Genetic Determinants For Cancer Risks With Racial Differences And Asthma

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GENETIC DETERMINANTS FOR CANCER RISKS WITH RACIAL DIFFERENCES AND ASTHMA

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April 2021
Abstract

Over the past decade, many studies have found disproportionally higher prostate cancer among men of African ancestry, and testicular cancer incidences among men of European ancestry, compared with men from other ethnicity/race groups. However, genetic determinants that could potentially explain this observation are unclear. This study collected single nucleotide polymorphisms (SNPs) related to the two cancer types and compared the frequencies of each risk allele of SNPs among men of African or European ancestry from several genetic databases. When comparing the frequencies of risk alleles that are associated with prostate and testicular cancers, significant differences were found between those of African descendants and European descendants. As the second part of this thesis, we investigated the roles of genetic in the reversal relationship observed between asthma and all cancer risks. Single Nucleotide Polymorphisms that were reported to be associated with asthma were collected and identified first and the cancer risks related to each variant were reviewed in the hope to provide genetic basis for future pathway analysis.
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Chapter 1: Racial Disparities in the Risk of Prostate and Testicular Cancers

Introduction

Prostate cancer (PCa) and testicular cancer, also known as testicular germ cell tumor (TGCT), are common cancers diagnosed in men globally. As the fourth most common cancer globally, prostate cancer has incidence rates that vary more than 25-fold worldwide. Within the United States, racial differences exist in prostate cancer incidence rates, with African American Men exhibiting the highest reported incidence rates. While Whites in the U.S. showed an incidence of 130.4 per 100,000 men, African American men showed a high yearly incidence of 214.5 per 100,000 men between 2008 and 2012.\(^1\) Although access to care and socioeconomic status may play a role in explaining this racial disparities, overall data suggests that increased androgen stimulation of the prostate among the black men could explain in part the higher incidence rates of prostate cancer in black than in white.\(^2\) Testicular cancer is a much less common disease when compared with prostate cancer. In 2012, the estimation was 5.6 per 100,000 men for new diagnose. However, it is still one of the most common cancer diagnosed in men aged 15 to 35 years.\(^1\) Similar to PCa, racial differences were also found in TGCT incidence rates, only with an opposite trend. Globally, Western and Northern European nations have the highest incidence rates (8.0 – 9.0 per 100,000) and African nations only have less than 1 per 100,000.\(^1\) Within the U.S., non-Hispanic Whites had the highest incidence rates followed by blacks, Hispanic Whites and Asians and Pacific Islanders.\(^3\) The biological mechanisms
behind this racial difference, however, is yet to be investigated, so is the opposite trend seen in the racial disparities in the risks of both cancers. Thus, to understand how genetic factors could play a role in the etiology of both cancers, this study analyzed genetic variants related to either prostate cancer or testicular cancer to examine whether the risk allele frequency could help investigate the observed incidence disparities in men of African ancestry and European ancestry.

**Literature Review**

The biological mechanisms behind this racial disparity in the prostate cancer risk among African descendants and European descendants have been investigated by some research studies. On the cellular level, for example, Nicolas et al. compared the molecular and genetic profiles of the normal epithelium and adenocarcinoma cells between a new African American prostate cell model and paired normal and cancer epithelial cells from the same patient. It was demonstrated that normal Conditionally Reprogrammed (CR) cells expressed high levels of basal cell markers, including KRT5 and TP63, but low androgen receptor (AR). Tumor CR cells from the African American patients on the other hand expressed a significantly high level of luminal marker and EMT markers (PD-L1, TIMP3 and PAI1). Another study, similarly, confirmed that there is a significant difference of AR protein expression between African men and white men. It was found that AR protein expression was 22% higher in the benign prostate and 81% higher in the PCa in black African men than in white men. On the genetic level, many studies have attempted to find the associations and mechanisms behind the observation. For example, a case-control analysis was conducted to determine if two polymorphisms within IGF-1 and one single-nucleotide polymorphism (SNP) in the IGFBP-3 gene were associated with serum IGF
level variations and risk for PCa in African American men. They revealed that variation in the 5’-untranslated region of the IGF-1 and IGFBP-3 genes may influence IGF serum levels and PCa risks in African American men.\textsuperscript{5}

With a 70% increasing incidence among Caucasian males in the last 20 years, TGCT is expected to have carcinoma in situ, originating from an embryonic germ cell blocked in its maturation process. Since 2009, several genome wide association studies (GWAS) have reported on SNPs that have significant associations with TGCT development, in or near the genes KITLG, SPRY4, BAK1, DMRT1, TERT, ATF7IP, HPGDS, MAD1L1, RFWD3, TEX14, and PPM1E.\textsuperscript{6} However, compared with prostate cancer, although multiple studies have observed and reported the racial disparity that men of European ancestry tend to have higher incidence rates of testicular cancer than men of African ancestry, few have dug deeper on the genetic mechanism that could potentially explain this relationship, not to mention the opposite trend that men of African ancestry and European ancestry have disproportionately higher incidences in prostate cancer and testicular cancer, respectively. Thus, by comparing the risk allele frequencies of the SNPs reported to have associations with these two cancers, this study takes the first step to understand this opposite trend of racial disparities on another genetic level, in the hope to provide building blocks for further genetic pathway analysis.

**Research Design**

Literature search was performed by using combinations of key words including, single nucleotide polymorphism (SNP), Genome Wide Associate Study (GWAS), genetic risk variant, prostate cancer, and testicular cancer. Genome-wide association studies and meta-analysis of genome wide association were analyzed to identify all the SNPs
associated studies with Testicular Cancer and Prostate Cancer. SNPs that present risk effects to the two cancer types at a statistically significant level were collected. A total of 230 risk SNPs significantly associated with prostate cancer and 80 risk SNPs associated with testicular cancer were identified (Supplementary Table 1, 2). One SNP (rs4624820) with conflicting results from two different studies was excluded from the further analysis. Data of risk and reference alleles, odds ratio (OR), confidence interval (CI), p-value, gene symbol, ethnic group, number of cases and controls, and citation of original publications were collected and included in supplementary tables. When there were multiple ORs present in the study, we only presented the ones from meta-analysis studies. Risk allele frequencies of these identified SNPs in populations of African and European ancestry were then obtained from 3 databases: 1000 Genomes Project, Allele Frequency Aggregator (ALFA), and the genome Aggregation Database (gnomAD). 1000 Genomes Project database contains data for 2,504 individuals from 26 populations. ALFA database has over 2 million subjects from 12 diverse populations. GnomAD has a total of 141,456 individuals in the 15,708 genomes sequenced. Number of individuals with available allele frequency data for each SNP in these 3 databases were included in Supplementary Table 1 and 2 as well.

The hypothesis that higher/lower incidence of prostate/testicular cancer could be associated with higher/lower average frequency of risk alleles was tested by comparing risk allele frequencies between European and African populations. Allele frequencies in different databases vary slightly and frequency of each risk allele (F) was calculated by averaging frequencies in these 3 databases with justification for sample sizes. To further account for attributable risk of risk alleles, weighted frequency (Fw) that was calculated...
with the equation: \(F_w = F \cdot \frac{OR}{OR_{max}}\), where OR is the corresponding odds ratio of the risk allele and ORmax is the largest odds ratio among risk alleles. Average weighted frequencies of risk alleles were then compared between the 2 racial/ethnic group using one-tailed student’s t-test because the testing hypotheses have one direction of interest for each cancer type.

**Results and Discussions**

The results showed that for prostate cancer, the average risk allele frequency (F) was significantly higher in men of African ancestry (45%) compared to men of European ancestry (42%) (\(p=0.043\)). After considering the odds ratio of risk alleles, the analysis of weighted frequencies (\(F_w\)) stayed highly significant (\(p=0.023\)) ([Figure 1.1a](#)). On the contrary, the average risk allele frequency of testicular cancer was significantly lower in men of African ancestry (46%) compared to men of European ancestry (51%) (\(p=0.029\)). The weighted analysis showed the same significant difference (\(p=0.014\)) ([Figure 1.1b](#)).

Moreover, frequencies of all risk alleles in African (Y axis of Figure 2) and European (X axis of Figure 2) populations showed significant linear regression relationships in both prostate cancer (\(Y=1.16X-0.012, p<0.0001\)) and testicular cancer (\(Y=0.71X+0.037, p<0.0001\)). Deming regression analysis was performed to find the line of best fit by accounting for frequency variations on both the x- and the y- axis. Regression lines from both cancer types were compared to a standard regression line that has equal allele frequencies in both African and European populations (slope=1). The differences between the slopes were highly significant where the regression line of prostate cancer data (slope=1.246, \(p=0.0051\), **Figure 1.2a**) skewed above the standard line towards the African
population and the regression line of testicular cancer data (slope=0.711, p<0.0001, Figure 1.2b) skewed below the standard line slope towards the European population.

Consistent with the results from international comparisons, the significant differences of risk allele frequencies in related SNPs demonstrated in the study suggests that the variations and racial disparities between African and European descendants could be underpinned by genetically determined variations in susceptibility or other constitutional factors. Moreover, epigenetic factors such as dietary or other modifiable factors could exert an important influence and potentially modify this observed association. For example, a study in UK found that unlike Asians in Asia and Bangladeshi and Chinese migrants to England, the Indian and Pakistani men in England were shown to have similar or even higher incidence rate of prostate cancer than White men.\textsuperscript{10} Thus, the convergence of incidence rates of prostate cancer among Indian and Pakistani people towards the local rate after a large number of migration suggests that there might be epigenetic factors behind the observation.

**Conclusion**

Results from both t-test and regression analysis are consistent with each other, which indicate that men of African ancestry are more likely to have risk alleles of prostate cancer and less likely to have risk alleles of testicular cancer compared to men of European ancestry. These findings suggest that genetic factors could partially explain the greater burden of prostate cancer on men of African ancestry and the higher incidence of testicular in men of European ancestry compared to other racial/ethnic groups. Cancer is a complex disease that normally involves multiple genes and environmental factors in its etiology. Therefore, in addition to understanding the influence of genetic factors, social and
environmental factors also need to be considered when analyzing the observed racial and ethnic disparities in the risk of prostate and testicular cancers.

Figure 1.1

Figure 1.1: Comparison of risk allele frequencies of prostate and testicular cancers between men of African descent and European descent. a) Average weighted risk allele frequency of prostate cancer was significantly higher in men of African descent compared to men of European ancestry descent (p=0.023). b) Average weighted risk allele frequency of testicular cancer was significantly lower in men of African descent compared to men of European descent (p=0.014).

Figure 1.2

Figure 1.2: Regression lines of risk allele frequencies between African and European descent for prostate and testicular cancers. a) The regression line of prostate cancer data (slope=1.16) skewed above the standard line (slope=1) towards African population. The differences between the slopes were highly significant (p<0.0001). b) The regression line of testicular cancer data (slope=0.71) skewed below the standard line slope (slope=1)
towards European population. The differences between the slopes were highly significant (p<0.0001).

Chapter 2: Asthma and Cancer Risks

Introduction

In the past decades, epidemiologic studies have shown that people with asthma present a significantly lower risk of several types of cancers, such as myeloma, melanoma, pancreatic cancer, non-Hodgkin’s lymphoma, stomach cancer, colorectal cancer, glioma and leukemia. However, the mechanisms responsible for the protective role of this atopic disease against certain malignancies are not fully understood. This study took advantage of available genome-wide association and expression data to identify genetic variants and possible biological pathways associated with both diseases that may play diametric roles in cancer and asthma development, in the hope to help explain the observed inverse relationship between them.

As a complicated condition with chronic airway inflammation and airway hyper-reactivity, asthma usually shows symptoms such as recurrent wheezing, coughing and
shortness of breath. The presence of immunoglobulin E (IgE)-mediated immune reactions is the main characterization of atopic disease such as asthma, and it is hypothesized that these IgE-mediated immune reactions may play a role in immunosurveillance against cancer. Therefore, it is possible that people with asthma, a condition commonly characterized by IgE-mediated atopic reactions, may develop an IgE-mediated response against neoplasms that could reduce cancer risks. While several studies have observed the inverse relationship between history of asthma and risk of various cancers, there is a lack of confirmation and consistency of this relationship. For example, some studies have shown that the inverse associations between atopic conditions including asthma and glioma were limited to white persons, with no association observed among the black population. However, genetic studies that could potentially explain the biological mechanisms and genetic pathways for this reversal relationship and the racial differences are very limited.

This study provides genetic bases for the reversal relationship between asthma and cancer risks by identifying genetic variants associated with asthma, searching and reviewing cancer risks related to the identified genetic variants, and detecting pathways of the genes that present the diametric role. This study also presents a thorough search of the cancer risks in the asthma-related genes for further haplotype investigations.

By leveraging recently available genome-wide genotyping and expression data, this study tackles a field that presented difficulties to study previously because comprehensive databases needed to identify clinical correlations between chronic disease and cancer risk were not commonly annotated for these anti-correlations. Understandings of the biochemical and genetic bases for the inverse asthma-cancer relationship may reveal novel
insights into the mechanisms underlying the etiology and development of these two diseases, which may, in turn, provide information to the development of therapeutic and preventive techniques for new molecular targets and form a powerful basis for future research.

**Literature Review**

As one of the first researchers who discovered the inverse relationship between asthma and cancer risks, in early 1960, Fisherman reported that atopic disease was significantly less common in patients with malignant disease than in age-matched controls. A few years later in 1974, a study of 765 men and 1127 women with asthma reported that deaths from all cancers excluding lung cancer were significantly reduced in both men and women. In 1993, a record-linkage study in Swedish hospitals for asthma revealed a marked reduction of cancer incidence among the 64,346 people treated compared with the general population. Risks of multiple myeloma, malignant melanoma, breast cancer, uterine body cancer and stomach cancer were observed to reduce. Moreover, a prospective cohort study in the U.S. with 1,102,247 subjects revealed a significant inverse association between overall cancer and colorectal cancer mortality and a history of both asthma and hay fever after 18 years of follow-up.

More specifically, atopic allergic conditions (AACs) including asthma appeared in many epidemiology studies to have protective roles in cancers such as colorectal cancer, pancreatic cancer, leukemia, glioma and Non-Hodgkin Lymphoma. According to a multiethnic cohort study with 4,834 incident colorectal cancer (CRC) cases and 1,363 CRC-related death in the U.S., AACs were associated with a reduced risk of CRC incidence among both men and women (RR=0.86). For pancreatic cancer, according to a
epidemiology review study, eight of the ten studies examining the associations between atopy and pancreatic cancer show a reversal relationship.\textsuperscript{19} A case-control study with 1297 ductal adenocarcinoma of the pancreas (PDAC) cases and 1024 controls found that asthma was associated with lower risk of PDAC (OR=0.64).\textsuperscript{20} Likewise, multiple studies found an inverse association between allergy, asthma or atopy with acute lymphoblastic leukemia (ALL), regardless of specific exposure.\textsuperscript{19} For example, a national registry-based case-control study carried out by France in 2003-2004 observed a negative association between ALL and history of asthma (OR=0.7).\textsuperscript{21} For primary brain tumors such as glioma, many studies suggested an inverse relationship as well. A 2007 analysis that investigated the relationship between allergic conditions and glioma prevalence in 1527 cases from Denmark, Finland, Norway, Sweden and the UK found a significant 30\% lower odds of glioma among adults with asthma history.\textsuperscript{22} Similarly, a US-based case-control study assessed the associations between self-reported asthma and glioma among 489 glioma patients, and found a significant result that asthma was associated with decreased odds of glioma (OR=0.6).\textsuperscript{23} As for non-Hodgkin lymphoma (NHL), recent pooled analyses support the inverse relationship as well. A pooled analysis of data on atopic disease and risk NHL from 13 case-control studies, including 13,535 cases and 16,388 controls, found that a history of asthma was associated with a 10\% reduction in overall NHL and B-cell NHL in individuals who reported at least one other atopic condition.\textsuperscript{24}

Despite the strong evidence for the inverse association between asthma and risk for certain cancer types, however, very few studies have investigated the molecular basis underlying this association. To provide building blocks for future pathway-based analysis to facilitate the identification of novel molecular networks, this his study explored GWAS
and genome-wide expression data to identify and study genes involved in the development of both diseases.

**Research Design**

Since it is hypothesized that some genes are involved but play diametric roles in both asthma and cancer development, identifying genes that are associated with both asthma and cancers is essential. More specifically, single nucleotide polymorphisms (SNPs) associated with both diseases should be identified, since they allow scientists to evaluate individuals’ genetic predispositions to develop diseases.\(^{25}\) Thus, as the first step, SNPs associated with increased risk of asthma but reduced risk of cancer were identified. Literature search was performed by using combinations of key words including, single nucleotide polymorphism (SNP), Genome Wide Associate Study (GWAS), genetic risk variant and asthma. GWAS and meta-analysis of genome wide association were analyzed to identify all the SNPs associated studies associated with asthma. SNPs that present risk effects to asthma at a statistically significant level were collected. With all the identified SNPs associated with asthma, literature search was then performed to find if any of the SNPs was associated with cancer risks by a combination of key words including the specific SNP number and cancer. Asthma related SNPs that were found to be associated with any cancer type were collected, regardless of the association direction.

Consequently, an exhaustive literature search was performed to find cancer risks related to all the genes that present risks to asthma with key words including the specific gene symbol, cancer and genetic variant, single nucleotide polymorphisms. Case-control studies that reveal the cancer risks associated with the specific genes and present genotype
information (SNPs) about the genes were included for future pathway analysis (Supplementary Table 4).

**Results**

A total of 169 SNPs that are reported to increase the risks of asthma incidents were identified and collected (Supplementary Table 3). Data of risk allele, reference allele, odds ratio (OR), confidence interval (CI), p-value, gene symbol (if applicable) and citation of original publications were included.

SNPs associated with both asthma and cancer risks were collected (Table 2.1). A total of 22 SNPs were found to have associations with cancers such as glioma, colorectal cancer and rectal cancer, lung cancer, breast cancer and cervical cancer. Among the 22 SNPs, 10 of them were reported to have statistical significances, and 7 (rs2284033, rs1800797, rs12956924, rs1801275, rs1800896, rs20541, rs1800925) of them were reported to show a reverse relationship between the two diseases because the risk alleles of asthma played a protective role in cancer risks. Such reversal association is represented when the odds ratio of the asthma risk allele is bigger than 1 while the odds ratio in cancer of the same allele is smaller than 1, or when the odds ratio of the reference allele for asthma is bigger than 1 for the cancer risk (rs1800896). For rs1800925, the reversal relationship is shown by the odds ratio of the heterozygous genotype CT (T as the risk allele for asthma) is smaller (OR=0.76) than that of the homozygous genotype CC (OR=1) for glioma risk.

4 SNPs that present significant associations between asthma and cancer risks are reported to have a positive relationship: rs1800925, rs1535, rs2066844 and rs1805010. The positive relationship is shown when the risk allele of asthma has an odds ratio that is greater than 1 for the cancer risks. For rs1805010, this relationship is shown by a different set of
alleles (C and T), instead of G and A seen in the asthma risk and reference alleles because the opposite trend of gene was genotyped in the original paper (PMID: 25785117). Among the 22 SNPs that present associations between the two diseases, 12 of them have results that are not statistically significant.

**Discussion**

Glioma is one of the cancer types that have been found the most frequently to have reversal relationships with asthma in this study. Four SNPs in this study are found to present this diametric role with a statistical significance (rs1801275, rs1800896, rs20541, rs1800925), and seven SNPs with insignificant results (rs62026376, rs10197862, rs1837253, rs7009110, rs72699186, rs17294280, rs62026376). As one of the most aggressive human tumors, glioma is responsible for 80% of primary malignant brain tumors with high mortality rates. In fact, it has been long suspected that a history of asthma and higher levels of immunoglobulin E (IgE) could play a protective role against glioma development and prognosis.26

In this study, two SNPs (rs20541 and rs1800925) (Table 2.1) that present this significantly reversal association are from a same gene: IL-13. Not surprisingly, it has been suggested that IL-13 is positively associated with asthma development and higher IgE levels, and individuals that are genetically capable of producing higher levels of IL-13 cytokine may be protected from glioma.27 Shin et al. found that by inducing death of activated microglia, which is the major inflammatory cell of the central nervous system, IL-13 controls brain inflammation and enhances neuronal survival.28 It is also indicated that IL-13 is central to a novel immunoregulatory pathway in which NKT cells suppress tumor immunosurveillance.29 Thus, although the functional relevance of IL-13 is not
completely understood, the negative associations between IL-13 and glioma collected and reviewed by this study adds more genetic proof to the protective role of IL-13 against glioma.

SMAD7 is another gene involved in inflammation-related pathways that shows a reversal association between cancer and asthma (rs12956924). SMAD7 modulates transforming growth factor-β, whose signaling pathway plays an important role in cancer initiation and progression, and Wnt signaling, which is central to the development of colorectal cancer (CRC).\textsuperscript{30} It is also indicated in another study that the SMAD7-mediated plastic effect on T-cell phenotype induces protection against colorectal cancer.\textsuperscript{31} However, SMAD7 polymorphisms can also be associated with increased risks of colon cancer. For example, rs12953717 in the SMAD7 gene is observed to have significant associations with increased risk of colon cancer.\textsuperscript{32} It is also reported that CRC patients with deletion of SMAD7 have a significantly better prognosis than patients with two copies of this gene, while increased copy numbers of SMAD7 are associated with a significantly worse prognosis.\textsuperscript{33} Thus, the contribution of SMAD7 in CRC is still unclear, and a better understanding of its role in future researches could help to determine if SMAD7 could serve as a molecular target for future CRC pharmacological interventions.

Interestingly, IL4R is observed to have SNPs related to both positive and negative associations with cancer risks and asthma: allele G of rs1801275 has a protective association against glioma whereas allele G of rs1805010 has a positive association with increased risk for renal cell cancer (Table 2.1). Though lacks further investigation, genetic explanations for the two phenomena were attempted by several studies. Genetic factors are likely to exist in linkage disequilibrium with particular haplotypes in IL4R and IL 13 that
affects the risk of brain cancer such as glioma and likely via an immune mechanism. On the other hand, type II IL4R, which consists of the IL13Rα1 and IL4Rα subunits, is overexpressed in many epithelial tumors, including renal cell carcinoma. In fact, the expression of IL4R is so robust on the cancer cells that it has been used for anti-cancer toxins as a targeting molecule. Therefore, future studies of the functionalities of IL4R and IL4/IL4R axis are warranted to understand their effects on cancer risks.

Conclusions

As the first step to investigate the molecular basis underlying the reversal association between asthma and risks for certain cancer types by literature reviewing, this study provided more genetic proof to the protective roles of genes such as IL13 against cancers such as glioma. Additionally, this study also demonstrated the contracting roles of a single gene (SMAD7 and IL4R) in the same or different types of cancers.

Although this study provides a fairly thorough list of SNPs associated with asthma, it is believed that more could be identified. Possible reasons for failure to find significant associations between some SNPs and asthma include both the relatively small numbers of controls reporting asthma and misclassification of the condition due to screening or self-report differences. For example, self-reported asthma history by questionnaire as a measure of asthma status could misclassify exposure, since the difference between asthma and conditions that exhibit similar symptoms may decrease the accuracy of exposure measurement. Similarly, due to differences in exposure definition or covariate adjustment, small sample sizes, multiple testing, and/or heterogeneity in study populations, it is possible that differences across studies of SNPs and cancer risks may arise. Additionally, epigenetic factors might also play important roles. For example, it is possible that some
genes that are associated with asthma can also interact with environmental factors and present different significant results in different studies. Similarly, heterogeneity in study environment might also confound the results as pollutant effect might amplify the results among those who are genetically susceptible. Thus, results that showed statistically insignificant were still presented for future investigation because of the methodological limitations existing in the individual epidemiological studies (Table 2.2).

Moreover, although this study provides a clear evidence for the reversal association between asthma and certain cancer risks, the temporal relationship between exposure and outcome is yet to be determined. Whether asthma is a protective/risk factor or the other way around still needs further investigation of the molecular pathways.
### Table 2. 1

Table 2. 1: SNPs associated with both asthma and cancer that have statistical significance

<table>
<thead>
<tr>
<th>SNP</th>
<th>Gene</th>
<th>Risk Allele</th>
<th>Ref Allele</th>
<th>OR</th>
<th>CI</th>
<th>Cancer related</th>
<th>Cancer OR</th>
<th>Cancer p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs2284033</td>
<td>IL2RB</td>
<td>G</td>
<td>A</td>
<td>1.12</td>
<td>1.08-1.16</td>
<td>Lung Cancer</td>
<td>0.56 (0.32–0.96)</td>
<td>0.031</td>
</tr>
<tr>
<td>rs1800797</td>
<td>IL6/LOC54147</td>
<td>G</td>
<td>A</td>
<td>1.04</td>
<td>1.03-1.06</td>
<td>Breast Cancer</td>
<td>0.77(0.57-1.04)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>rs12956924</td>
<td>SMAD7</td>
<td>A</td>
<td>G</td>
<td>1.04</td>
<td>1.02-1.05</td>
<td>Rectal Cancer</td>
<td>0.66(0.45-0.97)</td>
<td>0.03</td>
</tr>
<tr>
<td>rs12956924</td>
<td>SMAD7</td>
<td>A</td>
<td>G</td>
<td>1.04</td>
<td>1.02-1.05</td>
<td>Colorectal</td>
<td>0.77(0.59-1.00)</td>
<td>0.048</td>
</tr>
<tr>
<td>rs1801275</td>
<td>IL4R</td>
<td>G</td>
<td>A</td>
<td>2.12</td>
<td>1.39-3.22</td>
<td>Glioma</td>
<td>0.81 (0.69-0.95)</td>
<td>0.011</td>
</tr>
<tr>
<td>rs1800896</td>
<td>IL19</td>
<td>A</td>
<td>G</td>
<td>1.84</td>
<td>1.2–3.87</td>
<td>Glioma</td>
<td>GG: 1.39 (0.94–2.09)</td>
<td>0.021</td>
</tr>
<tr>
<td>rs20541</td>
<td>IL13</td>
<td>A</td>
<td>G</td>
<td>2.13</td>
<td>1.39-3.26</td>
<td>Glioma</td>
<td>TT: 0.39 (0.16–0.93)</td>
<td>0.023</td>
</tr>
<tr>
<td>rs1800925</td>
<td>IL13</td>
<td>T</td>
<td>C</td>
<td>1.46</td>
<td>0.98-2.19</td>
<td>Glioma</td>
<td>CT vs. CC: 0.76 (0.57-1.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>rs1800925</td>
<td>IL13</td>
<td>T</td>
<td>C</td>
<td>1.46</td>
<td>0.98-2.19</td>
<td>Breast Cancer (Same Direction)</td>
<td>2.08(1.32–3.28)</td>
<td>7.79 × 10^{-4}</td>
</tr>
<tr>
<td>rs1800925</td>
<td>IL13</td>
<td>T</td>
<td>C</td>
<td>1.46</td>
<td>0.98-2.19</td>
<td>Colon Cancer (Same Direction)</td>
<td>TT:2.27 (1.19–4.31)</td>
<td>0.012</td>
</tr>
<tr>
<td>rs1535</td>
<td>FADS2</td>
<td>A</td>
<td>G</td>
<td>1.05</td>
<td>1.04-1.06</td>
<td>Colorectal Cancer (Same Direction)</td>
<td>1.07 (1.04–1.11)</td>
<td>4.12 × 10^{-5}</td>
</tr>
<tr>
<td>SNP</td>
<td>Gene</td>
<td>Risk Allele</td>
<td>Ref Allele</td>
<td>OR</td>
<td>CI</td>
<td>Cancer OR</td>
<td>Cancer p-value</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>----------</td>
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<td>----------------</td>
<td></td>
</tr>
<tr>
<td>rs2066844</td>
<td>NOD2</td>
<td>T</td>
<td>C</td>
<td>1.09</td>
<td>1.06-1.12</td>
<td>Cancer Risk (Same Direction)</td>
<td>1.43(1.09–1.88)</td>
<td>0.01</td>
</tr>
<tr>
<td>rs2066844</td>
<td>NOD2</td>
<td>T</td>
<td>C</td>
<td>1.09</td>
<td>1.06-1.12</td>
<td>Colon Cancer (Same Direction)</td>
<td>8.7(2.2-23.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>rs1805010</td>
<td>IL4R</td>
<td>G</td>
<td>A</td>
<td>1.60</td>
<td>1.01-2.53</td>
<td>Renal Cell Cancer (Same Direction)</td>
<td>CC/CT vs. TT:1.266 (1.09-1.472)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table 2. 2

Table 2. 2: SNPs associated with both asthma and cancer that have no statistical significance (P-value > 0.05)
References


25. single nucleotide polymorphism / SNP | Learn Science at Scitable.
   https://www.nature.com/scitable/definition/snp-295/.


30. Song, B. et al. A case-control study: association of SMAD7 single nucleotide polymorphisms with colorectal cancer in the Han population. 9.


