0.048 | [ATP5G3, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, NEDD4L, NPSR1, ORAI3, SCN2A, SLC12A6, SLC1A4, SLC20A2, SLC24A4, SLC30A3, SLC30A4, SLC36A1, SLC39A11, SLC9A8, SLC9B2, STIM1, TESC, TPCN2, TRPC3, TRPV6] |
| GO\_BP:0098660 | inorganic ion transmembrane transport | 34 | 11.4 | 0.046 | [ATP5G3, CACNA1D, CACNG5, CACNG7, CLCA4, CNGA3, COX7A2L, FAM155A, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, NEDD4L, NPSR1, ORAI3, SCN2A, SLC12A6, SLC1A4, SLC20A2, SLC24A4, SLC30A3, SLC36A1, SLC39A11, SLC9A8, SLC9B2, STIM1, TESC, TPCN2, TRPC3, TRPV6] |
| GO\_BP:0098662 | inorganic cation transmembrane transport | 32 | 12.2 | 0.044 | [ATP5G3, CACNA1D, CACNG5, CACNG7, CNGA3, COX7A2L, FAM155A, ITGAV, ITPR1, ITPR3, KCND2, KCNIP4, KCNK3, LOC534223, NDUFA4L2, NEDD4L, NPSR1, ORAI3, SCN2A, SLC12A6, SLC20A2, SLC24A4, SLC30A3, SLC36A1, SLC39A11, SLC9A8, SLC9B2, STIM1, TESC, TPCN2, TRPC3, TRPV6] |
| ***1CL*** |  |  |  |  |  |
| GO\_BP:0051963 | regulation of synapse assembly | 9 | 34.6 | 0.027 | [ADGRL1, EFNA5, EPHB1, NTRK1, NTRK2, PTK2, PVRL1, WNT5A, WNT7A] |
| ***1CW*** |  |  |  |  |  |
| GO\_BP:0035418 | protein localization to synapse | 5 | 55.6 | 0.038 | [ASIC2, CDK5, DLG4, NSG1, SNAP47] |
| ***1EUS*** |  |  |  |  |  |
| GO\_BP:0014070 | response to organic cyclic compound | 31 | 14.2 | 0.029 | [BCL2, BMP4, BMP7, CSN3, CTNNB1, DDIT4, DROSHA, EFNA5, EGFR, GABRB1, GABRB3, GABRG2, GNG2, HCN1, HID1, HNF4G, IL10, IL1RN, KCNJ8, LRP6, LRRK2, NCOR1, NR1H2, PPP3CA, PRKCE, PRKCG, PRMT2, RECQL5, SLC9A1, SLIT3, UFSP2] |

%AG: percentage of genes associated with the significant pathways with respect to the total number of genes in the pathway; FDR: false discovery rate

1See Supplementary Table S1 for trait definition

**Supplementary Figure S1.** Haploview plot of pairwise D′ in the region at ~38.46-40.56 Mb on *Bos taurus autosome* (BTA6) in Piemontese beef cattle: red, Dʹ = 1.0 and logarithm of the odds (LOD) ≥ 2.0; blue, D′ = 1.0 and LOD < 2.0; white, D′ < 1.0 and LOD < 2.0; shades of pink/red, D′ < 1.0 and LOD ≥ 2.0. LD blocks are defined by a black line.

****