Role of Epidermal Growth Factor Receptor in Malignant Pleural Mesothelioma and its value for successful chemical pleurodesis

Thesis

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List of Abbreviations

Ab	Antibody
AHNP	anti-p185 $^{her2/neu}$ peptidomimetic
AHNP-SA	anti-p185 $^{her2/neu}$ peptidomimetic - streptavidin
AR	Amphiregulin
ARF	Alternate open reading frame
ATP	Adenosine triphosphate
Bcl-xL	B-cell lymphoma-extra large
BTC	Betacellulin
CALGB	Cancer and Leukemia Group B
CD	Cluster differentiation
CDKN2A	Cyclin-dependent kinase 2A
CF	Cystic fibrosis
CK	Cytokeratin
Cl	Chloride
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
Da	Dalton
DNA	Deoxyribonucleic acid
ECM	Extracellular matrix
ECOG	Eastern Cooperative Oncology Group
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EGFRvIII	epidermal growth factor receptor variant III
EMA	Epithelial Membrane antigen
EMT	Epithelial mesenchymal transition
EORTC	European Organization for Research and Treatment of Cancer
EPP	Extrapleural pneumonectomy
EPR	Epiregulin

Erb	erythroblastosis oncogene B
ERK	Extracellular signal–regulated kinases
Fab	Fragment antigen-binding
FAK	Focal Adhesion Kinase
FDA	U.S. Food and Drug Administration
Grb	Growth factor receptor-bound protein
Gy	Gray unit
HDM	House dust mite
Her	Human Epidermal Growth Factor Receptor
HB-EGF	Heparin-binding EGF-like growth factor
Ig	Immunoglobulin
IL	Interleukin
ILD	Interstitial lung disease
IMIG	International Mesothelioma Interest Group
IPF	Interstitial pulmonary fibrosis
IU	International Unit
Jak 2	Janus kinase 2
Jnk	Jun N-terminal kinases
K^+	Potassium ion
K-Da	Kilo dalton
LDH	Lactate dehydrogenase enzyme
mAb	Monoclonal Antibodies
MAP	Mitogen-activated protein
MAPK	Mitogen activated protein kinase
MIPC	Miliary intrapulmonary carcinomatosis
mm	millimeter
MMP	Matrix metalloproteinase
MPM	Malignant Pleural Mesothelioma
mRNA	Messenger ribonucleic acid
mTor	mammalian target of rapamycin
MUC5AC	Mucin 5AC
NF 2 gene	Neurofibromatosis type 2 gene

NF-KB	nuclear factor kappa-light-chain-enhancer of activated B cells
NRG	Neuregulin
NSCLC	Non small cell lung cancer
OS	overall survival
P-A	Postero-anterior
PAH	Pulmonary arterial hypertension
PCI	potato carboxypeptidase inhibitor
PDGF	Platelet derived growth factor
PI3K	Phospoinositide 3 kinase
PKB	Protein kinase B
PKC	Protein kinase C
PLC	Phospholipase C
PTEN	Phosphatase and tensin homolog
Raf	Rapidly Accelerated Fibrosarcoma.
RAS	Rat sarcoma
Rb	Retinoblastoma
RTKs	Receptor tyrosine kinases
ScFv	Single-chain variable fragment
SMRP	Serum Mesothelin–Related Protein
STAT	Signal transducer and activator of transcription
SV	Simian Virus
Tag	T antigen
TGF	Transforming growth factor
TKI	Tyrosine kinase inhibitor
TNF	Tumour necrosis factor
TRAIL	TNF-related apoptosis-inducing ligand
TS	Thymidilate synthase
TSG	Tumour suppressor gene
VATS	Video assisted thoracoscopic surgery
VEGF	Vascular endothelial growth factor
WBC	White blood cell count

WHO	World Health Organization
wt p53	wild-type p53 gene

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Abstract

Background The most common primary malignant tumor of the pleura is malignant mesothelioma, it is a highly aggressive tumour that has become a very important issue over recent years. Inhalational exposure to asbestos has been clearly established as the predominant cause of malignant mesothelioma in humans. Approximately 70 percent of cases of pleural mesothelioma are associated with documented asbestos exposure. Evidence suggests that the EGFR is involved in the pathogenesis and progression of different carcinoma types. In vivo and in vitro studies have shown that these proteins are able to induce cell transformation.

Aim of work: is to study the role of epidermal growth factor receptor in malignant pleural mesothelioma and to evaluate its value for successful chemical pleurodesis.

Subjects and methods: The study included fifty three cases selected from the Chest department inpatient Kasr El-Aini Hospital. All patients were subjected to full history taking, clinical examination, CT Chest, pleural biopsy, histopathhological examination and immunostainning by EGFR Ab.

Results: There was no statistical significance regarding age, sex smoking in the comparison between the 3 groups of the study population. There was no statistical significance regarding pleural fluid total proteins and LDH but there was statistical significance regarding pleural fluid sugar level between group I and II. There was a statistical significance regarding predominant cell pattern of pleural fluid cytological analysis. There was a statistical significance regarding immunostaining for detection of EGFRs in the pleural biopsy among study groups (100% positive in group I, 73.7% positive in group II and 46.2 % positive in group III). There was no statistical significance regarding the comparison between success rate of chemical pleurodesis and expression of EGFR in immunostaining in malignant groups of pleural effusion.

Conclusion: There is evidence that epidermal growth factor receptor is frequently over-expressed in malignant pleural mesothelioma samples and therefore may be a potential therapeutic target as Targeted EGFR therapy has been successful in non-small cell lung cancer and in colorectal cancer.

Key words:

Malignant Pleural Mesothelioma, Epidermal growth factor receptor Chemical Pleurodesis.

Introduction

The most common primary malignant tumor of the pleura is malignant mesothelioma. It arises from mesothelial surfaces of the pleural and peritoneal cavities, as well as from the tunica vaginalis and pericardium. ***(Sterman et al, 2008)***

Malignant pleural mesothelioma is a highly aggressive tumour that has become a very important issue over recent years. ***(Scherpereel et al, 2010)***.

Epidermal growth factor receptor exists on the cell surface and is activated by binding of its specific ligands, including epidermal growth factor and others. ***(Yarden and Schlessinger, 1987).***The resulting signalling network initiates diverse cellular pathways leading to proliferation, migration, gene transcription, cell cycle progression and cell survival. ***(Prenzel, 2001).***

Evidence suggests that the EGFR is involved in the pathogenesis and progression of different carcinoma types. In vivo and in vitro studies have shown that these proteins are able to induce cell transformation ***(Normanno et al, 2006)***.