B027

EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) GENE MUTATION TESTING FOR INTEGRATED CARE AND TREATMENT OF NON-SMALL CELL LUNG CANCER (NSCLC) PATIENT IN MALAYSIA

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1. INTRODUCTION

The testing for epidermal growth factor receptor (EGFR) mutation particularly in the tyrosine kinase domain is now a common practice worldwide as recommended by the guideline for the management of non-small cell lung cancer (NSCLC)[1,2]. The first generation EGFR tyrosine kinase inhibitor (TKI) drug approved by the FDA can block the signal from EGFR cells that tell the cells to grow. However, different mutation spanning from exon 18-21 of the EGFR gene gives different response to TKI drugs from first to fourth generation[3,4]. Thus, gene information regarding EGFR mutation is rather important after the histological assessment.

2. METHODOLOGY

Lung biopsy and relevant tissue fixed in formalin paraffin embedded were received. Manual specimen preparation were done to obtain genomic DNA using sample preparation kit from Cobas Roche. Real time polymerase chain reaction (RT-PCR) to target DNA using complementary primer pairs and oligonucleotide probes labelled with fluorescent dyes were run using Cobas Roche z480 analyser. Total of 42 mutations in EGFR gene can be detected and analysis of EGFR mutation were done (Figure 1).

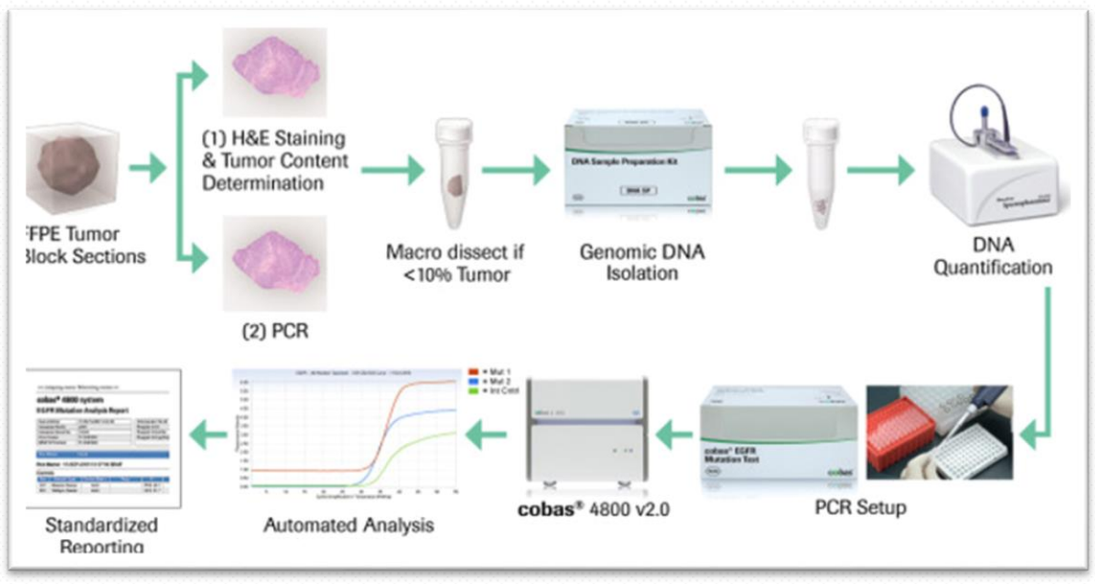

Figure 1 : EGFR mutation methodology using Cobas z480

4. DISCUSSION

Previous study reported the frequency of EGFR mutation is about 30% to 50% and commonly found among Asian female, never or light smoker[2]. With 37% of patients harbouring EGFR mutation positive tested in the our lab, we conclude that Malaysian patient have a high prevalence of EGFR activating mutation similar to that seen in other Asian population. Additionally, close to our finding, the most common activating mutation among Asian ie. exon 19 deletion and L858R can benefit from sensitivity to gefitinib, erlotinib and/or afatinib (1st & 2nd generation TKIs). Meanwhile, resistant mutation in exon 20 specifically T790M will respond to osimertinib (3rd generation TKI)[4].

5. CONCLUSION

Overview of EGFR mutation including different mutation; sensitizing and resistant patient were provided through a fast and reliable testing by the Genetics Laboratory, Women and Children Hospital Kuala Lumpur, Ministry of Health, Malaysia. This database will serve as baseline data by which more oncogenic driver gene testing will be introduced to the Malaysian lung cancer patients in the future.

3. RESULT

This is the first report published by the only lab offering EGFR testing in MOH facilities, a total of 3399 samples received for EGFR mutation testing since March 2014 until May 2019. 60% were female and 40% male patient, most of them were age 51-70 years old (62.2%). Overall, there were 37% patients with positive EGFR mutation meanwhile 58% were negative (Table 1). Exon 19 deletion (n=757, 59%) was the most common mutation type followed by exon 21 (L858R) point mutation (n=355, 28%) and the other type of mutation showed <5% details as shown in Table 2. Furthermore, 48 patients or tumours (4%) were identified having EGFR double mutation either in sensitizing mutation with favourable response to TKI or resistance mutations. List of mutations detected were shown in Table 2. From our collected data, mutations were found more in female compared to male patients (data not shown).

Clinical characteristics	n	%
Age		
10 to 30	32	<1
31 to 50	547	16.1
51 to 70	2116	62.2
71 to 90	702	20.6
91 above	2	<1
Sex		
Female	2047	60
Male	1352	40
Race		
Malay	1669	51
Chinese	1006	31
Indian	93	3
Others	631	19
EGFR mutation status		
No mutation	1968	58
Mutation detected	1273	37
Double mutation	48	4

Table 1 : Clinical characteristic of NSCLC patients received from March 2014 - May 2019 in Genetics Laboratory, WCHKL

Mutation in EGFR TKI domain	Frequency
Exon 18 : G719X	 33 (3%)
Exon 19 deletions	757 (59%)
Exon 20 : S768I **T790M** Insertions	 3 (<1%) 2 (<1%) 54 (4%)
Exon 21 : **L858R** L861Q	 355 (28%) 20 (2%)
Double mutation *drug resistance, *drug sensitive	48 (4%)

Table 2: Mutation type and frequency

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