Title: Atopic dermatitis-associated 6p21 variants regulate LOC100294145 expression and type 1 interferon signaling

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Background

Atopic dermatitis (AD) is a complex inflammatory disease with a strong genetic component. A singular approach of genome wide association studies (GWAS) can identify AD-associated genetic variants, but is unable to explain their functional relevance in AD.

Objective

This study aims to characterize AD-associated genetic variants and elucidate the mechanisms leading to AD, through the integration of genomic and transcriptomic studies.

Methods

GWAS was performed on 987 AD patients and 931 controls. Gene expression was measured in peripheral blood mononuclear cells (PBMCs) from 300 individuals. Promoter activity was measured with the dual-luciferase promoter assay. Biologically important hub genes were selected through co- expression analyses and clustering of protein-protein interactions. G:Profiler

was used to elucidate the function of these hub genes and their expression were investigated in independent GEO datasets.

Results

Minor alleles of rs241412 ($p = 7.45\times10\text{-}7$, OR = 1.42) and rs241410 ($p = 4.20\times10\text{-}7$, OR = 1.40) increased AD risk and LOC100294145 promoter activity in vitro. An increased expression of LOC100294145 in PBMCs was significantly associated with the minor genotypes of rs241412 and rs241410 and with AD. LOC100294145-regulated hub genes involved in type 1 interferon signaling were upregulated in AD skin lesions compared to healthy skin in GSE5667 and GSE32924, and downregulated following narrow-band ultraviolet B therapy in GSE27887.

Conclusion

Risk alleles of rs241410 and rs241412 associate with AD susceptibility through an increased LOC100294145 expression. LOC100294145 mediates AD pathogenesis through the dysregulation of hub genes involved in type 1 interferon signaling and is a potential target for AD treatment.

Title: Alternative Medical Systems – A Systematic review of Randomized Controlled Trials in Chronic Kidney Disease patients

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Aims

There is a growing interest in the use of alternative medical systems (AMS) such as Traditional Chinese Medicine (TCM), Ayuverda, homeopathy and naturopathy among chronic kidney disease patients. AMS has been demonstrated efficacy in reducing symptoms such as headache and fatigue in the general population. This review aims to summarize the efficacy and safety of AMS interventions in CKD patients.

Methods

A systematic review was conducted in Medline, Embase, Scopus, CINAHL, CENTRAL and PsycInfo in line with the PRISMA and SWiM guidelines. Randomised controlled trials (RCTs) which evaluated the use of AMS among adult CKD patients were included. The efficacy of each AMS was assessed based on improvement in biochemical markers or reduction in symptom severity scores. All adverse reactions were recorded.

Results

Of the 3259 articles retrieved, 23 RCTs were included. TCM (n=13) and naturopathy (n=5) were the most well studied AMS. Majority of studies (65%) had a sample size <100 patients. Common

indications evaluated included improvement in renal function (n=8) and uremic pruritus (UP) (n=4). Among TCM, acupuncture and the use of a ten-herb concoction and Qingshen granules were shown to improve estimated glomerular filtration rate (eGFR) by 5.1-15.5%, 26.6% and 17.8% respectively. Acupuncture was shown to reduced UP symptoms by 54.7%-60.2% while Huangkui and Shenqi granules reduced proteinuria by 18.6%-50.7% and 61.8% respectively. For naturopathy and Ayurveda, the use of alpha-keto amino acids and nigella sativa oil improved eGFR by 49.2% and 86.8% respectively. Adverse effects associated with the ten-herbs concoction included deranged liver function (4.55%) and hyperkalaemia (5.11%). Nausea was the most common adverse effect reported with alpha-keto amino acids (0.07%) and nigella sativa oil (7.04%).

Conclusion

TCM and naturopathy were more well-studied AMS therapies that demonstrated efficacy in CKD patients. RCTs with larger sample sizes are needed to verify the efficacy and safety of promising AMS.

Title: Allergic Rhinitis in Young Adult Chinese from the Singapore/Malaysia Cross-Sectional Genetics Epidemiology Study (SMCGES) Cohort: Prevalence, Patterns and Epidemiology of Allergic Rhinitis

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Background

Allergic rhinitis (AR) is characterized by the occurrence of at least two symptoms of nasal itching, nasal blockage, rhinorrhea, and sneezing, when not afflicted with a cold or flu, with defined atopic sensitization demonstrated by skin prick test or specific IgE responses. Besides the detriment to standard of living and economic burden of AR, both multicentre and single-cohort studies have observed an increase in AR prevalence in Asia over time.

Methods

In total, 12,872 individuals, with mean age 22.1 (SD = 4.8) were recruited from universities in Singapore and Malaysia. Each participant provided epidemiological databased on an investigator- administered questionnaire adapted from the validated ISAAC protocol, and atopy status was determined using a skin prick test (SPT) performed by qualified staff. AR was diagnosed according to ARIA guidelines and a positive SPT result.

Results

Sensitization (determined by SPT) to either Blomia tropicalis or Dermatophagoides pteronyssinus was prevalent in 66.5% of the cohort. Current rhinitis (manifesting ≥2 rhinitis symptoms, within the past 12 months) was observed in 48.9% of our population, while AR, which included atopy status, was estimated at 39.4%. Sneezing and rhinorrhoea were the most common symptoms among AR cases. AR prevalence decreased with increasing age (OR:0.979; 95% CI: 0.969-0.989; p-value<0.001), while male gender (OR: 2.053; 95% CI: 1.839-2.294; p-value<0.001), and a parental history of allergic diseases (OR: 2.750; 95% CI: 2.284-3.316; p-value<0.001) were significant risk factors for AR. Upon adjustment for age, gender, and parental history, housing type (OR: 0.632; 95% CI: 0.543-0.736; p- value<0.001) and income

level (>$6000 vs <$2000; OR: 2.461; 95% CI: 2.058-2.947; p-value<0.001) remained as significant risk factors for AR, while ever having kept a pet (OR: 1.167; 95% CI: 1.025- 1.328; p-value = 0.019) emerged as a risk factor. Conflicting results were obtained for indicators of sedentary lifestyle: frequent physical activity (OR: 1.394; 95% CI: 1.150-1.694;p-value<0.001) and increased duration spent using the TV/computer (OR: 1.224; 95% CI:1.006-1.489; p-value = 0.043) both increased the risk of AR. Lastly, using a novel food score, QDGIS, to estimate the overall glycaemic burden of diet, we identified lower dietary GI as a protective factor against AR manifestation (OR: 0.682; 95% CI: 0.577-0.807; p-value<0.001).

Conclusion

While the previously established non-modifiable risk factors for AR were present in our study population, the identification of modifiable risk factors, such as TV/computer usage, and dietary habits, opens a new area for research, both in the areas of gene-environment interaction, and management of AR.

Title: An Update on the Prevalence, Chronicity, and Severity of Atopic Dermatitis and the Associated Epidemiological Risk Factors in the Singapore/Malaysia Chinese Young Adult Population: A Detailed Description of the Singapore/Malaysia Cross-Sectional Genetics Epidemiology Study (SMCGES) Cohort

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Background

Atopic Dermatitis (AD) is a highly pruritic, chronic-recurrent inflammatory skin condition associated with erythematous lesions that affect a significant proportion of the population. Although AD is a non-communicable disease, AD can cause pain, unbearable itchiness, sleep

disturbance, loss of work productivity, and reduced quality of life. As a heterogeneous disease, AD is influenced by multiple genes and environmental triggers. As such, it is imperative to gain a deeper insight into the intricate gene-environment relationship that results in the manifestation of AD.

Methods

There are three objectives in our study. We first aim to update the epidemiological status of AD amongst young adults in Singapore and Malaysia, in particular amongst the Chinese ethnic background. Next, we re-evaluated the possible associated risk factors, identified in our previous meta-analysis and review studies, on the current cohort. Finally, we described here a detailed disease presentation and symptoms profile of our Singapore and Malaysia Cross-Sectional Genetics Epidemiology Study (SMCGES) cohort, which forms the base population for the discovery of associated genetic factors in relation to asthma, allergic diseases and skin conditions. Based on a skin prick test (SPT) and investigator-administered medical history responses, we assessed the AD profiles of 11494 participants and the significant modifiable and non-modifiable factors associated with disease presentation.

Results

The prevalence of AD in the combined population was 13.5%. Chronic and moderate/severe AD were observed in 35.5% and 40.5% of the individuals with AD, respectively. Family history of atopic diseases, prior history of drug allergies, a history of acne, increased household family monthly income, higher number of individuals in the shared household, parental education, sedentary lifestyle, physical activities, alcoholic consumption, and even quality of diet was

significantly associated with AD presentation, chronicity, and severity. Among all the factors evaluated, family and personal history of atopic diseases imposed the strongest associated risk.

Conclusion

These findings supported our previous review studies and affirmed that familial history or genetic factors critically influence the development of AD in our population and environment. Environmental and other modifiable factors can also trigger AD throughout the lifetime of individuals who have especially inherited the atopic disease disposition. A better understanding of how these risk factors affect AD individuals in our population can facilitate disease surveillance, monitor disease control, and serve as a description for our future genetic epidemiology studies.