

Maternal smoking during pregnancy affects adult onset of asthma in offspring: a follow up from birth to age 46 years

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Methods

The study population was based on the Northern Finland Birth Cohort in 1966 consisting of mothers and their children who were born in the northern Finland provinces of Oulu and Lapland in 1966 (1). The total number of births was 12058 in 1966, which covered 96.3% of all births in the area. In 1980, for the age 14 follow-up, 11764 alive subjects (97.6%) were traced and sent postal questionnaire, to which 11010 subjects responded. At the age of 31 in 1997, 10282 subjects were alive and traced. Among them, 8463 subjects who were still living in northern Finland or in the capital area were sent postal questionnaires and invited to clinical examinations to which 6025 subjects (71.2%) attended (2).

At the age of 46 in 2012-2013, 10300 subjects were alive and traced (85.4%). All subjects were given the opportunity to respond to two web based questionnaires (3,4) regarding background, lifestyle, health status, finances, work life and resources. If the participants did not have a computer, postal inquiries were sent to them. 7148 subjects completed data collection. The study was approved by the Ethics Committee of the Finnish Institute of Occupational Health and by the Ethics Committee of the Northern Ostrobothnia Hospital

District. At all stages of the study, the subjects gave written informed consent according to the Declaration of Helsinki.

Results

Exploring potential confounding factors and gender groups on offspring's asthma onset between 31 and 46 years

When analysing the potential confounding factors, parental asthma affected the risk of offspring's asthma development between 31-46 years (Table 1, S1). Mothers' education, ponderal index (in tertile), Apgar score at the 1st minute and parity showed no significant effects on development of asthma between the ages of 31-46 years (Table 1, S1). Offspring's education of 9 years or less or regular smoking at 31 years did not associate statistically significantly with asthma onset at 31-46 years (Table 1, S1). Mother's age at the time of delivery did not associate with offspring's cumulative incidence of asthma between 31-46 years (OR=0.99 95% CI 0.97-1.00, p=0.076)

The effect of maternal smoking on the asthma onset of offspring with past respiratory problems

When analysing the associations of potential confounding factors with adult onset asthma in the offspring subgroups reporting asthma, parental asthma increased the risk of offspring's asthma development between 31-46 years, but only in the offspring subgroup reporting as never having had asthma, not diagnosed by a physician (Table 1, S2). Mothers' education, ponderal index (in tertile), Apgar score at the 1st minute showed no significant effects on development of asthma between the ages of 31-46 years in any subgroup (Table 1, S2). Parity associated with offspring's onset of asthma between 31-46 years, in the subgroup who reported as having asthma, which is not doctor-diagnosed, at 31 years.

When analysing the potential confounding factors in the subgroups reporting wheeze, parental asthma affected the risk of offspring's asthma development between 31-46 years, but only in the offspring subgroup with beginning asthma at 31 years (Table 1, S3). Confounding factors showed no significant effects on development of asthma between the ages of 31-46 years in any subgroup (Table 1, S3). Parity associated with offspring's onset of asthma between 31-46 years, in the subgroup with current wheeze at 31 years.

Discussion

Several SNPs have been identified as being susceptibility genes affecting asthma risk due to tobacco smoke exposure. These single nucleotide polymorphisms are found in loci of genes encoding glutathione S-transferase (GSTM1, GSTT1, GSTP1), Gasdermin (GSDMB, GSDML), ORMDL3, Sm protein family (LSM14A), Protein Tyrosine Phosphatase, Receptor (PTPRT), and Runt Related Transcription Factor 1 (RUNX1) (5-12). A study group found suggestive evidence for an interaction between rs8094633 on chromosome 18 near EPB41L3 and in utero tobacco smoke exposure and an interaction between rs1575472 on chromosome 6 in PACRG and childhood tobacco smoke exposure. The SNPs found have not been identified previously in general genome-wide association studies on childhood asthma. Interestingly, the SNPs interacting with in utero and childhood tobacco smoke exposure were different and were not involved in the same pathway (13). A study in a pediatric population showed that effects of in utero exposure to maternal smoking on childhood asthma and wheezing occurrence in offspring were largely restricted to children with the GSTM1-null genotype (8). GSTM1 functions in detoxification of electrophilic compounds, including carcinogens, therapeutic drugs, environmental toxins and products of oxidative stress, by conjugation with glutathione (8). In Finnish population the SNP of GSTM1 gene is rare and thus we were not able to study it. Yet the findings of our group and other groups could imply the impact of interaction between foetal genome and gestational environment on development of asthma in adulthood.

Regarding potential confounding factors, the observed effect could not be explained by covariates such as maternal education, ponderal index, Apgar score at the 1st minute, parity, parental asthma, offspring's education and smoking at 31 years. However, the independent effect only remained significant among females. This could putatively reflect gender-based differences in utero and during postnatal life in programming airways towards asthma pathogenesis (14). Birth order associated with the cumulative incidence of asthma of adult offspring with current wheeze/beginning asthma so that if the birth order of the offspring was third, the

asthma risk was lower compared higher or lower birth order. This could be related to the offspring's exposure of infections and airway development. Another study showed that among Israeli children who were the only child in the family, the prevalence of asthma was 7.3% (15). The prevalence increased to 8.95% among subjects from families with three siblings, and then progressively decreased as the number of siblings increased, and reached a trough of 0.58% in conscripts from families of 15 to 20 siblings. Asthma prevalence was similar for all birth orders (15).

A study in a Scottish population of pregnant women showed that the prevalence of self-reported current smoking (24 %) was significantly lower than a cotinine-validated estimate of current smokers (30 %) pointing out a need to offer smoking cessation programs to all pregnant women, in order to target pregnant women who do not disclose their smoking status (16). The proportion of pregnant smokers in our study was lower (9 %) than in previous studies in other populations probably in part due to differences in population and health care. As our interest was new diagnoses of adult asthma, we dropped off mothers whose offspring had had childhood asthma or suspicion of asthma before the age of 31 years. When we evaluated the whole cohort, the proportion of mothers who reported smoking during the last three months of pregnancy was increased. It must also be taken into account that in our study smoking status relied only on self-report to identify pregnant smokers, which underestimates the true number of pregnant smokers as previously reported (16). Furthermore the same study showed that the prevalence of smoking was higher (40 %) in mothers with the two highest categories indicating the biggest deprivation, according to the Scottish Index of Multiple Deprivation (16). We found that neither offspring's education nor maternal education was associated with adult-onset asthma.

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Table S1. Cumulative incidence of physician-diagnosed asthma between the ages 31-46 years by maternal smoking during pregnancy, perinatal factors and selected factors at age 31 years - data from the 1966 Northern Finland Birth Cohort.

| Factors | In total | | | | Men | | | | Women | | | |
|---|------------------------|--------------------------------------|----------|---------|-------------------|--------------------------------------|----------|---------|---------------------|--------------------------------------|----------|---------|
| | All subjects n=5200 | Subjects with new DD asthma n=372 | % 9.1 | P | All men n=2314 | Subjects with new DD asthma n=118 | % 5.1 | P | All women n=2886 | Subjects with new DD asthma n=254 | % 8.8 | P |
| <hr/> | | | | | | | | | | | | |
| Maternal smoking during the last three months of pregnancy | | | | | | | | | | | | |
| No | 4727 | 322 | 6.8 | 0.004 | 2113 | 104 | 4.9 | 0.237 | 2614 | 218 | 8.3 | 0.009 |
| Yes | 473 | 50 | 10.6 | | 201 | 14 | 7.0 | | 272 | 36 | 14.2 | |
| Maternal smoking before the pregnancy | | | | | | | | | | | | |
| No | 4268 | 293 | 6.9 | 0.099 | 1893 | 90 | 4.8 | 0.167 | 2375 | 203 | 8.5 | 0.253 |
| yes | 885 | 75 | 8.5 | | 402 | 26 | 6.5 | | 483 | 49 | 10.1 | |
| Number of cigarettes the mother smoked per day before pregnancy | | | | | | | | | | | | |
| No | 4727 | 322 | 6.8 | 0.011** | 2113 | 104 | 4.9 | 0.133** | 2614 | 218 | 8.3 | 0.012 |
| 1-5 cigarette | 293 | 31 | 10.6 | | 134 | 7 | 5.2 | | 159 | 24 | 15.1 | |
| >=6 | 180 | 19 | 10.6 | | 67 | 7 | 10.4 | | 113 | 12 | 10.6 | |
| cigarettes/pipes | | | | | | | | | | | | |
| Change in smoking status during pregnancy | | | | | | | | | | | | |
| No smoking | 4265 | 292 | 6.8 | 0.113** | 1892 | 90 | 4.8 | 0.279** | 2373 | 202 | 8.5 | 0.035 |
| Gave up | 297 | 20 | 6.7 | | 145 | 10 | 6.9 | | 152 | 10 | 6.6 | |
| Cut down | 273 | 28 | 10.3 | | 128 | 6 | 4.7 | | 145 | 22 | 15.2 | |
| No change or increased | 306 | 27 | 8.8 | | 123 | 10 | 8.1 | | 183 | 17 | 9.3 | |
| Ponderal index | | | | | | | | | | | | |
| Lowest tertile | 1736 | 136 | 7.8 | 0.274 | 851 | 49 | 5.8 | 0.566 | 885 | 87 | 9.8 | 0.319 |
| Middle tertile | 1711 | 110 | 6.4 | | 741 | 34 | 4.6 | | 970 | 76 | 7.8 | |
| Highest tertile | 1709 | 123 | 7.2 | | 700 | 35 | 5.0 | | 1009 | 88 | 8.7 | |
| Apgar score at 1st minute | | | | | | | | | | | | |
| <=6 | 149 | 13 | 8.7 | 0.520 | 83 | 7 | 8.4 | 0.203 | 66 | 6 | 9.1 | 0.829 |
| 7-10 | 4762 | 345 | 7.2 | | 2098 | 108 | 5.1 | | 2664 | 237 | 8.9 | |
| Parity | | | | | | | | | | | | |
| 1 | 1641 | 121 | 7.4 | 0.582 | 736 | 33 | 4.5 | 0.505 | 905 | 88 | 9.7 | 0.454** |
| 2 | 1274 | 101 | 7.9 | | 586 | 35 | 6.0 | | 688 | 66 | 9.6 | |
| 3 | 848 | 58 | 6.8 | | 364 | 17 | 4.7 | | 484 | 41 | 8.5 | |
| 4 | 469 | 33 | 7.0 | | 220 | 15 | 6.8 | | 249 | 18 | 7.2 | |
| 5 or more | 961 | 59 | 6.1 | | 404 | 18 | 4.5 | | 557 | 41 | 7.4 | |
| Maternal education level | | | | | | | | | | | | |
| Matriculation examination | 263 | 17 | 6.5 | 0.490 | 128 | 6 | 4.7 | 0.836 | 135 | 11 | 8.1 | 0.689 |
| Secondary school or equivalent | 1209 | 78 | 6.5 | | 549 | 25 | 4.6 | | 660 | 53 | 8.0 | |
| Primary school or less | 3682 | 274 | 7.4 | | 1614 | 85 | 5.3 | | 2068 | 189 | 9.1 | |
| Parental asthma | | | | | | | | | | | | |
| Neither | 2885 | 187 | 6.5 | 0.01 | 1321 | 61 | 4.6 | 0.005 | 1564 | 126 | 8.1 | 0.059 |
| Either or both | 761 | 77 | 10.1 | | 304 | 27 | 8.9 | | 457 | 50 | 10.9 | |

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|--|------|-----|-----|-------|------|----|-----|-------|------|-----|-----|-------|
| Offspring's education level at 31 years | | | | | | | | | | | | |
| Matriculation examination | 2322 | 158 | 6.8 | 0.447 | 764 | 34 | 4.5 | 0.365 | 1558 | 124 | 8.0 | 0.112 |
| Less than matriculation examination | 2859 | 211 | 7.4 | | 1540 | 83 | 5.4 | | 1319 | 128 | 9.7 | |
| Offspring's regular smoking at 31 years*** | | | | | | | | | | | | |
| No | 4003 | 278 | 6.9 | 0.356 | 1671 | 78 | 4.7 | 0.194 | 2332 | 200 | 8.6 | 0.386 |
| Yes | 1111 | 86 | 7.7 | | 608 | 37 | 6.1 | | 503 | 49 | 9.7 | |

** trend test

*** smoking at least one cigarette per day for at least one year

Table S2. Cumulative incidence of physician-diagnosed asthma between the ages 31-46 years in three subgroups based on offspring's self-reported never/beginning/past asthma without doctor-diagnosed asthma at 31 years. Analyzed by maternal smoking during pregnancy, perinatal factors and selected factors at age 31 years - data from the 1966 Northern Finland Birth Cohort.

| Factors | Never asthma | | | | Beginning asthma | | | | Past asthma | | | |
|---|--------------|-----------------------------------|-------|---------|------------------|----------------------------------|--------|---------|-------------|----------------------------------|--------|---------|
| | n=4994 | Subjects with new DD-asthma n=325 | % 6.5 | P | n=128 | Subjects with new DD-asthma n=31 | % 24.2 | P | n=63 | Subjects with new DD-asthma n=15 | % 23.8 | P |
| <hr/> | | | | | | | | | | | | |
| Maternal smoking during the last three months of pregnancy | | | | | | | | | | | | |
| No | 4548 | 288 | 6.3 | 0.108 | 112 | 25 | 22.3 | 0.215 | 52 | 8 | 15.4 | 0.002 |
| Yes | 446 | 37 | 8.3 | | 16 | 6 | 37.5 | | 11 | 7 | 63.6 | |
| Maternal smoking before the pregnancy | | | | | | | | | | | | |
| No | 4112 | 261 | 6.3 | 0.146 | 101 | 24 | 23.8 | 1.00 | 42 | 7 | 16.7 | 0.120 |
| yes | 837 | 62 | 7.4 | | 26 | 6 | 23.1 | | 20 | 7 | 35.0 | |
| Number of cigarettes the mother smoked per day before pregnancy | | | | | | | | | | | | |
| No | 4548 | 288 | 6.3 | 0.253** | 112 | 25 | 22.3 | 0.290** | 52 | 8 | 15.4 | 0.001** |
| 1-5 cigarette | 278 | 24 | 8.6 | | 8 | 4 | 50.0 | | 7 | 3 | 42.9 | |
| >=6 cigarettes/pipes | 168 | 13 | 7.7 | | 8 | 2 | 25.0 | | 4 | 4 | 100.0 | |
| Change in smoking status during pregnancy | | | | | | | | | | | | |
| No smoking | 4110 | 261 | 6.4 | 0.474** | 100 | 23 | 23.0 | 0.500** | 42 | 7 | 16.7 | 0.007** |
| Gave up | 279 | 18 | 6.5 | | 11 | 2 | 18.2 | | 6 | 0 | 0.0 | |
| Cut down | 260 | 23 | 8.8 | | 6 | 3 | 50.0 | | 6 | 2 | 33.3 | |
| No change or increased | 288 | 19 | 6.6 | | 11 | 3 | 27.3 | | 7 | 5 | 71.4 | |
| Ponderal index | | | | | | | | | | | | |
| Lowest tertile | 1667 | 113 | 6.8 | 0.383 | 45 | 16 | 35.6 | 0.112 | 20 | 7 | 35.0 | 0.179 |
| Middle tertile | 1643 | 96 | 5.8 | | 39 | 8 | 20.5 | | 21 | 5 | 23.8 | |
| Highest tertile | 1644 | 114 | 6.9 | | 42 | 7 | 16.7 | | 20 | 2 | 10.0 | |
| Apgar score at 1st minute | | | | | | | | | | | | |
| <=6 | 140 | 11 | 7.9 | 0.493 | 6 | 2 | 33.3 | 0.631 | 3 | 0 | 0.0 | 0.561 |
| 7-10 | 4578 | 302 | 6.6 | | 114 | 27 | 23.7 | | 55 | 15 | 27.3 | |
| Parity | | | | | | | | | | | | |
| 1 | 1575 | 99 | 6.3 | 0.614 | 37 | 15 | 40.5 | 0.031 | 25 | 7 | 28.0 | 0.166 |
| 2 | 1233 | 92 | 7.5 | | 29 | 6 | 20.7 | | 12 | 3 | 25.0 | |
| 3 | 811 | 51 | 6.3 | | 26 | 2 | 7.7 | | 8 | 4 | 50.0 | |
| 4 | 457 | 30 | 6.6 | | 9 | 3 | 33.3 | | 3 | 0 | 0.0 | |
| 5 or more | 911 | 53 | 5.8 | | 27 | 5 | 18.5 | | 15 | 1 | 6.7 | |
| Maternal education level | | | | | | | | | | | | |
| Matriculation examination | 252 | 17 | 6.7 | 0.694 | 5 | 0 | 0.0 | 0.390 | 5 | 0 | 0.0 | 0.621 |
| Secondary school or equivalent | 1171 | 70 | 6.0 | | 24 | 5 | 20.8 | | 13 | 3 | 23.1 | |
| Primary school or less | 3526 | 235 | 6.7 | | 98 | 26 | 26.5 | | 45 | 12 | 26.7 | |
| Parental asthma | | | | | | | | | | | | |
| Neither | 2787 | 165 | 5.9 | 0.006 | 70 | 17 | 24.3 | 1.00 | 21 | 4 | 19.0 | 0.285 |
| Either or both | 709 | 63 | 8.9 | | 32 | 7 | 21.9 | | 18 | 7 | 38.9 | |

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|--|------|-----|-----|-------|----|----|------|-------|----|----|------|-------|
| Offspring's education level at 31 years | | | | | | | | | | | | |
| Matriculation examination | 2249 | 144 | 6.4 | 0.908 | 44 | 9 | 20.5 | 0.522 | 22 | 4 | 18.2 | 0.544 |
| Less than matriculation examination | 2726 | 178 | 6.5 | | 84 | 22 | 26.2 | | 41 | 11 | 26.8 | |
| Offspring's regular smoking at 31 years*** | | | | | | | | | | | | |
| No | 3851 | 245 | 6.4 | 0.527 | 95 | 21 | 22.1 | 0.354 | 44 | 11 | 25.0 | 0.738 |
| Yes | 1060 | 73 | 6.9 | | 33 | 10 | 30.3 | | 17 | 3 | 17.6 | |

** trend test

*** smoking at least one cigarette per day for at least one year

DD= doctor-diagnosed

Table S3. Cumulative incidence of physician-diagnosed asthma between the ages 31-46 years in three subgroups based on offspring's self-reported never/current/past wheeze at 31 years. Analyzed by maternal smoking during pregnancy, perinatal factors and selected factors at age 31 years - data from the 1966 Northern Finland Birth Cohort.

| Factors | Never wheeze | | | | Current wheeze | | | | Past wheeze | | | |
|---|--------------|-----------------------------------|-------|---------|----------------|----------------------------------|--------|---------|-------------|----------------------------------|--------|---------|
| | n=3702 | Subjects with new DD asthma n=188 | % 5.1 | P | n=550 | Subjects with new DD asthma n=84 | % 15.3 | P | n=643 | Subjects with new DD asthma n=78 | % 12.1 | P |
| <hr/> | | | | | | | | | | | | |
| Maternal smoking during the last three months of pregnancy | | | | | | | | | | | | |
| No | 3386 | 171 | 5.1 | 0.788 | 483 | 70 | 14.5 | 0.203 | 585 | 62 | 10.6 | 0.000 |
| Yes | 316 | 17 | 5.4 | | 67 | 14 | 20.9 | | 58 | 16 | 27.6 | |
| Maternal smoking before the pregnancy | | | | | | | | | | | | |
| No | 3056 | 158 | 5.2 | 0.763 | 437 | 63 | 14.4 | 0.374 | 528 | 55 | 10.4 | 0.005 |
| yes | 613 | 29 | 4.7 | | 111 | 20 | 18.0 | | 107 | 22 | 20.6 | |
| Number of cigarettes the mother smoked per day before pregnancy | | | | | | | | | | | | |
| No | 3386 | 171 | 5.1 | 0.978** | 483 | 70 | 14.5 | 0.377** | 585 | 62 | 10.6 | 0.002** |
| 1-5 cigarette | 197 | 11 | 5.6 | | 42 | 9 | 21.4 | | 36 | 10 | 27.8 | |
| >=6 cigarettes/pipes | 119 | 6 | 5.0 | | 25 | 5 | 20.0 | | 22 | 6 | 27.3 | |
| Change in smoking status during pregnancy | | | | | | | | | | | | |
| No smoking | 3055 | 158 | 5.2 | 0.922** | 437 | 63 | 14.4 | 0.528** | 527 | 54 | 10.2 | 0.009** |
| Gave up | 216 | 9 | 4.2 | | 31 | 6 | 19.4 | | 32 | 4 | 12.5 | |
| Cut down | 182 | 9 | 4.9 | | 40 | 9 | 22.5 | | 33 | 8 | 24.2 | |
| No change or increased | 210 | 10 | 4.8 | | 39 | 6 | 15.4 | | 41 | 10 | 24.4 | |
| Ponderal index | | | | | | | | | | | | |
| Lowest tertile | 1220 | 66 | 5.4 | 0.823 | 194 | 33 | 17.0 | 0.587 | 223 | 28 | 12.6 | 0.706 |
| Middle tertile | 1226 | 60 | 4.9 | | 168 | 22 | 13.1 | | 206 | 22 | 10.78 | |
| Highest tertile | 1229 | 61 | 5.0 | | 177 | 27 | 15.3 | | 209 | 28 | 13.4 | |
| Apgar score at 1st minute | | | | | | | | | | | | |
| <=6 | 102 | 5 | 4.9 | 1.00 | 20 | 5 | 25.0 | 0.212 | 20 | 3 | 15.00 | 0.726 |
| 7-10 | 3392 | 1762 | 5.2 | | 508 | 76 | 15.0 | | 589 | 72 | 12.2 | |
| Parity | | | | | | | | | | | | |
| 1 | 1173 | 57 | 4.9 | 0.455 | 175 | 35 | 20.0 | 0.027 | 209 | 22 | 10.5 | 0.795 |
| 2 | 903 | 56 | 6.2 | | 123 | 16 | 13.0 | | 161 | 23 | 14.3 | |
| 3 | 596 | 31 | 5.2 | | 98 | 8 | 8.2 | | 106 | 14 | 13.2 | |
| 4 | 337 | 14 | 4.2 | | 44 | 11 | 23.0 | | 62 | 8 | 12.9 | |
| 5 or more | 6901 | 30 | 4.3 | | 108 | 14 | 13.0 | | 105 | 11 | 10.5 | |
| Maternal education level | | | | | | | | | | | | |
| Matriculation examination | 184 | 11 | 6.0 | 0.646 | 27 | 2 | 7.4 | 0.391 | 39 | 4 | 10.3 | 0.596 |
| Secondary school or equivalent | 893 | 41 | 4.6 | | 109 | 20 | 18.3 | | 142 | 14 | 9.9 | |
| Primary school or less | 2593 | 134 | 5.2 | | 410 | 62 | 15.3 | | 457 | 60 | 13.1 | |
| Parental asthma | | | | | | | | | | | | |
| Neither | 2119 | 105 | 5.0 | 0.309 | 292 | 36 | 12.3 | 0.003 | 353 | 39 | 11.0 | 0.307 |
| Either or both | 491 | 30 | 6.1 | | 117 | 29 | 24.8 | | 107 | 16 | 15.0 | |

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|--|------|-----|-----|-------|-----|----|------|-------|-----|----|------|-------|
| Offspring's education level at 31 years | | | | | | | | | | | | |
| Matriculation examination | 1725 | 91 | 5.3 | 0.908 | 199 | 31 | 15.6 | 0.902 | 282 | 29 | 10.3 | 0.271 |
| Less than matriculation examination | 1965 | 96 | 4.9 | | 350 | 53 | 15.1 | | 351 | 47 | 13.2 | |
| Offspring's regular smoking at 31 years*** | | | | | | | | | | | | |
| No | 3006 | 151 | 5.0 | 0.619 | 317 | 56 | 17.7 | 0.070 | 496 | 57 | 11.5 | 1.00 |
| Yes | 632 | 35 | 5.5 | | 227 | 27 | 11.9 | | 137 | 16 | 11.7 | |

** trend test
 *** smoking at least one cigarette per day for at least one year
 DD= doctor-diagnosed

Table S4. List of the SNPs identified from a literature search associating with tobacco smoke exposure and asthma

| SNP_id | PMID (REF) | chromosome: position | ext_gene_name | transcript_count | allele | MAF for ALL | MAF for AFR | MAF for AMR | MAF for EAS | MAF for FIN | MAF for NFE | MAF for OTH | MAF for SAS |
|--|-------------------------------|----------------------------|----------------|------------------|------------|----------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| rs1042713 | 18558635 (12) | 5:148206156 | ADRB2 | 1 | G/A | 2.968 | 3.372 | 3.066 | 2.940 | 3.988 | 3.022 | 2.617 | 2.797 |
| rs11702779 | 21803869 (6) | 21:36160098 | RUNX1 | 19 | G/A | 2.601 | 2.467 | 3.706 | 2.851 | 3.154 | 2.788 | 2.503 | 2.684 |
| rs1759092 | 28253294 (5) | 19:34663409 | LSM14A | 8 | G/A | 4.094 | 4.692 | 3.481 | 3.794 | 1.101 | 3.788 | 4.184 | 4.053 |
| rs2305480 | 22626592 (7) | 17:38060848 | GSDMB | 15 | G/A | 2.440 | 0.985 | 2.243 | 2.920 | 1.810 | 3.562 | 3.047 | 3.160 |
| rs366631 | 12186820 (8) | 1:110252472 | GSTM1 | 8 | A/G | NA | NA | NA | NA | NA | NA | NA | NA |
| rs40401 | 24684517 (11) | 5:131396222 | IL3 | 1 | C/T | 2.413 | 3.643 | 1.765 | 2.024 | 3.678 | 2.213 | 1.677 | 2.015 |
| rs4795400 | 22626592 (7) | 17:38060848 | GSDMB | 15 | C/T | 2.477 | 1.106 | 2.235 | 2.920 | 1.803 | 3.562 | 3.056 | 3.182 |
| rs7262414 | 28253294 (5) | 20:40701392 | PTPRT | 8 | C/A | 1.082 | 0.715 | 0.638 | 0.966 | 0.0068 | 1.388 | 1.356 | 1.188 |
| rs8069176 rs1695 (previous id rs947894) | 22626592 (7) 20526719 (10) | 17:38060848 11:67352689 | GSDMB GSTP1 | 15 1 | G/A A/G | 2.865 0.354 | 2.499 0.450 | 2.320 0.375 | 2.913 0.172 | 1.816 0.270 | 3.566 0.335 | 3.040 0.317 | 3.132 NA |
| rs8076131 | 22626592 (7) | 17:38060848 | GSDMB | 15 | G/A | 4.409 | 5.713 | 4.657 | 4.047 | 5.097 | 3.378 | 3.853 | 3.720 |

SNP=single nucleotide polymorphism, CHR: POS= chromosome position, ext=external, AFR=African, AMR=Admixed American, EAS=East Asian, FIN=Finnish, MAF = minor allele frequency, NFE=Non-Finnish European, OTH=Other, SAS=South Asian, NA=not applicable.