

Effect of Tuberculin inhalation on the lung of Guinea pigs after experimental induction of allergic asthma

Thesis

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List of Abbreviations

ACQ	: Asthma control questionnaire
AHR	: Airway resistance
AMC	: Acid mammalian chitinase
APCs	: Antigen presenting cells
ASM	: Airway smooth muscle
BAL	: Broncho-alveolar lavage
BALF	: Broncho-alveolar lavage fluid
BCG	: Bacillus Calmette–Guérin
CCL	: Chemokine (C -C motif) ligand
CCR3	: C-C chemokine receptor type 3
Cdyn	: Dynamic compliance
CI 95%	: 95% confidence interval
CRTH	: Chemo-attractant homologous receptor
CXCL	: Chemokine (C-X-C motif) ligand
cys-LTs	: Cysteinyl leukotrienes
DCs	: Dendritic cells
EAR	: Early allergic response
EDN	: Human eosinophil-derived neurotoxin
FcεRI	: Fc receptor for IgE

List of Abbreviations (Cont.)

FEV1	: Forced expiratory volume in the first second
FOXP3	: Forkhead box P3
FVC	: Forced vital capacity
GATA3	: GATA-binding protein 3
GM-CSF	: Granulocyte-macrophage colony-stimulating factor

List of Abbreviations (Cont.)

H&E	: Haematoxylin and eosin
HR	: Histamine receptors
i.p.	: Intraperitoneal
I.U.	: International unit
i.v.	: Intravenous
ICS	: Inhaled corticosteroid
IFN-γ	: Interferon-gamma
IgE	: Immunoglobulin E
IL	: Interleukin
IL-4Rα	: IL-4 alpha chain receptor
L.M.	: Light microscopy
LABAs	: Long acting beta 2 agonists
LAR	: Late allergic response
LTC4	: Leukotriene C4
M.vaccae	: Mycobacteria vaccae
MAPK	: Mitogen-Activated Protein Kinases

MCs : Mast cells

List of Abbreviations (Cont.)

MHC : Major histocompatibility complex

NFAT : Nuclear factor of activated T cells

NKT cells : Natural killer T cells

OVA : Ovalbumin

PAMPs : Pathogen-associated molecular patterns

PBS : Phosphate buffered saline

PEF : Peak expiratory flow

PG : Prostaglandin

PPD : Purified protein derivative

List of Abbreviations (Cont.)

RL : Pulmonary resistance

ROR γ t : Retinoic acid orphan receptor- γ t

RT-PCR : Real- Time PCR

SCIT : Subcutaneous immunotherapy

SD : Standard deviation

SEM : Standard error of the mean

SEM : Scanning electron microscopy

SIT : Specific immunotherapy

SLIT : Sublingual immunotherapy

sRaw : Specific airway resistance

STAT6 : Signal Transducer And Activator Of Transcription 6

TCR : T-cell receptor

List of Abbreviations (Cont.)

TGF- β : Transforming growth factor beta

Th cell : T-helper cell

TLR : Toll-like receptor

TNF : Tumor necrosis factor

Tregs : T regulatory cells

TSLP : Thymic stromal lymphopoietin

V_T : _____Tidal volume

WT animal: _____Wild type animal

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Introduction

Asthma is a heterogeneous inflammatory disorder of the airways characterized by chronic airway inflammation, airway hyper-reactivity (AHR) and by symptoms of recurrent wheezing, coughing and shortness of breath. Asthma is a major public health problem affecting 300 million people worldwide and has increased considerably in prevalence over the past three decades (**Wilson et al., 2006**).

Clinically, although several distinct forms of asthma are recognized, the major focus of treatment and research over the past 25 years has been on allergic asthma, the most common form of asthma. Allergen-specific T helper type 2 (Th2) cells are thought to be present in the lungs of almost all patients with asthma, particularly patients with allergic asthma (**Robinson et al., 1992**).

~~Th2 cells produce cytokines that regulate the allergen-specific synthesis of immunoglobulin E (IgE), the recruitment of eosinophils, the recruitment and growth of mast cells, and AHR, a cardinal feature of asthma (Holgate and Polosa, 2008).~~

Also, it has been assumed that Treg cells play an important role in controlling ~~such T-helper typeh-2-~~biased

responses both in animal models and studies in humans (Strickland et al., 2006; Gogishvili et al., 2007).

At the present, the most effective standard anti-asthmatic drugs available include inhaled β 2-agonists and glucocorticoids; these control asthma in about 90-95% of patients (Caramori et al., 2008). The remaining 5% to 10% of asthma patients have severe disease that is difficult to control despite optimum management of co-morbid conditions and environmental triggers; optimum therapy and good adherence to conventional treatment regimens (Stewart et al., 2010).

Hence, there is a great need for new therapies of allergic asthma. In the last few years many studies were concerned by the role of BCG in asthma management; it showed promising results in animal models. However, its mode of action is still controversial. Zuany-Amorim et al. (2002) stated that BCG regulates the allergic host immune responses through the induction of Treg cells rather than affecting the Th1/Th2 balance.

Based on the good results of BCG in animal models of asthma, the present thesis worked upon inhaled tuberculin as a new suggested therapy to asthma. Asthma animal model is