**Supplemental Table 2. *NAT2* genetic variants associated with differential urinary or serum metabolite levels and other traits (Complete list)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variant** | **Type** | **Risk Allele** | **P-value** | **RAF\*** | **Increase/****decrease** | **Reported trait** | **Reference** | **Location**† |
| rs10109552 | Non-coding | G | 2 x 10-8 | 0.69 | NA | Essential tremor | (Müller et al., 2016) | 8:18451300 |
| rs11784251 | Non-coding | G | 2 x 10-17 | 0.56 | ↑ | Blood metabolite levels (*N*-acetylputrescine) | (Rhee et al., 2022) | 8:18402503 |
| rs1390360 | Non-coding | A | 7 x 10-13 | 0.56 | ↑ | Serum albumin levels | (Sakaue et al., 2021) | 8:18403983 |
| rs146812806 | Non-coding | Ins | 9 x 10-32 | 0.35 | ↑ | Serum metabolite levels (5-acetylamino-6-amino-3-methyluracil) | (Feofanova et al., 2020) | 8:18414994 |
|  |  | Ins | 9 x 10-14 |  | ↓ | Mean corpuscular hemoglobin concentration | (Chen et al., 2020) |  |
| rs1495741 | Non-coding | NR | 4 x 10-11 | - | NA | Bladder cancer | (Rothman et al., 2010)  | 8:18415371 |
|  |  | A | 1 x 10-27 | 0.65 | ↑ | Blood metabolite levels (1-methylurate) | (Shin et al., 2014) |  |
|  |  | A | 2 x 10-10 | . | NA | Bladder cancer | (Figueroa et al., 2014) |  |
|  |  | A | 7 x 10-11 |  | NA | Liver injury in anti-tuberculosis drug treatment | (Suvichapanich et al., 2019) |  |
|  |  | A | 1 x 10-24 |  | ↓ | *N*-acetylputrescine levels (blood) | (Rhee et al., 2022) |  |
|  |  | A | 2 x 10-15 |  | ↓ | 4-acetamidobutanoate levels (blood) | (Rhee et al., 2022) |  |
|  |  | G | 4 x 10-8 | 0.35 | NA | Youthful appearance (self-reported) | (Roberts et al., 2020) |  |
|  |  | G | 6 x 10-21 |  | ↓ | Urinary metabolite levels in chronic kidney disease | (Schlosser et al., 2020) |  |
| rs1495743 | Non-coding | NR | 6 x 10-16 | - | ↓ | Serum metabolite levels (1-methylxanthine) | (Krumsiek et al., 2012) | 8:18415371 |
|  |  | NR | 7 x 10-9 | - | ↑ | 4-acetamidobutanoate levels (serum) | (Yet et al., 2016) |  |
|  |  | G | 2 x 10-40 | 0.35 | ↓ | Metabolic traits (SM-7 + 11 other traits) | (Suhre et al., 2011a) |  |
|  |  | G | 9 x 10-14 |  | ↓ | Iron status biomarkers (total iron binding capacity) | (Bell et al., 2021) |  |
| rs1495745 | Non-coding | T | 9 x 10-12 | 0.38 | ↑ | C-reactive protein levels | (Han et al., 2020) | 8:18405213 |
| rs1495747 | Non-coding | C | 3 x 10-8 | 0.56 | ↑ | Calcium levels | (Sakaue et al., 2021) | 8:18405351 |
| rs1995003 | Non-coding | T | 6 x 10-6 | 0.23 | ↑ | Serum tin levels | (Yang et al., 2022) | 8:18475599 |
| rs35246381 | Non-coding | C | 3 x 10-35 | 0.35 | ↑ | Urinary metabolite levels in chronic kidney disease (*N*-acetylputrescine) | (Schlosser et al., 2020) | 8:18415025 |
|  |  | C | 2 x 10-25 |  | ↑ | Urinary metabolite modules in chronic kidney disease (4-acetamidobutanoate, allo-threonine, *N*-acetylputrescine) | (Schlosser et al., 2020) |  |
|  |  | C | 1 x 10-72 |  | ↑ | Urinary metabolite levels in chronic kidney disease (5-acetylamino-6-formylamino-3-methyluracil) | (Schlosser et al., 2020) |  |
|  |  | C | 7 x 10-128 |  | ↑ | Serum metabolite levels (5-acetylamino-6-formylamino-3-methyluracil) | (Feofanova et al., 2020) |  |
|  |  | C | 6 x 10-24 |  | ↑ | Urinary metabolite levels in chronic kidney disease (5-acetylamino-6-amino-3-methyluracil)  | (Schlosser et al., 2020) |  |
|  |  | C | 3 x 10-202 |  | ↑ | Urinary metabolites  | (Raffler et al., 2015) |  |
| rs35570672 | Non-coding | T | 4 x 10-40 | 0.35 | ↓ | Serum metabolite levels (1-methylxanthine) | (Feofanova et al., 2020) | 8:18415125 |
|  |  | T | 1 x 10-100 |  | ↑ | Serum metabolite levels (*N*-acetylputrescine) | (Feofanova et al., 2020) |  |
| rs4646248 | Non-coding | C | 5 x 10-11 | 0.39 | ↓ | Liver enzyme levels (alkaline phosphatase) | (Pazoki et al., 2021) | 8:18402845 |
|  |  | T | 2 x 10-10 | 0.61 | ↑ | Serum albumin levels | (Sinnott-Armstrong et al., 2021) |  |
| rs4921913 | Non-coding | NR | 7 x 10-9 | - | ↓ | 1-methylxanthine levels (serum) | (Yet et al., 2016) | 8:18414867 |
|  |  | NR | 2 x 10-19 | - | ↑ | 5-acetylamino-6-formylamino-3-methyluracil levels (serum) | (Bar et al., 2020) |  |
|  |  | C | 6 x 10-44 | 0.35 | ↑ | Serum metabolite levels (4-acetamidobutanoate) | (Feofanova et al., 2020) |  |
|  |  | C | 5 x 10-19 |  | ↑ | Liver enzyme levels (gamma-glutamyl transferase) | (Pazoki et al., 2021) |  |
| rs1495743 | Non-coding | T | 3 x 10-47 | 0.35 | ↓ | Blood metabolite ratios (4-acetamidobutanoate/N1-methyladenosine) | (Shin et al., 2014) | 8:18414867 |
| rs4921914 | Non-coding | NR | 6 x 10-18 | - | ↑ | *N*-acetylputrescine levels (serum) | (Bar et al., 2020) | 8:18414928 |
|  |  | C | 1 x 10-28 | 0.35 | NA | Urinary metabolites (Formate/succinate ratio) | (Suhre et al., 2011b) |  |
|  |  | C | 5 x 10-18 |  | NA | Urinary metabolite levels in chronic kidney disease (X - 12410) | (Schlosser et al., 2020) |  |
|  |  | C | 1 x 10-11 |  | ↓ | Urinary metabolite levels in chronic kidney disease (1-methylurate) | (Schlosser et al., 2020) |  |
|  |  | T | 4 x 10-32 | 0.65 | ↑ | Urinary metabolites (H-NMR features; unknown) | (Rueedi et al., 2014) |  |
|  |  | T | 1 x 10-60 |  | ↑ | Blood metabolite levels (1-methylxanthine) | (Shin et al., 2014) |  |
| rs4921915 | Non-coding | G | 1 x 10-19 | 0.35 | ↑ | Urinary metabolite levels in chronic kidney disease (4-acetamidobutanoate) | (Schlosser et al., 2020) | 8:18414956 |
| rs66477371 | Non-coding | T | 6 x 10-6 | 0.07 | ↓ | Academic attainment (math) | (Donati et al., 2021) | 8:18456207 |
| rs7006687 | Non-coding | T | 2 x 10-6 | 0.57 | NA | QT interval (drug interaction; sulfonylurea hypoglycemic agents) | (Avery et al., 2014) | 8:18376073 |
| rs721399 | Non-coding | T | 4 x 10-58 | 0.56 | ↓ | Blood metabolite levels (4-acetamidobutanoate) | (Shin et al., 2014) | 8:18401856 |
|  |  | T | 2 x 10-10 |  | ↓ | 4-acetamidobutanoate levels (blood) | (Rhee et al., 2022) |  |
|  |  |  |  |  |  |  |  |  |

\*, Based on 1000 Genomes Project (phase 3)

†, Human GRCh38/hg38

RAF, relative allele frequency. NR, not reported. NA, not available.

Ins, insertion

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