
# SERUM LEVEL OF INTERFERON–GAMMA & INTERLEUKIN–22 IN LEPROSY PATIENTS

## THESIS

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***Dermatology and Venereology***

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# وَقُل رَّبِّ زِدْنِي عِلْمًا

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# مستوى إنترلوكين 22 وإنترفيرون جاما في مصل مرضى الجذام

رسالة مقدمة للحصول على درجة الماجستير في
**الأمراض الجلدية والتناسلية وأمراض الذكورة**

**من**


طبيبة/ شيماء عامر مفتاح

بكالوريوس الطب والجراحة العامة


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# LIST OF CONTENTS

# LIST OF ABBREVIATIONS

- **aa:** Amino acids.
- **AD**: Atopic dermatitis
- **APCs**: Antigen-presenting cells
- **BB:** Borderline borderline
- **BCG:** Bacillus Calmette-Guerin.
- **BI:** Bacteriological index
- **BL:** Borderline lepromatous
- **BT:** Borderline tuberculoid
- **TYK :**Tyrosine kinase
- **CCR4:** Chemokine receptors 4
- **CLE**: Conserved lymphokine element
- **CMI:** Cell-mediated immunity
- **CSF:** Cerebrospinal fluid.
- **CXCL10:** CXC-chemokine 10.
- **ELISA**: Enzyme-linked immunosorbent assay.
- **EM**: Electron microscopy.
- **ENL:** Erythema nodosum leprosum
- .**HBV:** Hepatitis B virus
- **HCV**: Hepatitis C virus.
- **HIES:** Hyper-IgE syndrome
- **HLA:** Human leucocytic antigens
- **ID:** Indeterminate leprosy
- **IFN-γ:** Interferon gamma
- **Ig**: Immunoglobulin.
- **IL:** Interleukin.
- **iNOS:** Inducible nitric oxide synthetase
- **JAK:** Janus kinase family.
- **LL:** lepromatous leprosy.
- **LLp:** Polar lepromatous leprosy.
- **LLs:** Subpolar lepromatous leprosy.
- **MB:** Multibacillary.
- **MCP-1:** Monocyte chemoattractant protein-1
- **MDT:** Multi drug therapy.

- **MHC:** Major histocompatibility complex
- **MI:** Morphological index.
- ***M. leprae***: Mycobacterium lepra.
- **MoAb:** Monoclonal antibodies.
- **Foxp3**: Master regulatory transcription factoforkhead fox p3
- **NK:** Natural killer.
- **Non-RL**: Non reactional
- **PAF:** Platelet activating factor
- **PB:** Paucibacillary
- **PCR:** Polymerase chain reaction.
- **PDGF:** Platelet-derived growth factor
- **PG:** Prostaglandin.
- **Pg/ml:** Picogram/milliliter**.**
- **PGL-1:** Phenolic glycolipid 1.
- **PNL:** Pure neuritic leprosy.
- **qRT-PCR**: quantitative Reverse transcriptase-PCR.
- **RA:** Rheumatoid arthritis.
- **RL**: Reactional leprosy.
- **ROR-c:** Thymus specific nuclear receptor.
- **rRNA:** Ribosomal (r) RNA.
- **SCs:** Schwann cells.
- **SD:** Standard deviation.
- **SPSS**: Statistical program for social science.
- **SSS**: Slit-Skin Smear
- **STAT3**: Signal transducer and activator of transcription 3.
- **T-bet:** lineage-specific transcription factors required for the differentiation of Th1.
- **TCR:** T cell's receptor.
- **TGF-β:** Transforming growth factor- beta.
- **Th cells:** T helper cells
- **TLR2:** Toll-like receptor 2.
- **T Regs**: T regulatory**TNF:** Tumor necrosis factor.
- **TT:** Tubercloid leprosy.
- VCAM**:** Vascular cell adhesion molecule Negative.
- **WHO:** World Health Organization.

# LIST OF FIGURES

# LIST OF TABLES

# INTRODUCTION

Leprosy is a chronic infectious disease caused by the obligate intracellular microorganism *Mycobacterium leprae (M. leprae)*. It is still considered a major health problem in some countries of Asia, Latin America, and Africa, including Egypt. According to the World Health Organization (WHO), approximately 260,000 new patients were affected in 2006 ***(WHO, 2008).***

The **Ridley–Jopling** classification of leprosy is based on clinical and histopathological criteria, which suggest a disease spectrum with five clinical categories: tuberculoid (TT), borderline tuberculoid (BT), borderline borderline (BB), borderline lepromatous (BL), and lepromatous (LL) leprosy ***(Ridley and Jopling, 1966).*** At one pole, TT leprosy is characterized by few well-defined skin patches, few bacilli (paucibacillary; PB), and vigorous cell-mediated immunity (CMI) ***(Fitness et al., 2002).*** At the other pole, LL presents with many skin lesions with uncontrolled proliferation of leprosy bacilli (multibacillary; MB), and inefficient CMI ***(Britton and Lockwood, 2004).*** Borderline leprosy manifests clinical and immunological features with characteristics between the two forms ***(Sasaki et al., 2001).***

Th subsets play a discriminative role in translating antigen-immunopathology. The identification of novel T cell subsets, such as Th17 cells, is important in order to define the role of the specific immune response in human disease. Across the board of different pathologies, distinct T cell subsets secrete cytokines that not only function on other immune cells, but also instruct target cell ***(Burgler S., 2009 and Eyerich, K., 2009*)**.

Each T cell subset secretes tissue-instructing cytokines such as IFN-γ (Th1), IL-4 (Th2), andIL-17, IL-22 (Th17***)( Weber et al., 2007).***

A less well-defined tissue-instructing cytokine is IL-22, which is expressed by Th17 cells ***(Kreymborg, 2007)*** but also by NK cells ***(Cupedo, 2009)***. There are many studies have determined that some T cells express IL-22 independently of IL-17, particularly CCR10+ T cells ***( Eyerich K , 2009 ; Nograles K.E , 2009 and Trifari et al , 2009).***

The function of IL-22 is difficult to generalize: It is not antiinflammatory, nor is it necessarily proinflammatory.In the skin, IL-22 induces antimicrobial peptides, promotes keratinocyte proliferation, and inhibits differentiation, which suggests a role in remodeling wound healing and in innate defense mechanisms ***(Boniface , 2005).***

The immune response against intracellular pathogens (including *M. leprae*) is mainly regulated by interferon-γ (IFN-γ). This cytokine activates macrophages through the production of reactive oxygen intermediates (ROIs), nitric oxide (NO), and enhanced expression of class I and II MHC molecules and costimulatory molecules involved in antigen presentation. IFN-γ also modulates the expression of other antigen processing mechanisms, which promote optimum activation of CD4 and CD8 T cells ***(*Huang *et al., 2002).***