Data Article

Dataset of allele and genotype frequencies of the three functionally significant polymorphisms of the MMP genes in Russian patients with primary open-angle glaucoma, essential hypertension and peptic ulcer

Oksana Minyaylo, Dina Starikova, Maria Moskalenko, Irina Ponomarenko, Evgeny Reshetnikov, Volodymyr Dvornyk, Mikhail Churnosov

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A B S T R A C T

Data on the allele and genotype frequencies of the three functionally significant single nucleotide polymorphisms (SNPs) of the matrix metalloproteinases (MMP) genes (rs1799750 MMP1, rs3918242 and rs17576 MMP9) in Russian patients with primary open-angle glaucoma (POAG), essential hypertension (EH) and peptic ulcer (PU) are presented. Association studies identified these SNPs as possible significant markers associated with many multifactorial disorders, including POAG, EH, and PU. The frequencies of alleles and genotypes of the three SNPs in Russian patients with POAG, EH, and PU were presented separately for the entire study sample, females, and males, respectively. The data can be used as a reference for the Russian population.

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Specifications Table

| Subject                  | Biology                     |
|--------------------------|-----------------------------|
| Specific subject area    | Genetics                    |
| Type of data             | Table and figure            |
| How data were acquired   | MALDI/TOF mass spectrometry using the Sequenom MassARRAY 4.0 platform (Agena Bioscience™) |
| Data format              | Raw and analyzed data       |
| Parameters for data      | Whole blood (5 ml) was drawn to a plastic vial (Vacutainer®) containing 0.5 M EDTA (pH=8.0). Genomic DNA was isolated by the standard phenol-chloroform method. DNA samples were first checked for quality (concentration 10–15 ng/mL, purity A260/A280=1.7–2.0) and then used for genotyping. About 5% of blind replicate samples were used for genotyping quality control; the repeatability test indicated a 100% concordance rate. |
| collection               | Description of data collection |
|                          | The quality of isolated DNA was checked by the Nanodrop-2000 spectrophotometer. Genotyping was performed on the Sequenom MassARRAY® iPLEX platform using the MALDI-TOF (matrix-assisted laser desorption/ ionization time-of-flight) mass spectrometry. Assay Design Suite 1.0 was used to design a multiplex genotyping assay (http://agenabio.com/assay-design-suite-10-software). |
| Data source location     | Belgorod, Russia            |
| Data accessibility       | The data is available with this article |

Value of the data

- The frequencies of alleles and genotypes of rs1799750 MMP1, rs3918242 and rs17576 MMP9 in Russian patients with POAG, EH, and PU are presented separately for the entire cohort, male and female participants.
- The polymorphisms rs1799750 MMP1, rs3918242 and rs17576 MMP9 may be associated with POAG, EH, and PU.
- The data on the allele and genotype frequencies of the MMP genes can be used for meta-analyses of genetic studies on POAG, EH, and PU.
- The presented data of the MMP genes polymorphisms can serve as a reference for population and genetic association studies of the common disorders.

1. Data description

The dataset contains the raw data (supplementary Table), frequencies of alleles and genotypes (Table 1) for three SNPs of two MMP genes (rs1799750 MMP1, rs3918242 and rs17576 MMP9) in Russian patients diagnosed with POAG, EH, and PU. These polymorphisms were previously reported for their association with POAG, EH, and PU (Table 2) [1–45]. The studied SNPs manifest the regulatory potential (Table 3), which is evidenced by several eQTLs (Table 4) and splicing QTLs (Table 5). The allele and genotype frequencies are provided separately for the whole study cohort, females, and males, respectively. No significant differences in the frequencies of alleles and genotypes were found between the male and female participants for each of the studied diseases.

2. Experimental design, materials, and methods

2.1. Study subjects

The study cohort consisted of 1556 Russian participants, including 536 patients diagnosed with POAG (290 females and 246 males), 621 patients with EH (359 females and 262 males), and 399 patients with PU (211 females and 188 males). The study participants were clinically
| Diseases | SNP genotype or allele rs1799750 | All n | frequency | Male n | frequency | Female n | frequency |
|----------|----------------------------------|-------|-----------|--------|-----------|----------|-----------|
| POAG     | 1G1G                             | 152   | 0.2836    | 73     | 0.2968    | 79       | 0.2724    |
|          | 1G2G                             | 267   | 0.4981    | 131    | 0.5325    | 136      | 0.4690    |
|          | 2G2G                             | 117   | 0.2183    | 42     | 0.1707    | 75       | 0.2586    |
|          | 1G                               | 571   | 0.5327    | 277    | 0.5630    | 294      | 0.5069    |
|          | 2G                               | 501   | 0.4673    | 215    | 0.4370    | 286      | 0.4931    |
|          | rs3918242                        |       |           |        |           |          |           |
|          | CC                               | 385   | 0.7183    | 175    | 0.7114    | 210      | 0.7241    |
|          | CT                               | 133   | 0.2482    | 65     | 0.2642    | 68       | 0.2345    |
|          | TT                               | 18    | 0.0335    | 6      | 0.0244    | 12       | 0.0414    |
|          | C                                | 903   | 0.8424    | 415    | 0.8435    | 488      | 0.8414    |
|          | T                                | 169   | 0.1576    | 77     | 0.1565    | 92       | 0.1586    |
|          | rs17576                          |       |           |        |           |          |           |
|          | AA                               | 205   | 0.3825    | 110    | 0.4472    | 95       | 0.3276    |
|          | GA                               | 260   | 0.4851    | 108    | 0.4390    | 152      | 0.5241    |
|          | GG                               | 71    | 0.1324    | 28     | 0.1138    | 43       | 0.1483    |
|          | A                                | 670   | 0.6250    | 328    | 0.6667    | 342      | 0.5897    |
|          | G                                | 402   | 0.3750    | 164    | 0.3333    | 238      | 0.4103    |
| EH       | rs1799750                        |       |           |        |           |          |           |
|          | 1G1G                             | 169   | 0.2721    | 65     | 0.2481    | 104      | 0.2987    |
|          | 1G2G                             | 309   | 0.4976    | 140    | 0.5334    | 169      | 0.4707    |
|          | 2G2G                             | 143   | 0.2303    | 57     | 0.2175    | 86       | 0.2396    |
|          | 1G                               | 647   | 0.5209    | 270    | 0.5153    | 377      | 0.5251    |
|          | 2G                               | 595   | 0.4791    | 254    | 0.4847    | 341      | 0.4749    |
|          | rs3918242                        |       |           |        |           |          |           |
|          | CC                               | 444   | 0.7150    | 189    | 0.7214    | 255      | 0.7103    |
|          | CT                               | 149   | 0.2399    | 64     | 0.2443    | 85       | 0.2368    |
|          | TT                               | 28    | 0.0451    | 9      | 0.0343    | 19       | 0.0529    |
|          | C                                | 1037  | 0.8349    | 442    | 0.8435    | 595      | 0.8287    |
|          | T                                | 205   | 0.1651    | 82     | 0.1565    | 123      | 0.1713    |
|          | rs17576                          |       |           |        |           |          |           |
|          | AA                               | 229   | 0.3688    | 100    | 0.3817    | 129      | 0.3593    |
|          | GA                               | 311   | 0.5008    | 131    | 0.5000    | 180      | 0.5014    |
|          | GG                               | 81    | 0.1304    | 31     | 0.1183    | 50       | 0.1393    |
|          | A                                | 769   | 0.6192    | 331    | 0.6317    | 438      | 0.6010    |
|          | G                                | 473   | 0.3808    | 193    | 0.3683    | 280      | 0.3899    |
| PU       | rs1799750                        |       |           |        |           |          |           |
|          | 1G1G                             | 121   | 0.3033    | 45     | 0.2394    | 76       | 0.3602    |
|          | 1G2G                             | 195   | 0.4887    | 98     | 0.5212    | 97       | 0.4597    |
|          | 2G2G                             | 83    | 0.2080    | 45     | 0.2394    | 38       | 0.1801    |
|          | 1G                               | 437   | 0.5476    | 188    | 0.5000    | 249      | 0.5901    |
|          | 2G                               | 361   | 0.4524    | 188    | 0.5000    | 173      | 0.4099    |
|          | rs3918242                        |       |           |        |           |          |           |
|          | CC                               | 277   | 0.6942    | 129    | 0.6862    | 148      | 0.7014    |
|          | CT                               | 115   | 0.2883    | 58     | 0.3085    | 57       | 0.2701    |
|          | TT                               | 7     | 0.0017    | 1      | 0.0053    | 6        | 0.0285    |
|          | C                                | 669   | 0.8383    | 316    | 0.8404    | 353      | 0.8365    |
|          | T                                | 129   | 0.1617    | 60     | 0.1596    | 69       | 0.1635    |
|          | rs17576                          |       |           |        |           |          |           |
|          | AA                               | 142   | 0.3559    | 69     | 0.3670    | 73       | 0.3460    |
|          | GA                               | 184   | 0.4612    | 83     | 0.4415    | 101      | 0.4787    |
|          | GG                               | 73    | 0.1829    | 36     | 0.1915    | 37       | 0.1753    |
|          | A                                | 468   | 0.5865    | 221    | 0.5878    | 247      | 0.5853    |
|          | G                                | 330   | 0.4135    | 155    | 0.4122    | 175      | 0.4147    |

Abbreviations: POAG - primary open-angle glaucoma, EH - essential hypertension, PU - peptic ulcer.
Table 2
The literature data about associations of the studied polymorphisms of the MMP genes with POAG, PU and some digestive diseases (gastric and esophageal cancer), EH and IS with EH.

| SNP       | Gene | Number of publications in PubMed/PubMed Central | Phenotype       | Association (significance) (associated allele) | Reference |
|-----------|------|-------------------------------------------------|-----------------|-----------------------------------------------|-----------|
| rs1799750 | MMP1 | 70/119                                          | POAG            | **OR = 1.64, p = 0.01**                         | [1]       |
| rs1799750 | MMP1 |                                                 | POAG            | **OR = 1.64, p = 0.002**                        | [2]       |
| rs1799750 | MMP1 |                                                 | POAG            | **OR = 1.34, p = 0.017 (2 G)**                  | [3]       |
| rs1799750 | MMP1 |                                                 | POAG            | **OR = 2.04, p<0.001 (2 G)**                    | [4]       |
| rs1799750 | MMP1 |                                                 | POAG            | **OR = 1.35, p = 0.017 (2 G)**                  | [5]       |
| rs1799750 | MMP1 |                                                 | peptic ulcer    | **OR = 3.46, p = 0.03 (1 G/1 G)**               | [6]       |
| rs1799750 | MMP1 |                                                 | gastric cancer  | **OR = 3.34, p = 0.016 (2 G/2 G)**              | [7]       |
| rs1799750 | MMP1 |                                                 | gastric cancer  | **OR = 1.05, p = 0.013 (2 G)**                  | [8]       |
| rs1799750 | MMP1 |                                                 | IS with hypertension | **OR = 1.54, p = 0.005 (2 G)** | [9]       |
| rs1799750 | MMP1 |                                                 | IS with hypertension | **OR >1; p<0.05 (2 G)** | [10]      |
| rs1799750 | MMP1 |                                                 | IS with hypertension | **p>0.05** | [11]      |
| rs1799750 | MMP1 |                                                 | essential hypertension in men | **OR = 2.58; p = 0.04 (together with rs11568818, rs1320632, rs11225395)** | [12–17, 18] |
| rs3918242 | MMP9 | 106/127                                         | POAG            | **OR = 1.63; p = 0.002 (T)**                    | [19]      |
| rs3918242 | MMP9 |                                                 | POAG            | **OR = 1.55, p = 0.012 (T)**                    | [20]      |
| rs3918242 | MMP9 |                                                 | POAG            | **OR = 1.46, p = 0.032 (CT+TT)**                | [21]      |
| rs3918242 | MMP9 |                                                 | peptic ulcer    | **p>0.05**                                     | [22]      |
| rs3918242 | MMP9 |                                                 | gastric cancer  | **OR = 2.60; p<0.05 (together with rs17576 and rs17577)** | [23]      |
| rs3918242 | MMP9 |                                                 | esophageal cancer | **OR = 2.71; p = 0.02 (CC)** | [24]      |
| rs3918242 | MMP9 |                                                 | gastric cancer  | **p>0.05**                                     | [25]      |
| rs3918242 | MMP9 |                                                 | IS with hypertension | **OR = 2.76; p = 0.003 (TT)** | [26]      |
| rs3918242 | MMP9 |                                                 | IS with hypertension | **OR = 1.73; p<0.05 (T)** | [27]      |
| rs3918242 | MMP9 |                                                 | IS with hypertension | **OR = 2.20; p<0.05 (TT)** | [28]      |
| rs3918242 | MMP9 |                                                 | IS with hypertension | **OR = 2.08; p = 0.016 (T)** | [29]      |
| rs3918242 | MMP9 |                                                 | IS with hypertension | **OR<1; p = 0.001 (CC)** | [30]      |

(continued on next page)
| SNP     | Gene | Number of publications in PubMed/PubMed Central | Phenotype                                                                 | Association (significance) (associated allele)                                                                 | Reference |
|---------|------|-----------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|-----------|
|         |      |                                               | IS with hypertension                                                     | OR > 1; $p = 0.009$ (T)                                                                                     | [31]      |
|         |      |                                               | IS with hypertension                                                     | OR = 5.53; $p = 0.001$ (CC)                                                                                 | [32]      |
|         |      |                                               | IS with hypertension                                                     | OR = 1.43; $p = 0.001$ (T)                                                                                  | [33]      |
|         |      |                                               | IS with hypertension                                                     | OR = 5.47; $p < 0.05$ (TT)                                                                                 | [34]      |
|         |      |                                               | IS with hypertension                                                     | OR = 1.27; $p = 0.01$ (T)                                                                                  | [12]      |
|         |      |                                               | IS with hypertension                                                     | $p > 0.05$                                                                                                  | [35]      |
|         |      |                                               | essential hypertension                                                  | OR = 1.30; $p = 0.002$                                                                                      | [36]      |
|         |      |                                               | isolated systolic hypertension                                          | OR > 1; $p = 0.009$ (T)                                                                                     | [37]      |
|         |      |                                               | left ventricular hypertrophy in hypertensive patients                    | OR > 1; $p = 0.0015$ (together with rs2234681 and rs17576)                                                | [38]      |
|         |      |                                               | hypertension of pregnancy                                               | OR < 1; $p = 0.007$ (CC)                                                                                   | [39]      |
|         |      |                                               | essential hypertension in children                                       | OR > 1; $p < 0.05$ (TT)                                                                                     | [40]      |
|         |      |                                               | essential hypertension                                                  | $p > 0.05$                                                                                                  | [41]      |
| rs17576 | MMP9 | 78/97                                          | POAG                                                                      | OR = 1.96; $p = 0.0005$ (AG)                                                                               | [20]      |
|         |      |                                               | POAG                                                                      | OR = 0.66; $p = 0.03$ (A)                                                                                   | [21]      |
|         |      |                                               | POAG                                                                      | OR = 1.53; $p = 0.034$ (GG)                                                                                 | [42]      |
|         |      |                                               | POAG in men                                                               | OR = 0.56; $p = 0.003$ (together with rs2250889)                                                            | [43]      |
|         |      |                                               | POAG                                                                      | OR = 2.34; $p = 0.01$ (GG)                                                                                  | [4]       |
|         |      |                                               | POAG                                                                      | $p > 0.05$                                                                                                  | [6]       |
|         |      |                                               | peptic ulcer                                                              | OR = 0.49; $p = 0.007$ (AA)                                                                                  | [7]       |
|         |      |                                               | gastric cancer                                                            | OR = 4.34; $p < 0.05$ (Q)                                                                                   | [23]      |
|         |      |                                               | gastric cancer                                                            | $p > 0.05$                                                                                                  | [44]      |
|         |      |                                               | IS with hypertension                                                      | OR = 0.91; $p = 0.04$ (GG)                                                                                  | [45]      |
|         |      |                                               | IS with hypertension                                                      | $p > 0.05$                                                                                                  | [46]      |
|         |      |                                               | left ventricular hypertrophy in hypertensive patients                    | OR > 1; $p = 0.0015$ (together with rs2234681 and rs3918242)                                                | [38]      |
|         |      |                                               | essential hypertension                                                   | OR > 1; $p < 0.05$ (AA)                                                                                     | [41]      |
|         |      |                                               | isolated systolic hypertension                                           | $p > 0.05$                                                                                                  | [37]      |

Abbreviations: POAG - primary open-angle glaucoma, EH - essential hypertension, IS - ischemic stroke, PU - peptic ulcer.
Table 3
Regulatory effects of the 3 SNPs of the MMP genes (HaploReg, v4.1, update 05.11.2015) ([https://pubs.broadinstitute.org/mammals/haploreg/haploreg.php](https://pubs.broadinstitute.org/mammals/haploreg/haploreg.php)).

| c chr | pos (hg38) | variant | R ref | AM R | AS N | EU R | GE RP | Sip hy | Prom oter histone marks | Enhancer histone marks | DNA see | Prote ins boun ded | Motif s changed | GWAS hits | NHGRI/ EBI | GRA SP QTL | Selec ted eQTL | GENC ODE | RefSeq | dbSN P | func annot |
|-------|------------|---------|-------|------|------|------|-------|-------|-----------------------|-----------------------|---------|------------------|-------------|------------|-------------|-------------|---------------|-----------|--------|--------|-------------|
| 1     | 102799 764 | rs1799 750 | T     | C    | 0.5  | 0.4  | 0.3  | 0.4  | 5 tissues             | 5 tissues             | CFOS    | GATA 2           | 21 altered motifs | 8 hits      | 1.6kb 5' of MMP1 | LOC10028 8077 | intronic      |
| 2     | 460073 37  | rs3918 342 | C     | 0.1  | 0.0  | 0.1  | 0.1  | 1 tissues             | 1 tissues             | BLD, THYM, SPLN IPS C     | 4 altered motifs | 1 hit    | 6 hits           | 1.6kb 5' of MMP9 | 1.6kb 5' of MMP9 | missense |
| 2     | 460115 86  | rs1757 8  | A     | 0.3  | 0.2  | 0.7  | 0.3  | 17 tissues            | 4 tissues             | ESC      | Pax-4  | 12 hits          | MMP9        | MMP9       | missense |
| Chr | SNP   | Reference allele | Alternative allele | Gene expression | Effect Size ($\beta$) | P-Value | Tissue                                |
|-----|-------|------------------|-------------------|-----------------|----------------------|---------|---------------------------------------|
| 11  | rs1799750 | TC               | T                 | MMP1            | $-0.66$              | 9.6E-84 | Cells - Cultured fibroblasts          |
|     |       |                  |                   | MMP1            | $-0.52$              | 1.3E-25 | Thyroid                               |
|     |       |                  |                   | MMP1            | $-0.42$              | 1.9E-25 | Lung                                  |
|     |       |                  |                   | MMP1            | $-0.58$              | 5.8E-23 | Heart - Atrial Appendage              |
|     |       |                  |                   | MMP1            | $-0.45$              | 0.0000000000000000000017 | Adipose - Visceral (Omentum) |
|     |       |                  |                   | MMP1            | $-0.46$              | 0.0000000000000000000066 | Heart - Left Ventricle          |
|     |       |                  |                   | MMP1            | $-0.36$              | 0.0000000000000000000022 | Heart - Left Ventricle          |
|     |       |                  |                   | MMP1            | $-0.32$              | 0.000000013 | Esophagus - Muscularis                |
|     |       |                  |                   | MMP1            | $-0.35$              | 0.000000015 | Artery - Aorta                        |
|     |       |                  |                   | MMP1            | $-0.28$              | 0.000000024 | Adipose - Subcutaneous                |
|     |       |                  |                   | MMP1            | $-0.22$              | 0.000000038 | Artery - Tibial                       |
|     |       |                  |                   | MMP10           | $-0.19$              | 0.0000025 | Lung                                  |
|     |       |                  |                   | MMP1            | $-0.3$               | 0.0000028 | Esophagus - Gastroesophageal Junction |
|     |       |                  |                   | MMP1            | $-0.28$              | 0.00000075 | Breast - Mammary Tissue               |
|     |       |                  |                   | WTAPP1          | $-0.15$              | 0.00004 | Testis                                |
| 20  | rs3918242 | C                | T                 | SLC12A5         | 0.61                 | 0.0000000000000000000059 | Lung                              |
|     |       |                  |                   | SLC12A5         | 0.8                 | 0.0000000000000000000016 | Adipose - Visceral (Omentum)    |
|     |       |                  |                   | SLC12A5         | 0.6                 | 0.0000000000000000000045 | Adipose - Subcutaneous           |
|     |       |                  |                   | SLC12A5         | 0.69                | 0.0000000000000000000045 | Breast - Mammary Tissue          |
|     |       |                  |                   | SLC12A5         | 0.63                | 0.0000000000000000000082 | Artery - Aorta                   |
|     |       |                  |                   | SLC12A5         | 0.78                | 0.000000018 | Spleen                              |
|     |       |                  |                   | SLC12A5         | $-0.61$             | 0.000000019 | Adrenal Gland                        |
|     |       |                  |                   | SNX21           | 0.21                | 0.000000999 | Muscle - Skeletal                    |
|     |       |                  |                   | SLC12A5         | 0.45                | 0.00000029 | Thyroid                              |
|     |       |                  |                   | SLC12A5         | 0.43                | 0.00000037 | Nerve - Tibial                       |
|     |       |                  |                   | SLC12A5         | 0.43                | 0.00000038 | Uterus                               |

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| Chr | SNP     | Reference allele | Alternative allele | Gene expression | Effect Size ($\beta$) | P-Value        | Tissue                                                                 |
|-----|---------|------------------|--------------------|-----------------|----------------------|-----------------|------------------------------------------------------------------------|
| 20  | rs17576 | A                | G                  | SLC12A5         | 0.41                 | 0.0000053       | Skin - Sun Exposed (Lower leg)                                         |
|     |         |                  |                    | SLC12A5         | 0.48                 | 0.000001        | Skin - Not Sun Exposed (Suprapubic)                                    |
|     |         |                  |                    | PLTP            | −0.25               | 0.0000028       | Nerve - Tibial                                                        |
|     |         |                  |                    | SLC12A5         | −0.57               | 0.0000000000043  | Adrenal Gland                                                        |
|     |         |                  |                    | PLTP            | −0.26               | 0.00000000033   | Lung                                                                  |
|     |         |                  |                    | PLTP            | −0.32               | 0.000000026      | Heart - Left Ventricle                                                |
|     |         |                  |                    | PLTP            | −0.24               | 0.000000034      | Nerve - Tibial                                                       |
|     |         |                  |                    | PLTP            | −0.2                | 0.000000021      | Adipose - Subcutaneous                                                |
|     |         |                  |                    | NEURL2          | −0.3                | 0.000000026      | Adipose - Visceral (Omentum)                                          |
|     |         |                  |                    | PLTP            | −0.2                | 0.000000046      | Thyroid                                                              |
|     |         |                  |                    | PLTP            | −0.19               | 0.000000055      | Artery - Tibial                                                      |
|     |         |                  |                    | PLTP            | −0.37               | 0.000000066      | Adrenal Gland                                                        |
|     |         |                  |                    | NEURL2          | −0.24               | 0.0000015        | Adipose - Subcutaneous                                                |
|     |         |                  |                    | PLTP            | −0.25               | 0.000002         | Artery - Aorta                                                       |
|     |         |                  |                    | NEURL2          | −0.31               | 0.0000021        | Artery - Aorta                                                       |
|     |         |                  |                    | PLTP            | −0.18               | 0.0000024        | Adipose - Visceral (Omentum)                                          |
|     |         |                  |                    | PLTP            | −0.3                | 0.0000025        | Colon - Sigmoid                                                     |
|     |         |                  |                    | PLTP            | −0.22               | 0.0000033        | Brain - Frontal Cortex (BA9)                                         |
|     |         |                  |                    | PCIF1           | 0.35                | 0.0000041        | Adrenal Gland                                                        |
|     |         |                  |                    | ZSWIM1          | −0.26               | 0.0000068        | Adipose - Visceral (Omentum)                                          |
|     |         |                  |                    | RP3–337018.9    | −0.22               | 0.0000076        | Lung                                                                 |
|     |         |                  |                    | PLTP            | −0.32               | 0.0000091        | Pituitary                                                           |
|     |         |                  |                    | SNX21           | 0.14                | 0.0000012        | Muscle - Skeletal                                                   |
|     |         |                  |                    | RP3–337018.9    | −0.2                | 0.0000028        | Adipose - Subcutaneous                                               |
|     |         |                  |                    | NEURL2          | −0.22               | 0.000036         | Lung                                                                 |
|     |         |                  |                    | NEURL2          | −0.22               | 0.000073         | Thyroid                                                             |
Table 5
The sQTL values of the 3 SNPs of the MMP genes. (according to Genotype-Tissue Expression (GTEx) (http://www.gtexportal.org/)).

| Chr | SNP   | Reference allele | Alternative allele | Gene Symbol | Intron Id                         | Effect Size (β) | P-Value       | Tissue                        |
|-----|-------|------------------|--------------------|-------------|-----------------------------------|----------------|---------------|-------------------------------|
| 11  | rs1799750 | TC               | T                  | WTAPP1      | 102,832,906:102,833,452:clu_16,168 | -0.51          | 0.000000000065 | Testis                       |
| 20  | rs3918242 | C                | T                  | CD40        | 46,126,741:46,128,138:clu_33,045  | 0.5            | 0.00000000029  | Thyroid                      |
|     |        |                  |                    | CD40        | 46,126,741:46,128,138:clu_32,508  | 0.45           | 0.00000000067  | Lung                          |
|     |        |                  |                    | CD40        | 46,126,741:46,128,138:clu_32,508  | 0.45           | 0.00000000067  | Lung                          |
|     |        |                  |                    | SLC12AS     | 46,021,886:46,023,369:clu_29,529  | 0.79           | 0.00000000098  | Pituitary                    |
|     |        |                  |                    | CD40        | 46,126,741:46,128,138:clu_27,442  | 0.49           | 0.000000041    | Artery - Aorta               |
|     |        |                  |                    | ACOT8       | 45,841,956:45,844,263:clu_24,540  | 0.58           | 0.00000011     | Heart - Left Ventricle       |
|     |        |                  |                    | CD40        | 46,126,741:46,128,138:clu_22,055  | 0.74           | 0.00000015     | Cells - EBV-transformed lymphocytes |
|     |        |                  |                    | ACOT8       | 45,841,956:45,844,263:clu_27,123  | 0.49           | 0.00000041     | Heart - Atrial Appendage     |
| 20  | rs17576 | A                | G                  | SLC12AS     | 46,021,886:46,023,369:clu_29,529  | 0.63           | 0.000000000093 | Pituitary                    |
|     |        |                  |                    | SLC12AS     | 46,023,071:46,023,369:clu_24,852  | -0.45          | 0.000000033    | Brain - Cortex               |
|     |        |                  |                    | SLC12AS     | 46,021,886:46,023,369:clu_26,648  | 0.46           | 0.000002       | Brain - Cerebellum            |
|     |        |                  |                    | SLC12AS     | 46,021,886:46,023,369:clu_53,353  | 0.38           | 0.000011       | Testis                       |
examined at the Department of Eye Microsurgery (patients with POAG), Department of Cardiology (patients with EH), and Department of Gastroenterology (patients with PU) of St. Isaaf Belgorod Regional Clinical Hospital. All participants were self-reported unrelated Russians born in Central Russia [46]. The study was approved by the Regional Ethics Committee of Belgorod State University. All participants signed an informed consent prior to the enrolment to this study.

2.2. DNA analysis

Phlebotomy was performed by a certified nurse. Blood (5 ml) was drawn from the ulnar vein to a plastic vial (Vacutainer®) with 0.5 M EDTA (pH = 8.0). Total genomic DNA was isolated from the buffy coat by the standard phenol-chloroform protocol [47] and then checked for quality using Nanodrop 2000 spectrophotometer (Thermo Scientific, Inc.). Only samples with A260/A280 = 1.7–2.0 were used for the analysis. The isolated DNA was stored at −80°C.

Three SNPs of the MMP genes (rs1799750 MMP1, rs3918242 and rs17576 MMP9) were selected for the analysis. The following selection criteria were applied [48,49]: 1) Previously reported associations with POAG, EH and PU (Table 2), 2) Regulatory potential (regSNP) (Table 3), 3) Effect on gene expression (eSNP) (Table 4), 4) Splicing QTLs (sSNP) (Table 5), and 5) MAF > 5%.

The selected loci were associated with POAG, EH and PU in previously published candidate gene association studies (Table 2) and have functional significance: significant regulatory potential (Table 3) (determined using the online tools HaploReg, v4.1 update 05.11.2015, https://pubs.broadinstitute.org/mammals/haploreg/haploreg.php), influence gene expression level (Table 4) and involved in splicing QTLs (Table 5) (determined using the GTExportal data, http://www.gtexportal.org/).

The DNA samples used for the analysis had concentration 10–15 ng/ml. A single well iPLEX SNP genotyping assay was designed using the Assay Design Suite 1.0 (http://agenabio.com/assay-design-suite-10-software). For this purpose, three SNPs of interest were retrieved from dbSNP of NCBI and imported into the software according to their IDs. DNA genotyping was performed on the MALDI-TOF mass spectrometry iPLEX platform (Agena Bioscience Inc, San Diego, CA).

For quality control of genotyping, 5% of blind replicate samples were included. The concordance for replicate samples was 100%.

2.3. Statistical analysis

The studied SNPs were checked for their correspondence to the Hardy-Weinberg equilibrium (HWE) using the chi-square test. The frequencies of alleles and genotypes were analyzed for possible differences between the females and males in the study sample using the Kruskal-Wallis test.

Declaration of Competing Interest

The authors have no known competing financial interests or personal relationships that might have, or could be perceived to have influenced the results reported in this article.

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Supplementary materials

Supplementary material associated with this article can be found in the online version, at doi:10.1016/j.dib.2020.106004.

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