



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Correlation of Stool Lactobacillus Acidophilus and Leaky Gut Syndrome in Patients with Hashimoto Thyroiditis

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
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AIRE	<i>Autoimmune regulator</i>
AITDs	<i>Autoimmune thyroid diseases</i>
AMPs	<i>Antimicrobial proteins</i>
ANA	<i>Antinuclear antibodies</i>
anti-Tg	<i>Anti thyroglobulin</i>
anti-TPO	<i>Anti-thyroid peroxidase</i>
APCs	<i>Antigen-presenting cells</i>
APS 1	<i>Autoimmune polyglandular syndrome type I</i>
ATD	<i>Autoimmune thyroid disease</i>
CTLA-4	<i>Cytotoxic T lymphocyte-associated 4</i>
DCs	<i>Dendritic cells</i>
ELISA	<i>Enzyme-linked immunosorbent assay</i>
FOXP3	<i>Forkhead box protein 3</i>
FT4	<i>Free thyroxine</i>
GABA	<i>γ-amino butyric acid</i>
GAPs	<i>Cell-associated antigen passages</i>
GF	<i>Germ-free</i>
HLA	<i>Human leukocyte antigen</i>
HS	<i>Highly significant</i>
HSP	<i>Heat shock proteins</i>
HT	<i>Hashimoto thyroiditis</i>
IAP	<i>Intestinal alkaline phosphatase</i>
IBD	<i>Inflammatory bowel disease</i>
IBM SPSS	<i>Statistical Package for Social Science</i>
IECs	<i>Intestinal epithelial cells</i>
IFN-α	<i>Interferon-α</i>
IL-10	<i>Interleukin-10</i>
IPEX	<i>Immune dysregulation, polyendocrinopathy, Enteropathy, X-linked</i>

List of Abbreviations (Cont...)

Abb.	Full term
ITregs	<i>Inducible Tregs</i>
LPSs	<i>Lipopolysaccharides</i>

MS	<i>Multiple sclerosis</i>
MUC2	<i>Mucin</i>
NLRs	<i>NOD-like receptors</i>
NS	<i>Non significant</i>
NSAIDs	<i>Non-steroidal anti-inflammatory drugs</i>
nTregs	<i>Natural Tregs</i>
PCR	<i>Polymerase chain reaction</i>
PRRs	<i>Pattern recognition receptors</i>
PTM	<i>Pretibial myxoedema</i>
PTMP	<i>Posttranslational modification of proteins</i>
PTPN22	<i>Protein tyrosine phosphatase, non-receptor type 22</i>
RA	<i>Rheumatoid arthritis</i>
S	<i>Significant</i>
SIgA	<i>Secretory IgA</i>
SLE	<i>Systemic lupus erythematosus</i>
T1D	<i>Type 1 diabetes</i>
TBII	<i>TSH receptor-blocking antibodies</i>
TEDs	<i>Transepithelial dendrites</i>
TG	<i>Thyroglobulin</i>
TgAb	<i>Tg antibodies</i>
TGF-β	<i>Transforming growth factor beta</i>
TLR	<i>Toll-like receptor</i>
TLRs	<i>Toll-like receptors</i>
TPO	<i>Thyroid peroxidase</i>
TPOAb	<i>Thyroperoxidase antibodies</i>
TRAb	<i>TSHR antibody</i>
tTg	<i>Tissue trans glutamimnase</i>
ZO-1	<i>Zonula occludens-1</i>

INTRODUCTION

Leaky gut, also known as increased intestinal permeability, is a digestive condition in which bacteria and toxins are able to "leak" through the intestinal wall. The walls of the intestines act as barriers, controlling what enters the bloodstream to be transported to our organs. Small gaps in the intestinal wall called tight junctions allow water and nutrients to pass through, while blocking the passage of harmful substances. Intestinal permeability refers to how easily substances pass through the intestinal wall (*Camilleri, 2019*).

When the tight junctions of intestinal walls become loose, the gut becomes more permeable, which may allow bacteria and toxins to pass from the gut into the bloodstream. When the gut is "leaky" and bacteria and toxins enter the bloodstream, it can cause widespread inflammation and possibly trigger a reaction from the immune system (*Mu et al., 2017*).

A protein called zonulin is a known regulator of intestinal permeability. When it's activated in genetically susceptible people, it can lead to leaky gut. Two factors that trigger the release of zonulin are bacteria in the intestines and gluten, which is a protein found in wheat and other grains (*Fasano, 2012*). However, There are

likely multiple contributing factors to leaky gut syndrome as Excessive sugar intake, Non-steroidal anti-inflammatory drugs (NSAIDs) Excessive alcohol intake, Nutrient deficiencies, Inflammation, Stress, Poor gut health: Yeast overgrowth (*Konturek et al., 2011*).

Hashimoto thyroiditis is an autoimmune disease that destroys thyroid cells by cell and antibody-mediated immune processes. It is the most common cause of hypothyroidism in developed countries. In contrast, worldwide, the most common cause of hypothyroidism is an inadequate dietary intake of iodine. This disease is also known as chronic autoimmune thyroiditis and chronic lymphocytic thyroiditis. The pathology of the disease involves the formation of antithyroid antibodies that attack thyroid tissue, causing progressive fibrosis (*Mincer and Jialal, 2019*).

Gut shows diverse microbial communities in different parts. Streptococcaceae and Lactobacillaceae populate the proximal region, whereas the distal portion of the small intestine is home to Lactobacillaceae, Erysipelotrichaceae, and Enterobacteriaceae. The colon is inhabited by members of Bacteroidaceae, Prevotellaceae, and Clostridiaceae families. The epithelial lining of stomach harbors Lactobacillaceae and Streptococcaceae. The term dysbiosis is commonly used to describe the situation that arises whenever there is a structural or

functional change in gut micro biota configuration, which disturbs homeostasis of the gut ((*Kennedy et al., 2020*).

Lactobacillus is a genus of Gram-positive, aero tolerant anaerobes or microaerophilic, rod-shaped, non-spore-forming bacteria. They are a major part of the lactic acid bacteria group (i.e., they convert sugars to lactic acid). In humans, they constitute a significant component of the microbiota at a number of body sites, such as the digestive system (*Makarova et al., 2006*).

Protection of the gut barrier from disruption by induction of changes in expression and distribution of tight junction proteins and mucus may be the key mechanism of probiotic function (*Ewaschuk et al., 2008*).

Alterations in the gut micro biota are associated with autoimmune diseases development. The molecular mimicry, bystander T-cell activation, post-translational modification of luminal proteins by altered micro biota, and a shift to proinflammatory milieu in gut mucosa could contribute to autoimmunity as in hashimoto thyroiditis (*Straub, 2015*).

