CCOMPUTO : Collaborative Computational Tools for Dutch Molecular Tumor Boards

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Lung cancer is associated with high mortality rates

Lung cancer is responsiblse for over 135,000 deaths annually and can be classified into Small Cell Lung Cancer (SCLC) and Non-Small Lung Cancer (NSCLC) with the latter being diagnosed in 85% of lung cancer patients (1).

NSCLC is often linked with genetic events in kinases

Driver Oncogenic mutations are often found in kinases such as the EGFR, ALK and BRAF. Luckly , these kinases are druggable and pharmaceutical companies introduced various inhibitors in the market (2).

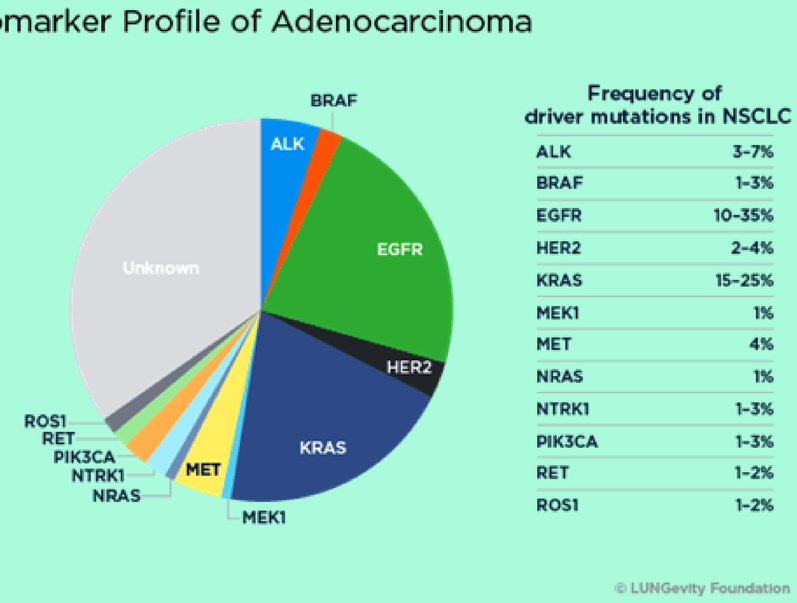

Figure 1. Pie chart representation of muatational biomarkers for NSCLC. Adapted from (3)

Figure 2 . Molecular Tumor Board as from 2018. From right to left : Dr Harry Groen (lung doctor), Dr. Anthoine van wekken (lung doctor), Dr Leon van Kempen (Principal investigator), Dr Maarten Niemantsverdriet (clinical molecular biologist) (4).

Urge for a rapid aproach that is user friendly for the medical staff.

Due to the scarce time to set up the therapeutic approach (around 10 days), Dutch MTBs cannot rely on experimental set up. They often can only review the published literature.

Computational tools have been used sporadically in clinical mutational analysis

Scanning medical and tranbslational medicine journals, one can spot a timid use of 3D-structures to provide insight into a mutation or prediction to treatment. however, data is scarced. Another big concern is the lack of uniformity and reproducibility from this data (6)

Novel mutation are emerging at a fast pace

Despite five approved drugs in the european markets, a porcentage of patients rapidly progress under targeted therapy often presenting mutations not described in the literature. MEdical teams are challenged by the unkown response to available treatment (5).

Molecular Tumor Boards are focused on challenging mutations

Dutch oncology centers are gathering scientists and medical professionals into multidisciplinary boards to discuss challenging cases involving novel NSCL kinase-linked mutations. The so called Molecular Tumor Boards (MTB) (4).

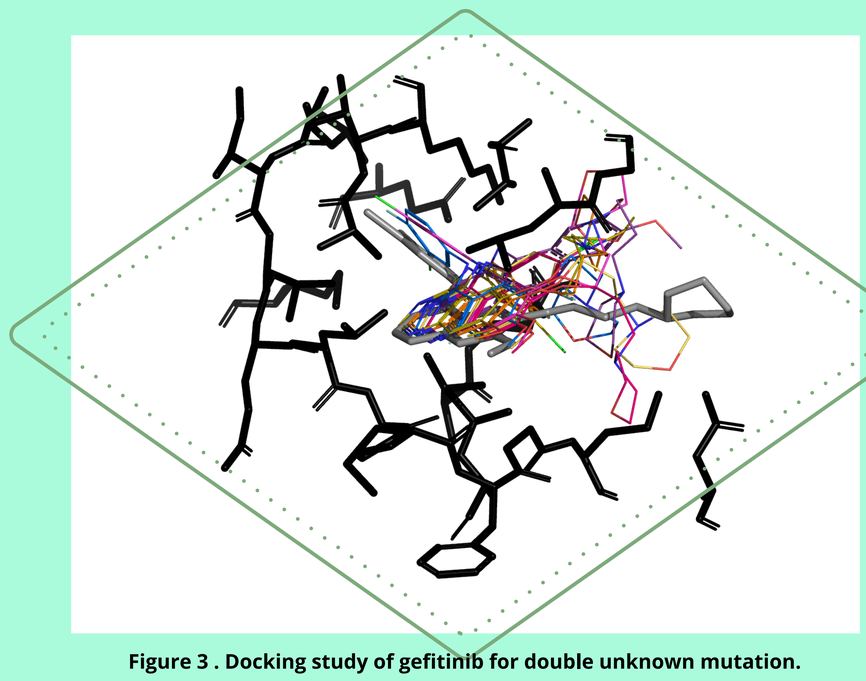

Figure 3 . Docking study of gefitinib for double unknown mutation.

CCOMPUTO has been developed and applied since 2018 at the Molecular Tumor Board (UMCG)

Using reliable ans mostly open source tools, CComputo offers an affordable approach to generate models of unkwon mutations diagnosed in NSCLC. Alterations in EGFR, ALK, and BRAFare currently the main genes for which molecular modeling can be performed in a clin- ical setting. In 2018, modeling was performed for 22 NSCLC cases (20%) in the UMCG-MTB, which led to a targeted therapy recommendation in 18 (including 11 off-label recommendations) and resulted in 11 treated patients (5).

Due to its success , collaborations with other Dutch Medical Centers florished.

Worth to read

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university of groningen

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umcg

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