



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



Ain Shams University
Faculty of Pharmacy
Biochemistry Department

“Investigation of Adipolin and Subfatin in Osteoarthritis Patients”

A Thesis

Submitted in Partial Fulfillment of the Requirements for the
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In Pharmaceutical Sciences
(Biochemistry)

By

Basma Hamdi Mahmoud Kamel Hassaneen Sobieh
B. Ph. Sci., Ain Shams University (2013)
Demonstrator of Biochemistry, Faculty of Pharmacy,
Ain Shams University

Under Supervision of

Prof. Dr. Hala Osman El- Mesallamy
Dean of Faculty of Pharmacy, Sinai University
Professor of Biochemistry
Faculty of Pharmacy, Ain Shams University

Associate Prof. Dr. Zeiad Mohamed Zakaria
Associate Professor of Orthopedic Surgery
Faculty of Medicine
Ain Shams University

Dr. Dina Hamada Kassem
Lecturer of Biochemistry
Faculty of Pharmacy
Ain Shams University

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كلية الصيدلة
قسم كيمياء حيوية

" دراسة الأديبولين و السيفاتين في مرضى خشونة المفاصل "

رسالة مقدمة

لاستكمال متطلبات الحصول علي درجة الماجستير في العلوم الصيدلانية
تخصص (كيمياء حيوية)

إعداد

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معيدة بقسم الكيمياء الحيوية- كلية الصيدلة-جامعة عين شمس

تحت إشراف

أ.د/ هالة عثمان المسلمي
عميد كلية الصيدلة-جامعة سيناء
أستاذ الكيمياء الحيوية
كلية الصيدلة-جامعة عين شمس

أ.م.د/ زياد محمد زكريا
استاذ مساعد جراحة العظام
كلية الطب جامعة عين شمس

د/ دينا حماده قاسم
مدرس الكيمياء الحيوية
كلية الصيدلة جامعة عين شمس

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
" وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ
عَلَيْكَ عَظِيمًا "

صدق الله العظيم

سورة النساء- الآية (١١٣)

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Publications Related to the Thesis

1) Sobieh BH; Kassem DH; Zakaria ZM; El-Mesallamy HO, “Potential Emerging Roles of the Novel Adipokines Adipolin/CTRP12 and Meteorin-like/METRNL in Obesity-Osteoarthritis Interplay” CYTOKINE. Accepted 2020 November.

Impact Factor=**2.952**

Publications Related to the Thesis

2) METRNL: A Novel Adipokine with Potential Emerging Role in the Pathogenesis of Osteoarthritis and its Interplay with Obesity. Live Poster in Keystone Symposia (Obesity: From Cell to Patient (EK17)), USA 1 February 2021.



Publications Related to the Thesis

METRNL: A Novel Adipokine with Potential Emerging Role in the Pathogenesis of Osteoarthritis

Basma H. Sobieh ^a, Dina H. Kassem ^a, Zeiad M. Zakaria ^b, and Hala O. El-Mesallamy

a, c *

^a Biochemistry Department, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt

^b Orthopedic Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

^c Faculty of Pharmacy, Sinai University, Sinai, Egypt

Background: Osteoarthritis (OA) is one of the ten most disabling diseases worldwide. Obesity is one of the major risk factors for OA. Adipokines are potential candidates that link obesity with OA, and may serve as putative targets for disease-modifying OA drugs, especially for obese patients. Among these adipokines, METRNL is a newly discovered adipokine not only expressed by adipose tissue but also by chondrocytes. Recent studies also suggest its role as an anti-inflammatory adipokine. However, its role in obesity-OA interplay has not been adequately studied.

Methods: Circulating as well as synovial fluid (SF) METRNL and insulin levels, and matrix-metalloproteinase-13 (MMP-13) SF-levels were all measured by ELISA in obese osteoarthritic patients (n=30) and obese non-osteoarthritic subjects (n=25). The severity of the knee articular cartilage damage was evaluated by X-ray radiographs.

Results: Serum METRNL was found to be significantly decreased in OA-patients compared to non-OA-subjects; 31.85 ± 5.09 pg/ml and 51.85 ± 6.29 pg/ml, respectively, $p=0.012$. Serum METRNL levels were also found to be relatively decreased with the advancing of OA. The higher the serum METRNL levels, the less likelihood to have OA. Furthermore, SF METRNL levels were found to be significantly elevated in OA patients compared to non-OA subjects; 912 [367-1524] and 315 [125-484] pg/ml, respectively, $p=0.007$

Publications Related to the Thesis

Conclusions: Our results highlight a possibly pivotal role for METRNL in OA pathogenesis. METRNL could provide a new biomarker to for OA state, and disease severity. Different regulatory mechanisms are strongly suggested for regulation of METRNL secretion from different tissues. Conclusively, METRNL is a potential novel therapeutic target for OA.



Obesity: From Cell to Patient (EK17)
February 2021, CO, USA

Contact information: Basma.Hassaneen@pharma.asu.edu.eg

METRNL: A Novel Adipokine with Potential Emerging Role in the Pathogenesis of Osteoarthritis and its Interplay with Obesity

Basma H. Sobieh^a, Dina H. Kassem^a, Zeiad M. Zakaria^b, and Hala O. El-Mesallamy^{a, c}

^aFaculty of Pharmacy, Biochemistry Department, Ain Shams University, Cairo, Egypt

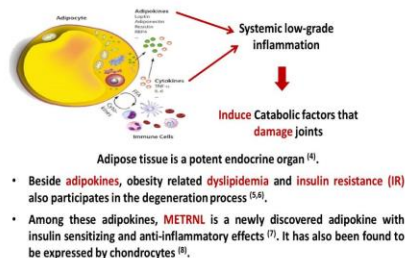
^bFaculty of Medicine, Orthopedic Department, Ain Shams University, Cairo, Egypt

^cFaculty of Pharmacy, Sinai University, Sinai, Egypt



Background

- Obesity, with its associated complications, is a growing health problem worldwide^[1].
- Obesity is one of the most significant risk factors for osteoarthritis (OA)^[2].
- As the theory of mechanical loading failed to explain the relation between obesity and OA in non-weight bearing joints, scientists speculated that **adipose tissues** play a crucial role in this context^[3].

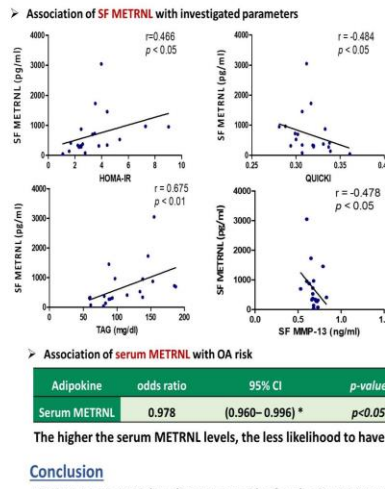
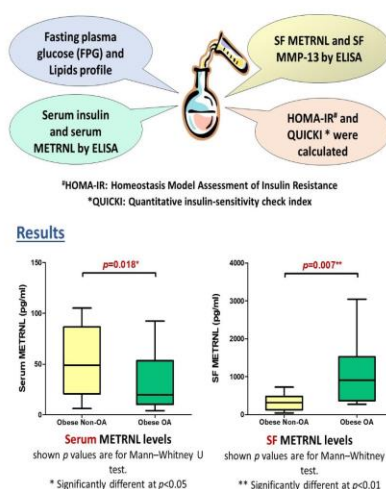


Aim of the work

- 1) To investigate the levels of METRNL in both serum and synovial fluid (SF) of obese patients with and without OA.
- 2) To study the possible association of this new adipokine with insulin resistance and dyslipidemia.
- 3) To study the association of this adipokine with OA severity, and with other prominent markers in OA like matrix metalloproteinase-13 (MMP-13).

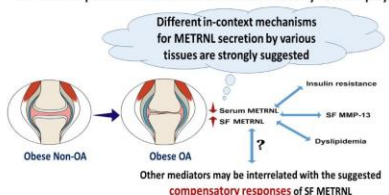
Subjects and Methods

- Weight & Height were recorded to calculate body mass index (BMI).
- Knee-radiographs using X-ray were done to determine OA-severity (based on Kellgren-Lawrence (KL) criteria).



Conclusion

METRNL is a potential mediator to consider for obesity-OA interplay



Future Work

- 1) Experimental mechanistic studies to further elucidate the role of METRNL in obesity-OA interplay.
- 2) Large-scale studies to determine if there is a cut-off value for METRNL to predict obese subjects who are more likely to develop OA.
- 3) Further studies to investigate the effect of various anti-inflammatory drugs on METRNL.

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Related Publication

Potential Emerging Roles of the Novel Adipokines Adiponin/CTRP12 and Meteorin-like/METRNL in Obesity-Osteoarthritis Interplay (2020). Cytokine, E-Pub Ahead of Print.

List of Abbreviations

ABCA-1	Adenosine triphosphate (ATP)-binding cassette transporter-1
ACL	Acute cruciate ligament
ACR	American College of Rheumatology
AGEs	Advanced glycation end products
Akt	Protein kinase B
AMPK	Adenosine monophosphate-activated protein kinase
ANOVA	Analysis of variance
Apo	Apolipoprotein
BAT	Brown adipose tissue
BMI	Body mass index
CI	Confidence intervals
C1qdc2	C1q domain-containing protein
CRP	C-reactive protein
CTRP-12	C1q/tumor necrosis factor-related protein-12
CVD	Cardiovascular disease
ECM	Extracellular matrix
ELISA	Enzyme-Linked Immuno-Sorbent assay
FFA	Free fatty acids
FPG	Fasting plasma glucose
GLM	General linear modelling
HDL-C	High-density lipoprotein-cholesterol
HIF-2α	Hypoxia inducible factor 2 α
HOMA-IR	Homeostasis model assessment-insulin resistance
IL	Interleukin
IR	Insulin resistance
JSN	Joint space narrowing
KL	Kellgren–Lawrence

List of Abbreviations

LCAT	Lecithin–cholesterol acyltransferase
LDL-C	Low density lipoprotein cholesterol
LXR	Liver X receptor
MCP-1	Monocyte chemotactic protein-1
Metrn1	Meteorin-like
MMP	Matrix metalloproteinase
MT	Meniscal tear
mtROS	Mitochondrial-ROS
NF-κB	Nuclear factor-Kappa B
OA	Osteoarthritis
ORs	Odds ratio
Ox-LDL	Oxidized LDL
PGC-1α	Peroxisome proliferator-activated receptor gamma coactivator-1alpha
PPAR γ	Peroxisome proliferator-activated receptor gamma
QUICKI	Quantitative insulin-sensitivity check index
RA	Rheumatoid arthritis
RAGE	Receptor of AGE
ROS	Reactive oxygen species
Runx2	Runt-related transcription factor-2
SEM	Standard error of mean
SF	Synovial fluid
STAT3	Signal transducer and activator of transcription protein 3
TC	Total cholesterol
T2DM	Type 2 diabetes mellitus
TAG	Triacylglycerols
TIMP	Tissue inhibitor of metalloproteinases
TKA	Total knee arthroplasty
TLR	Toll-like receptor
TNF-α	Tumor necrosis factor-alpha
