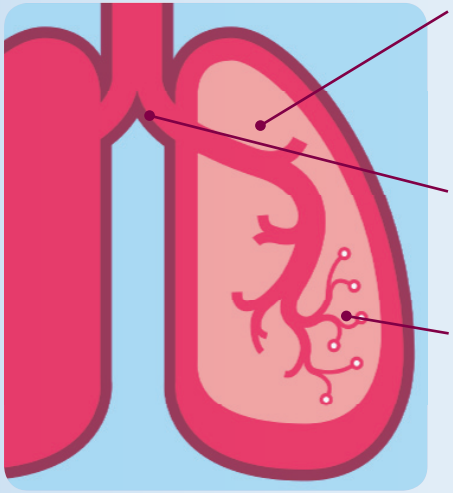
Lung Cancer

Lung cancer is the leading cause of cancer death globally. Each year 1.3 million people die as a result of the disease[1], equating to more than 3,000 deaths worldwide every day[2]. In Europe, lung cancer accounted for an average of 20% of all cancer deaths in 2008[3].

Lung cancer can be broadly divided into two major types, non-small cell lung cancer (NSCLC) and small cell lung cancer. NSCLC is the most prevalent and accounts for approximately 85% of all cases[4]. Early-stage NSCLC does not always have obvious symptoms and so the majority of patients are not diagnosed until the disease is at an advanced stage[4], when the chances for cure or significant clinical benefit are limited.

Some NSCLC tumours have activating mutations in the epidermal growth factor receptor (EGFR) gene, changing the structure of the EGFR proteins such that they have increased activity. EGFR activating mutation-positive (Act MUT+) NSCLC is considered to be a genetically distinct form of lung cancer[5]. Anywhere between 10 and 30% of people with NSCLC have tumours that harbour EGFR activating mutations[6,7].

Types of Non-Small Cell Lung Cancer

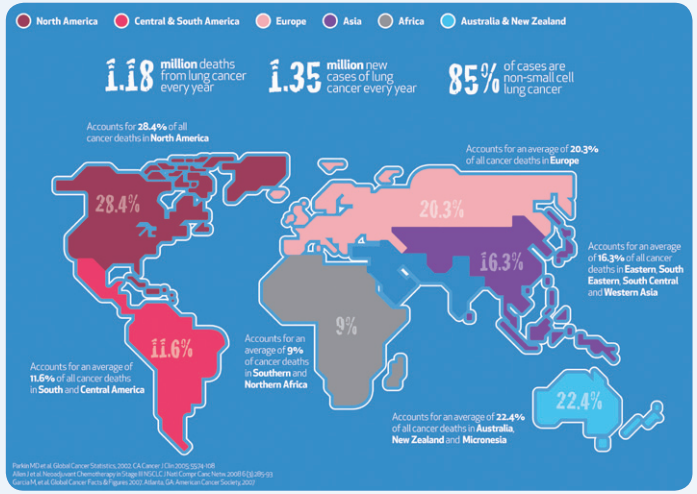


Squamous cell carcinoma
- Develops from cells that line the airways
- Often found near the centre of the lung in one of the main airways (the left or right bronchus)
- Associated with smoking

Large cell carcinoma
- Cells appear large and round when viewed under a microscope
- Tumours tend to be larger than 2.5-4 centimetres

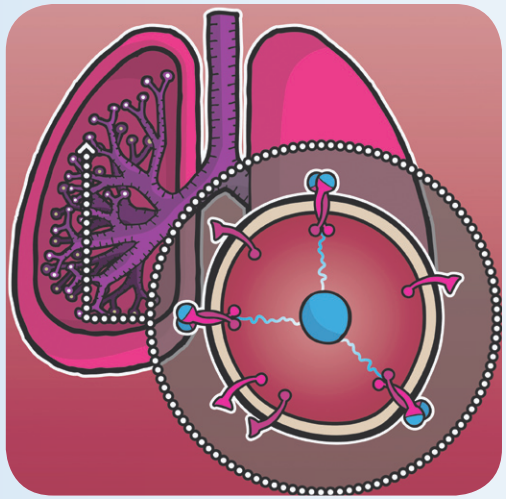
Adenocarcinoma
- Develops from a particular type of cell which produces mucous (phlegm), which lines the airways
- Often found in the periphery (outer areas) of the lungs

Global Lung Cancer Figures



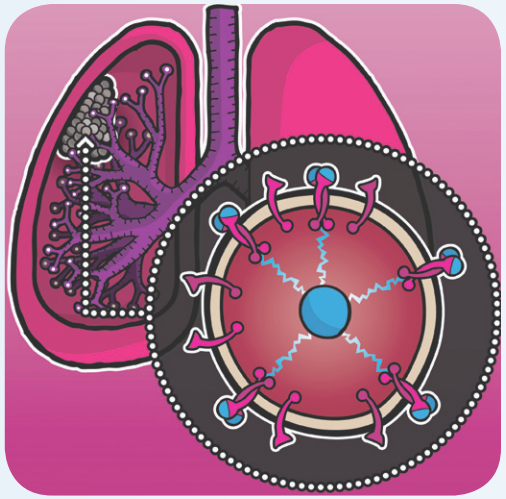
Introduction to EGFR Act MUT+ NSCLC

What is EGFR?
Epidermal Growth Factor Receptor (EGFR) is a protein that sits across the cell membrane to which Epidermal Growth Factor (EGF) binds[8]. When EGF binding happens the tyrosine kinase of the EGFR is activated and triggers a complex signalling cascade in and between cells that is part of normal cell activity, however in lung cancers it can lead to accelerated cell growth and division, development of metastases and angiogenesis[9,10].



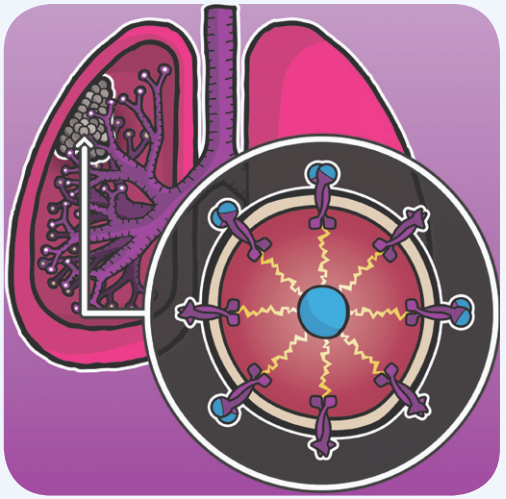
Normal EGFR signalling

- The activity of Epidermal Growth Factor Receptors (EGFRs) forms part of normal cell functioning.



Signalling in lung cancer without EGFR activating mutations

- In most lung cancers, more EGFRs than normal are present leading to enhanced EGFR signalling.
- EGFR signalling is one of several factors that contribute to cancer growth in lung cancer without EGFR activating mutations.



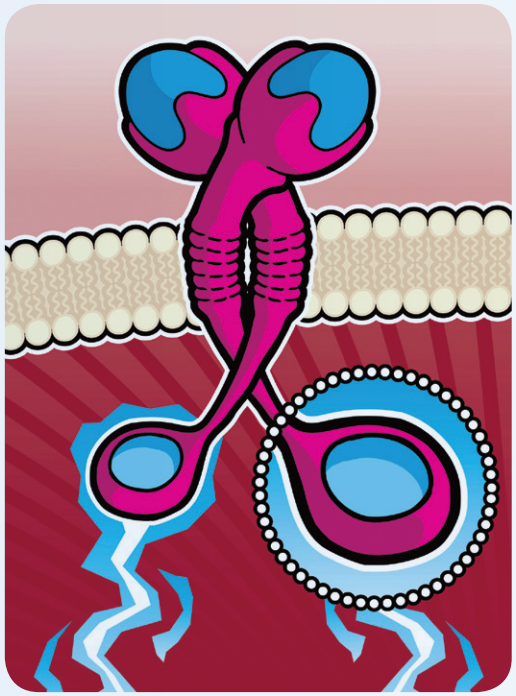
Signalling in EGFR Act MUT+ lung cancer

- In EGFR Act MUT+ lung cancer EGFR signalling is constantly active and is the key driver of tumour growth.
- EGFR Act MUT+ lung cancer is a distinct form of lung cancer.

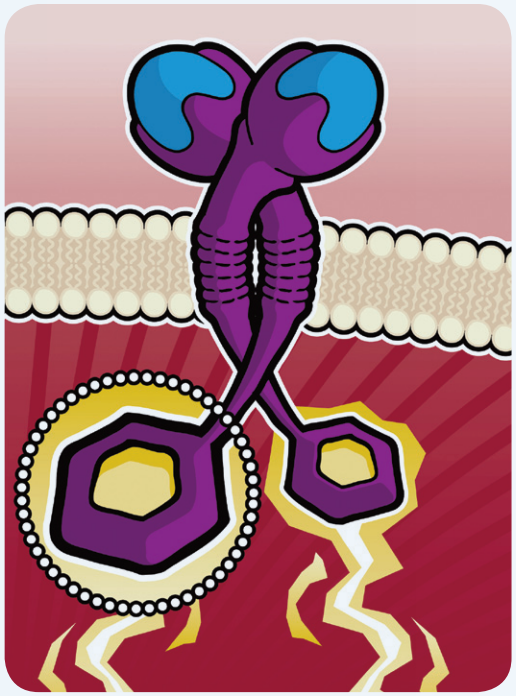
Introduction to EGFR Act MUT+ NSCLC

What is an EGFR activating mutation?
A mutation is a random change to the DNA sequence of a particular gene. Mutations occur as insertions (when one or more new subunits of DNA are inserted into the DNA sequence), deletions (when one or more new subunits are deleted from the DNA sequence) or substitutions/point mutations (when an existing subunit is replaced).

EGFR activating mutations are found in specific areas of DNA in the EGFR gene (exon 19 and exon 21). These mutations lead to changes in the structure and function of the EGFR proteins giving them new or greater activity. As many as one in three (30%) Asian patients with lung cancer and an estimated one in ten (10%) lung cancer patients in the Western population have EGFR activating mutation-positive NSCLC.



EGFR without activating mutations



EGFR with activating mutations

EGFR activating mutations occur in a region of the EGFR called the tyrosine kinase domain. These mutations change the shape of the tyrosine kinase domain and trigger altered signalling inside the cell which can result in uncontrolled cell division and cancer.

References

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