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Genome-wide association study of Atopic dermatitis in Hong Kong

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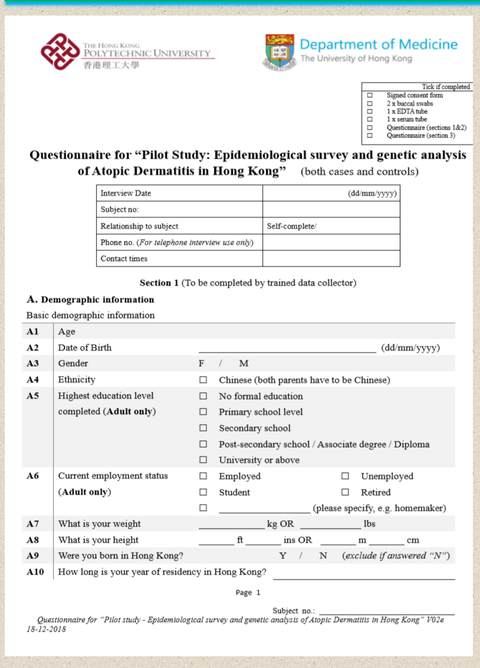
Introduction

Atopic dermatitis (AD) is a common, incurable chronic inflammatory skin disorder that can significantly impact the quality of life of patients. There is an incomplete understanding of the underlying pathogenesis, with no genome-wide association study (GWAS) conducted in Hong Kong, and previous clinical studies were limited to childhood AD. The aim of this study was to carry out a pilot study to search for Hong Kong population specific genetic variants and environmental risk factors across childhood and adult AD.

We hypothesize that differences in subgroups of AD patients (eczema severity, age, IgE, eosinophil count, and age of onset), and different environmental risk factors maybe conferred by different genetic risk factors.

Method



The Hong Kong Polytechnic University 香港理工大學 — Department of Medicine, The University of Hong Kong

Tick if completed	
☐	Signed consent form
☐	2 x buccal swabs
☐	1 x EDTA tube
☐	1 x serum tube
☐	Questionnaire (sections 1&2)
☐	Questionnaire (section 3)

Questionnaire for "Pilot Study: Epidemiological survey and genetic analysis of Atopic Dermatitis in Hong Kong" (both cases and controls)

Interview Date	(dd/mm/yyyy)
Subject no:	
Relationship to subject	Self-complete/
Phone no. (*For telephone interview use only*)	
Contact times	

Section 1 (To be completed by trained data collector)

A. Demographic information

Basic demographic information

A1	Age	
A2	Date of Birth	_____ (dd/mm/yyyy)
A3	Gender	F / M
A4	Ethnicity	☐ Chinese (both parents have to be Chinese)
A5	Highest education level completed (**Adult only**)	☐ No formal education ☐ Primary school level ☐ Secondary school ☐ Post-secondary school / Associate degree / Diploma ☐ University or above
A6	Current employment status (**Adult only**)	☐ Employed ☐ Unemployed ☐ Student ☐ Retired ☐ _____ (please specify, e.g. homemaker)
A7	What is your weight	_____ kg OR _____ lbs
A8	What is your height	_____ ft _____ ins OR _____ m _____ cm
A9	Were you born in Hong Kong?	Y / N (*exclude if answered "N"*)
A10	How long is your year of residency in Hong Kong?	_____

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Subject no.: _____

Questionnaire for "Pilot study - Epidemiological survey and genetic analysis of Atopic Dermatitis in Hong Kong" V02e 18-12-2018

43 child and 33 adult AD subjects were recruited from Queen Mary Hospital and 44 controls were recruited from the Hong Kong Polytechnic University campus. Demographic and clinical details were collected via questionnaire interview

Blood and buccal samples were taken from subjects to undergo total serum IgE, eosinophil count and GWAS for genetic variant profiling.

Results

Through subgrouping, SCORAD correlated with eosinophil among subjects with more severe AD or with higher immunological predisposition: high SCORAD subgroup (p=0.039), high eosinophil subgroup (p=0.006) and high IgE subgroup (p=0.008). This study has identified novel child-onset factors such as caesarean section and non-smoking parent(s). GWAS has identified 6 candidate single-nucleotide polymorphism (SNPs) in association with the duration of AD and 5 potential SNPs in association with IgE.

Discussion

- Novel child-onset factors:
  1. Caesarean section
  2. Non-smoking parent(s)
- 6 significant SNPs in association with the duration of AD:
  1. Astn2 gene: rs10982272, rs12380425, rs146392873, rs140693157, rs12378473
  2. Intron variant rs73123810
- 5 Significant SNPs in association with IgE:
  1. Intron variant rs10753681
  2. Unknown functions: rs12524729, rs2988685, rs4706269 and rs4707264

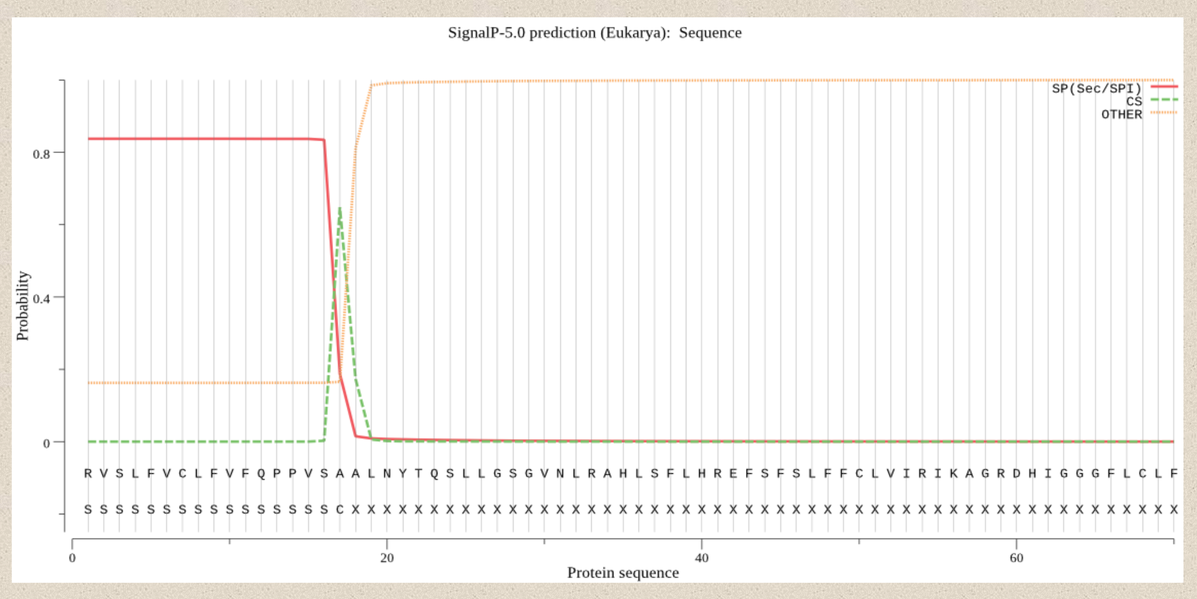

Figure 1. Likelihood of rs12378473 being the signal peptide transported and cleaved by Sec/SPI at each amino acid position.

Conclusion

This pilot study supported our hypothesis that different AD subgroups based on AD severity, age of onset, IgE levels, and eosinophil count, may be associated with different environmental risk factors. Further fine mapping and functional studies shall be conducted to elucidate the exact roles of these candidate genes and environmental risk factors. Larger sample sizes are needed to validate the conclusion.

Reference

1. Deckers, I.A., et al., Investigating international time trends in the incidence and prevalence of atopic eczema 1990-2010: a systematic review of epidemiological studies. PLoS One, 2012. 7(7): p. e39803.
2. Hon, K.L., A.K. Leung, and B. Barankin, Barrier repair therapy in atopic dermatitis: an overview. Am J Clin Dermatol, 2013. 14(5): p. 389-99.

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