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Evaluation of current methods to detect the mutations of epidermal growth factor receptor in non-small cell lung cancer patients

Jasmina Obradovic[1] and Vladimir Jurisic[2*]

Abstract

Many different methods were developed to detect commonly known mutations and to screen new mutations of the epidermal growth factor receptor in non-small cell lung cancer patients. Some of these methods are so sensitive as to be able to detect even one epidermal growth factor receptor mutant tumor cell among up to 1000–2000 normal cells. We have considered current methods chronologically reported to detect mutations in epidermal growth factor receptor in patients with non-small cell lung cancer. We also gave a short preview of their significance for routine clinical works. A Pub Med literature search was performed in order to demonstrate what methods are mostly used in mutation detection and to show their distribution through the last 10 years.

Keywords: EGFR, Methods, Mutations, NSCLC

Review

Introduction

An extensive genetic research has provided a lot of useful information about molecular genetic abnormalities, including chromosomal aberrations, over-expression of oncogenes, and deletions or mutations in tumor suppressor genes. These results have been applied to early detection, classification, and prognosis of NSCLC [1].

Epidermal growth factor receptor (EGFR) is a trans-membrane receptor protein with a ligand-binding extracellular domain, trans-membrane domain, and cytoplasmic tyrosine kinase (TK) domain. EGFR is a member of a family of four tyrosine kinase receptor (RTK) molecules. Several ligands bind with receptor(s) and activate them inducing autophosporilation of TK domain, which is usually affected with mutations. This leads to a series of intracellular signaling pathways, which in turn result in cancer proliferation, reduced apoptosis, invasion, metastasis, and stimulation of tumor-induced angiogenesis [1].

* Correspondence: vdvd@mailcity.com
[2]Faculty of Medicine, University of Kragujevac, Svetozara Markovica 69, 34 000, Kragujevac, Serbia
Full list of author information is available at the end of the article

Non-small cell lung cancer (NSCLC) is the most common cause of cancer-related death in the world [2]. EGFR is over-expressed in several tumor types, including NSCLC, and it was one of the molecules that were recognized as a biomarker for the development of targeted therapies [3,4]. The deletion of the four amino acid sequence (del 746–750) in the exon 19 and the substitution of leucine by arginine at codon 858 (L858R) in exon 21 are two of the most common mutations in the kinase domain of EGFR gene in NSCLC patients [5].

The small-molecule tyrosine kinase inhibitors including gefitinib and erlotinib have recently been approved for the treatment of patients with NSCLC [4,6-9]. In addition, mutations in the epidermal growth factor receptor (EGFR) have been confirmed as predictors of the efficacy of treatment with EGFR-tyrosine kinase inhibitors. The results from several randomized phase III trials have emphasized the importance of molecular testing prior to initiating first-line therapy for advanced NSCLC. Increasing evidence demonstrates that patients with EGFR mutations experience a more significant benefit with gefitinib or erlotinib compared to standard chemotherapy, whereas an opposite effect occurred in patients with EGFR-mutation negative tumors [7-9].

We have considered several methods to detect EGFR mutation reported in literature and come into use in the