
شبكة المعلومات الجامعية


# بسم الله الرحمن الرحيم


# شبكة المعلومات الجامعية

# التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

# جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

## قسم

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# بالرسالة صفحات لم ترد بالاصل

# *Study of soluble Receptor Activator Nuclear Factor Kappa β Ligand (sRANKL) In Patients with Bone Metastases*



**Thesis**

**Submitted for the Partial Fulfillment of the Requirements of the Master Degree in "Clinical Pathology"**

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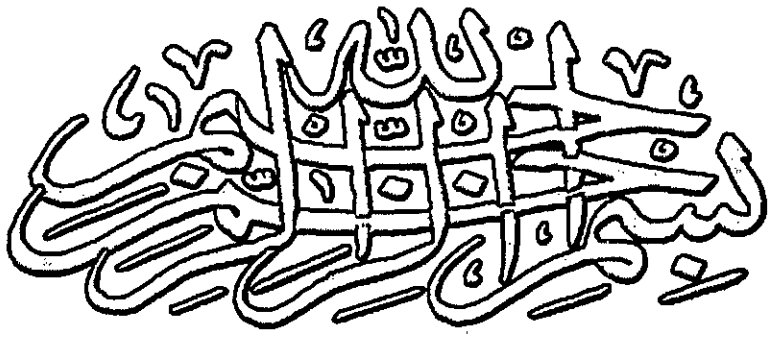

وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم
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**Emad Abd El-Moneim Ragab**

# *Dedicated*

*I wish to express my particular thanks to*

*My Father,* *My Mother*

*My Wife*

*and all My Love and Wishes to*

*My Son*

*To all I Would Say Thank You*

# *Study of Soluble Receptor Activator Nuclear Factor Kappa β Ligand (sRANKL) in Patients with Bone Metastases*

Biochemical markers of bone remodeling are more accurate non-invasive means for diagnosis of bone metastases. The aim of this work was to study the serum level of soluble form of the receptor activator for nuclear factor (NF)KB(sRANKL) in patients with bone metastases and compare them with non-metastatic cancer patients. sRANKL was measured in 34 patients with carcinoma of the breast, prostate, lung, kidney and colorectum. Including 16 cancer patients without bone metastases and 18 cancer patients, with bone metastases. It was found that the mean values of serum sRANKL were significantly increased in metastatic patients (2.94±0.34) when compared with both control group (0.69±0.07) and non-metastatic group (1.23±0.19). There were insignificant correlation between sRANKL and age, ALP and total calcium. From this study it can be concluded that sRANKL is considered a specific recent marker in metastatic bone disease and useful in assessing the early onset of bone micrometastases.

# دراسة مرتبط المكون الذائب لمنشط مستقبلات العامل النووى كابا - ب (اس - رانك - ال) فى مرضى السرطان المنتشر بالعظام

الهدف من هذا البحث هو دراسة المرتبط المكون الذائب لمنشط مستقبلات العامل النووى كابا - ب (اس - رانك - ال) فى مرضى السرطان المنتشر بالعظام ومقارنتهم بمرضى السرطان الغير منتشر بالعظام .وقد اشتمل البحث على ٣٤ مريضاً بسرطان الثدى والبروستاتا والرئة والكلى والقولون ، ١٦ مريضاً منهم بالسرطان الغير منتشر بالعظام ، ١٨ مريضاً منهم بالسرطان المنتشر بالعظام ، وهذه الدراسة أظهرت ارتفاع مستوى (اس - رانك - ال) فى مجموعة مرضى السرطان المنتشر بالعظام ارتفاع ذو دلالة إحصائية إذا ما قورن بمستواه فى مجموعتى الأصحاء ومرضى السرطان الغير منتشر بالعظام.

وتتلخص نتائج البحث فى الآتى استخدام (اس - رانك - ال) كإحدى دلالات الكيمياء الحيوية الحديثة والدقيقة فى الكشف المبكر عن الثانويات السرطانية المنتشرة بالعظام فى مرضى السرطان.

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# List of Abbreviations

| | |
|---|---|
| **(1,25 $(OH)_2D$)** | Vitamin D. |
| **BGP** | Bone gla protein. |
| **BSP** | Bone sialoprotein. |
| **CRD** | Cysteine-rich domains. |
| **CT** | Calcitonin. |
| **CTX** | C-terminal telopeptide. |
| **DC** | Dendritic cells. |
| **DPD** | Deoxy-pyridinoline. |
| **FADD** | Fas-associated with death domain. |
| **FDG** | Fluorine-18-fluoro deoxy glucose. |
| **GHYL** | Galactosyl hydroxy lysine. |
| **HHM** | Humoral Hypercalcema of malignancy. |
| **ICTP** | Pyridinoline cross-linked carboxy terminal telopeptide. |
| **IGF** | Insulin like growth factor. |
| **MAP** | Mitogen activated protein. |
| **M-CSF** | Macrophage-colony stimulating factor. |
| **MMPs** | Matrix metalloproteinases. |
| **MRI** | Magnetic resonance imaging. |
| **MSCs** | Marrow stromal cells. |
| **NF** | Nuclear factor. |
| **NTX** | N-terminal telopeptide. |
| **ODAR** | Osteoclast differentiation and activation receptor. |
| **ODF** | Osteoclast differentiation factor. |

| | |
|---|---|
| **OPG** | Osteoprotegerin. |
| **OPGL** | Osteoprotegerin ligand. |
| **PDGF** | Platelet derived growth factor. |
| **PET** | Positron emission tomography. |
| **PICP** | C-terminal propeptide fragment. |
| **PLAD** | Pre-ligand assembly domain. |
| **PTH** | Para thyroid hormone. |
| **PTHRP** | PTH related protein. |
| **PYP** | Urine pyridinoline. |
| **RANKL** | Receptor activator nuclear factor kappa-B ligand. |
| **SRANKL** | Soluble receptor activator nuclear factor kappa-B ligand. |
| **TGF** | Transforming growth factor. |
| **TMB** | Tetra methyl benzidine. |
| **TNF** | Tumour necrosis factor. |
| **TNFR** | Tumor necrosis factor receptor. |
| **TRAFs** | Tumour necrosis factor receptor-associated factors. |
| **TRANCE** | Tumour necrosis factor related activation-induced cytokines. |
| **TRAP** | Tartrate-resistent acid phosphatase. |

# Introduction

# Introduction

Carcinoma is an invasive disease process that spreads to other tissues throughout the body, producing metastases and abnormal tissue growth. Carcinoma of the breast, prostate and kidney have a particularly high rate of invasion to bone, resulting in bone metastases and causing considerable bone destruction ***(Galasko, 1981)***.

Biochemical markers of bone remodeling have been used as surrogate markers to manage patients with metastatic bone disease. Markers of the bone resorptive process, such as the bone collagen breakdown products N-telopeptide and C-telopeptide are useful markers for monitoring the response and efficacy of anti-resorptive therapy and to assess disease progression in patients with osteolytic bone disease.

Recently discovered markers of osteoclastogenesis, osteoprotegrin (OPG) and the soluble form of the receptor activator for nuclear factor (NF)-κb (RANK-L), also are candidate markers of the bone metastases process and offter potential as surrogate markers of tumour-induced osteoclastogenesis ***(Laurence, 2003)***.

RANK ligand (RANK-L) is both necessary and sufficient for osteoclast differentiation, provided that permissive concentrations of macrophage colony stimulating factor (M-CSF) are present and also enhances activity and prolongs the lifespan of osteoclasts by decreasing apoptosis. In bone marrow, RANKL is expressed on the surfaces of marrow stromal cells (MSCs) of the osteoblasts lineage ***(Yasuda et al., 1998)***, T-lymphocytes ***(Cenci et al., 2000)*** and B-lymphocytes ***(Kanematsu et al., 2000)***.