Research Study Application Form

For official use only:
Ref. No:_____

PART I: Study Description

1. Title of Study

Assessment of mast cell activation diagnostic test in patients with allergic disease(s)

2. Principal Investigator

Name	Designation	Department/Division
Tak Hong Lee	HK Sanatorium & Hospital	Allergy Centre

Please attach curriculum vitae

3. Co-investigators

Name	Designation	Department/Division
Hang Yung Alaster Lau	Chinese University of Hong Kong	School of Biomedical Sciences
See-Ying Tam	Stanford University	Pathology

Please attach curriculum vitae

4. Duration of Study

4.1 Proposed study starting date: ___1____ /____02____ /____18____ (dd/mm/yy)

4.2 Proposed study completion date: _____31__ /___1_____ /____19____ (dd/mm/yy)

5. Participants

5.1 Is the study done in collaboration with other units/institutions? X Yes □ No

5.2 If so, please specify which unit/institution:

The Chinese University of Hong Kong

6. Brief summary of study (use language understood by a lay person)

Activation of mast cells in the immune system is known to cause allergic reactions sometimes with severe systemic symptoms. Professor Lau and Dr. Tam have recently developed a blood-based mast cell activation diagnostic test in which levels of functional activation in-vitro in primary cultured mast cells generated from the peripheral blood of single individuals can be assessed. It is our hypothesis that the test can be used to predict the potential state of in-vivo mast cell activation in any individual based on the functional activation profiles exhibited by their cultured mast cells. We now wish to translate our in-vitro findings in a pilot study to disease groups where mast cell activation is expected to be high. These include highly allergic individuals; those with chronic idiopathic urticaria; those with mastocytosis; and those with the mast cell activation syndrome. Furthermore, we will use the functional genomics approach to identify gene expression biomarkers that are correlated with such diseases. The results will be compared with data that have been collected from a cohort of healthy control blood donors.

7. Aim of the Study and Expected Outcome

The objective of this study is to assess whether patients with severe allergic diseases exhibit high levels of mast cell activation as determined by the mast cell activation diagnostic test developed by Lau and Tam. We anticipate that patients with history of severe allergic reactions will show up as high responders in the blood-based mast cell activation diagnostic test. Moreover, using microarray analysis as the approach for gene expression studies, we anticipate further that genomics biomarkers that are correlated with the high functional activation of the in-vitro mast cells derived from these patients can be readily identified.

8. Study Design & Methodology

8.1 Non-experimental / Observational study ***(omit PART II, Experimental study)***

- [ ] Prospective, observational study
- [ ] Retrospective, chart review study
- [ ] Other, specify: _____

8.2 Prospective, Experimental Study

- [ ] Randomized controlled trial
- [x] Non-randomized controlled trial
- [ ] Uncontrolled trial
- [ ] Other, specify: _____

9. Research Plan and Methodology

Attach the research protocol instead, if available

About 100 ml of peripheral venous blood from individual patients will be drawn into heparinized syringes and collected in a blood-collecting bag/tube containing silica. The bag/tube will be promptly transported to Professor Lau's laboratory at CUHK in Shatin to be processed for the generation of primary human mast cell cultures using the protocol that has previously been developed by his group

[Inflammation Research 66: 25 (2017); publication attached to this application]. After culturing for 9 weeks, the resulting human mast cells will be analyzed for both their functional activity in terms of histamine release in response to the activation of high-affinity IgE receptors in these cells and their gene expression profiles using microarray analysis. The in-vitro functional and genomics data will be correlated with specific diagnoses and measurements of blood PGD2, PGD2 metabolites, tryptase and histamine levels in blood. For mediator assays, plasma from each subject will be collected after the CD34+ isolation step and the samples will be aliquoted and frozen at -80°C for subsequent analysis.

10. Study Subjects

10.1 How many subjects will be recruited locally? Explain rationale for sample size calculation if possible.

The numbers of patients recruited will depend on the types of patients who attend the allergy centre during the year and who are willing to participate in the research. We hope to recruit at least 6 patients in each group in this pilot study. For the rarer conditions such as mastocytosis and mast cell activating syndrome it may not be possible to recruit 6 patients.

10.2 How will subjects (patients/controls) be identified and recruited?

The patients that we will study initially will be those with chronic idiopathic urticaria, severe asthma, severe eczema, multiple food allergies, anaphylaxis, mast cell activating syndrome, mastocytosis.

10.3 What are the inclusion and exclusion criteria?

The exclusion criteria are children (<18 years old); those who are unwilling or unable to donate 100 mls blood; and pregnant mothers.

10.4 If randomization is used, explain the process:

N/A

➢ ***Non-experimental Study Omit Part II. Go directly to PART III***

PART II: EXPERIMENTAL STUDY *(to be completed for Experimental Study only)*

11. Product/Procedure: Drug, Appliance, Device or Diagnostic Test

11.1	Will any product be administered to subjects for the purpose of this study? *i.e. in addition to treatment the subjects would receive if not participating in research* Go to Q 13.2 if "no", specify if "yes" □ Drug. The drug trial is Phase □ Medical device	□ Yes	X No □ Others
11.2	Is this study sponsored by industry/commercial agency? If yes, specify nature of sponsorship:	□ Yes	□ No
11.3	Is the product licensed in Hong Kong?	□ Yes	□ No
11.4	Is the product licensed in other countries? If yes, specify where:	□ Yes	□ No
11.5	Is the product being studied for licensed indications?	□ Yes	□ No
11.6	Has the procedure been undertaken before elsewhere? If yes, please give short description:	□ Yes	□ No
11.7	Is there a plan to apply for a clinical trials certificate?	□ Yes	□ No

12. Benefits, potential hazards and risks to study subjects

12.1	State possible benefits to study subjects: There is no direct benefit to the study patients.

12.2 Describe potential discomfort, distress and hazards entailed by study procedures, and how these will be minimised:

The only discomfort is the venepuncture and this will be minimized by expert technique.

13. Financial costs and payment to subjects

13.1	Will there be any financial cost to the subjects?	□ Yes	X No
13.2	Will the subjects receive payment or other benefits?	□ Yes	X No

If yes, specify nature and amount:

14. Indemnity and Compensation

14.1	Is there an external indemnity/insurance provided?	□ Yes	x No
14.2	Is the indemnity supported by an insurance policy?	□ Yes	x No
14.3	If yes, is an insurance certificate available for review?	□ Yes	x No

PART III

15. Confidentiality, consent and research ethics

15.1 What measures are taken to protect the identity of the subjects?

Samples will be anonymised.

15.2 Will a written informed consent be obtained from study subjects? x Yes □ No

If "yes", please attach a copy of consent form in English and one in Chinese

15.3 Has the research project been submitted for review to an external Ethics Committee? □ Yes x No

If yes, specify which Committee:

16. Source of Funding (external), Resources Implication and Conflict of Interest

16.1 Research Fund: Company Sponsored □ No Funding x

Other □

If "other", specify:

16.2 Is there any payment to the investigator or study site for conducting the study?

None

PART IV: OTHER CONSIDERATIONS

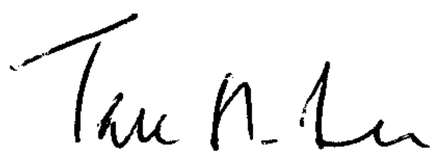
17. Are there any other types of assistance required?

Statistical support	□ specify:	None
Clerical	□ specify:	None
I.T.	□ specify:	None
Financial support	□ specify:	None
Other	□ specify:	None

PART V: DECLARATIONS

Declaration by Investigators

1. The information supplied is to the best of my/our knowledge and belief accurate.
2. I/We shall comply with the principles enunciated in the 1996 or a later version of the Declaration of Helsinki, the Good Clinical Practice and whenever applicable the U.S. Code of Federal Regulations.
3. I/We understand that approval by the HKSH Ethics/Research Committee shall be renewed every 12 months and that the project can be stopped by the HKSH Ethics/Research Committee at any time before the end of the study if the protocol is not strictly adhered to.
4. I/We agree to report study progress to the HKSH Ethics/Research Committee as requested, and to submit a final report at the end of the project.
5. I/We agree to report all serious adverse events to the Hospital Management as soon as these are discovered.
6. I/We agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.
7. I/We agree to maintain adequate accurate records and to make them available for audit/ inspection.
8. I/We undertake to adhere strictly to the research protocol.
9. I/We agree that due acknowledgment will be made to HKSH in any publication of the results of the Research Study.
10. I/We undertake to take all reasonable steps to keep all information confidential and secure and that all data collected is for the purpose of research study only.

	Name	Signature	Date
Principal Investigator:	Tak Hong Lee		21/11/2017
Co-investigators:	Hang Yung Alaster Lau		17 Nov 2017
	See-Ying Tam		18/11/2017

Appendix A: INFORMED CONSENT CHECKLIST

Please indicate where the following items may be found.

	Patient Information Sheet	Consent Form	Not Included
That the trial involves research and those aspects of the trial that are experimental	✓		
The purpose of the trial	✓	✓	
The trial treatment(s) and the probability for random assignment to each treatment			✓
The subject's responsibilities	✓	✓	
The trial procedures to be followed, including all invasive procedures	✓	✓	
The reasonably foreseeable risks or inconveniences to the subject and when applicable, to an embryo, foetus, or nursing infant	✓		
The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this	✓		
The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks			N/A ✓
The compensation and/or treatment available to the subject in the event of trial-related injury			N/A ✓
The anticipated pro-rated payment, if any, to the subject for participating in the trial	✓		
The anticipated expenses, if any, to the subject for participating in the trial			✓
That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled	✓	✓	
That the monitor (s), and REC will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.	✓	✓	

	Patient Information Sheet	Consent Form	Not Included
That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and /or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential	✓	✓	
That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial			✓
The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury	✓		
The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated			✓
The expected duration of the subject's participation in the trial	✓		
The approximate number of subjects involved in the trial			✓
That the Investigator includes the statement "The Institution will receive payment to cover the administrative costs and trial related expense" or similar	✓		