# IMMUNOHISTOCHEMICAL DETECTION OF EPIDERMAL GROWTH FACTOR RECEPTOR IN LARYNGEAL SQUAMOUS CELL CARCINOMA

*Thesis Submitted for the Partial Fulfillment of the M.D. Degree in Otorhinolaryngology*


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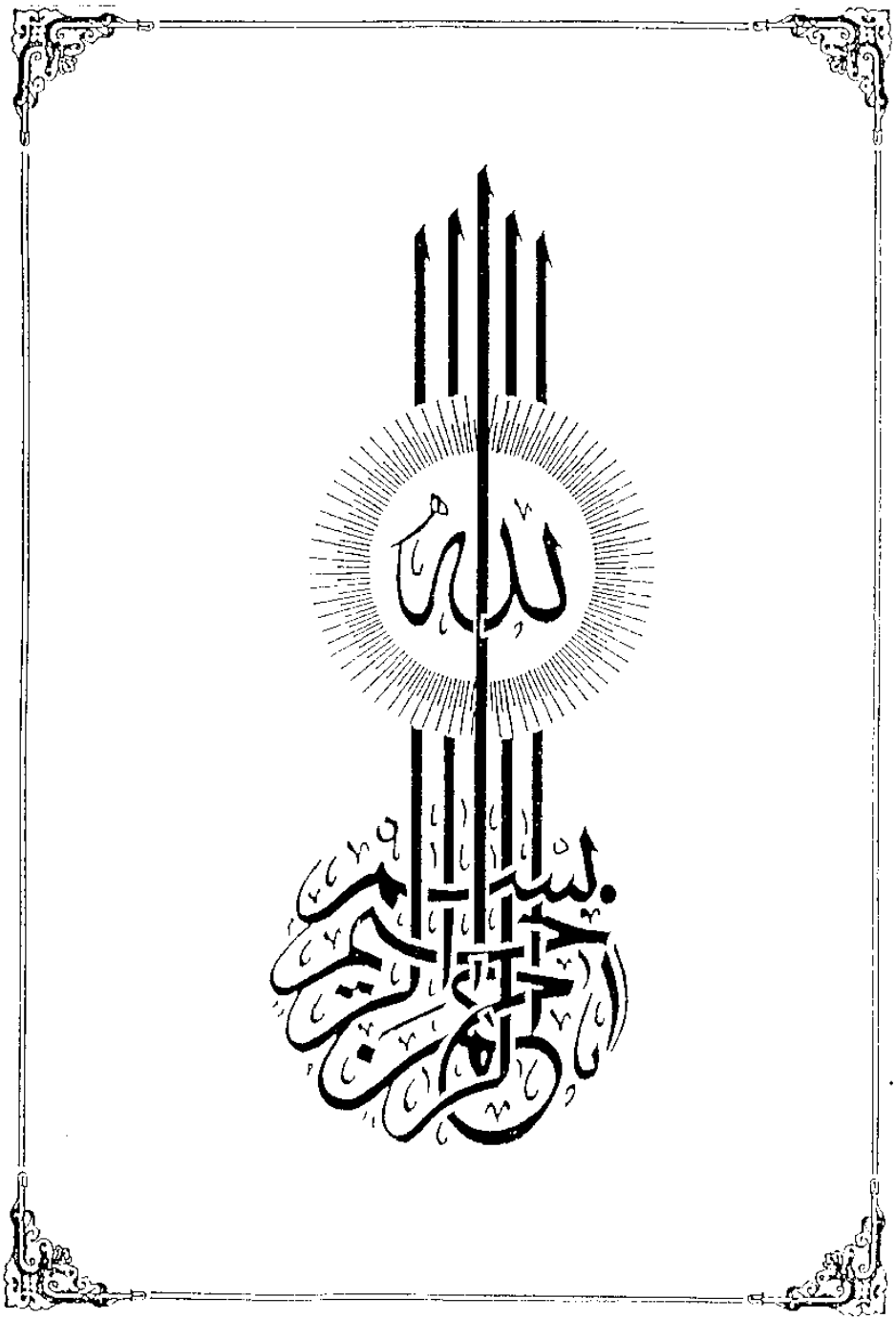
بسم الله الرحمن الرحيم

**قالوا سبحانك لا علم لنا إلا ما علمتنا،**
**إنك أنت العليم الحكيم**

صدق الله العظيم

سورة البقرة-الآية:٣٢



To My Family

## Acknowledgment

First of all, thanks to God, without his help, this work could not be accomplished.

I would like to present my sincere thanks and appreciation to Professor Dr. Mohamed Nassar, Professor of Otorhinolaryngoloy, Faculty of Medicine-Ain Shams University, for his great help, continuous support, meticulous supervision and fruitful guidance throughout this work.

I would like to express my gratitude to Prof. Dr. Maisa El Maraghi, Professor of Pathology, Faculty of Medicine, Ain Shams University who gave me the privilege of working under her supervision, her continuous guidance and worthy remarks are beyond words of thanks.

Also I would like to thank Prof. Dr. Ossama Abdul Hamid, Professor of Otorhinolaryngology, Faculty of Medicine-Ain Shams University, for his sincere help and thorough revision of every detail in this work. I am truely grateful for him for his unlimited support and help through the whole work.

Words stand short when coming to express my gratefulness to Prof. Dr. Magdy Samir, Professor of Otorhinolaryngology, Ain Shams University for his unlimited knowledge and kind criticism.

Last but not least, my great thanks and respect to Dr. Sabry Magdi, Lecturer of Otorhinolaryngology, Ain Shams University who saved no time nor effort in helping me throughout this work.

Mgdy Shedid

# ABSTRACT

The application of the technique of molecular biology to the study of cancer has produced dramatic advances in the understanding of the basic biology and behaviour of these diseases.

Epidermal growth factor receptor (EGFR) is a protein product of C-erb-B oncogene . Activation of this receptor by binding of epidermal growth factor leads to cell division. In this study, EGFR expression increases with increasing grade of malignancy. In mucosa nearby malignant lesions, EGFR expression was positive in about 75% of cases. In minor pathological lesions and normal controls, EGFRs were negative, so EGFR could be an early sign of dysplasia.

It will be helpful to use EGFR expression as a guide for safety margin, postoperative irradiation and follow up for early detection of recurrence.

**Key words: Epidermal growth factor receptors (EGFRs) – Immunohistochemistry – Laryngeal carcinoma.**

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## List of Abbreviations

| | |
|---|---|
| BMP: | Bone marrow protein |
| CSFs: | Colony stimulating factors |
| DNA: | Deoxy ribonucleic acid |
| DSF: | Disease free survival |
| ECGF: | Endothelial cell-derived growth factor |
| EGF: | Epidermal growth factor |
| EGFR: | Epidermal growth factor receptor |
| F G Fs: | Fibroblast growth factors |
| G-CSF: | Granulocyte colony stimulating factors |
| GMCSFs: | Granulocyte-macrophage colony stimulating factors |
| H&E: | Haematoxylin and Eosin |
| HNSCC: | Head and neck squamous cell carcinoma |
| IL-1: | Interleukin-1 grwoth cytokine |
| IL-2: | Interleukin-2 growth cytokine |
| M-CSF: | Macrophage colony stimulating factors |
| MAB: | N-Methyl-4-aminoazobenzene |
| MPL: | Minor pathological lesion |
| NGF: | Nerve growth factor |
| PDGF: | Platelet derived growth factor |
| Rb gene: | Retinoblastoma gene |
| RNA: | Ribonucleic acid |
| TGF-α: | Transforming growth factor α |
| TGF-β: | Transforming growth factor-β |
| TNF: | Tumor necrosis factor |
| V. myc: | Virus in myeloproliferative disorder of chicken |
| V. ras: | Virus in sarcoma of rats |
| V. src: | Virus from sarcoma of chicken |
| V P F.: | Vasopermeability factor |

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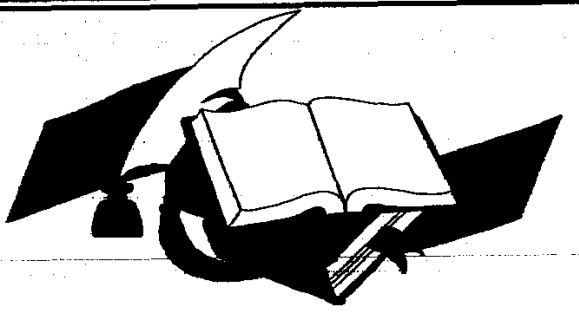

# Introduction and Aim of the Work

# INTRODUCTION

Carcinomas of head and neck constitute about 5-7% of all new malignancies diagnosed annually in North America. The treatment of head and neck cancer during the last 20 years has been marked by significant advancement in those areas that impact on improvement in patient morbidity. Unfortunately, mortality statistics during the same period have shown little change. The failure to improve overall patient survival has emphasized the need to seek new methods of attacking this disease *( Varmus , 1989 )*.

The recent emphasis on the study of the molecular biology, genetics and immunology of cancer is motivated by the belief that understanding the fundamental mechanisms that underlie the origins of human cancer will lead to more rational means of treating these malignancies *(Gullick, 1991)*.

Tumors arise and progress through a series of genetic changes in cancer-associated genes known as oncogenes or tumor suppressor genes. It is the accumulation of mutations in oncogenes that leads to clonal outgrowth and tumor progression. Recently, more precise molecular techniques identified specific point mutations within oncogenes that lead to tumor progression. These point mutations occur in proto-oncogenes; normal cellular genes that are activated to induce tumor growth and in tumor suppressor genes-cellular genes whose normal

suppressor function is inactivated allowing tumor progression. Because these mutations are an integral part of the clonal population of cells that allow tumor outgrowth, the detection of these specific changes in clinical samples is diagnostic for the presence of cancer ***(Anderson, 1992).***

Already in some hematological malignancies, lung and breast cancer, oncogenes expression has been linked to various clinical parameters including tumor aggressiveness, radioresistance and propensity to tumor metastases ***(Irish and Bernstein, 1993).***

Previous studies have suggested that activation of C-reb B, K-ras, myc and int-2 oncogenes in malignant head and neck tumors may be important in the development of these cancers ***(Christensen et al., 1992).***

Epidermal growth factor (EGF) is a polypeptide stimulating growth and presumably, differentiation of a variety of mamalian epithelial tissues and cell types. EGF binds to a specific membrane receptor and thereby activates a tyrosine-specific protein kinase which is part of the intracellular domain of the receptor. This in turn leads to a variety of biochemical and physiological events and ultimately to DNA replication and cell division. The EGF receptor is detectable on a large variety of cell types and tissues including the proliferative component of epithelia. A close similarity between the amino acid sequence from the erb-B oncogene and the cytoplasmic and