Peer Review File

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Reviewer Comments

The manuscript entitled "Molecular pathways of kinase fusions and diagnostic approaches for their detection in non-small cell lung carcinomas" focused the attention on the role of gene rearrangements in advanced stage non small cell lung cancer patients.

In particular, careful attention was paid on the different methods (IHC; FISH, NGS, RT-PCR) able to detect gene rearrangements.

Comment 1: The Authors described different methodologies (IHC, RT-PC, NGS, FISH) able to detect gene rearrangements. In order to cover all the main technologies involved in this field, please could the Authors add a paragraph regarding nCounter technology, and its role in gene rearrangements detection?

Response to comment 1:

We agree with reviewer 1 that the nCounter technology is of increased interest. As requested, we added a paragraph about this method in the new version of our manuscript.

Comment 2: The Authors should provide the extensive forms for all the acronyms through the text, including gene acronyms, when they first appear. Please control.

Response to comment 2

We thank reviewer 2 for this comment. We checked for all the acronyms used in the manuscript and wrote them in the extensive form when they appeared first in the manuscript.

Comment 3: Gene acronyms should be written in italics.

Response to comment 3:

We completely agree with reviewer 2 and appreciate this comment. We wrote all gene acronyms in italics, unless they are protein names.

Comment 4: In the paragraph "tyrosine kinase fusions in lung cancer and molecular mechanisms", could the Authors briefly describe the principal clinic-pathological features of advanced stage NSCLC harboring a gene rearrangement?

Response to comment 4

We thank the reviewer for the comment to include more clinic-pathological information. We agree that it is an important aspect and added a paragraph on this topic.

Comment 5: Page 4 line 100 "In ADC or not otherwise specified non-small cell cancer (NSCC, NOS) of the lung,", please modify with "In ADC or not otherwise specified NSCLC (NSCLC, NOS)".

Response to comment 5:

We thank reviewer 1 for this comment. However, NSCC-NOS is the recommended abbreviation for not otherwise specified non-small cell lung cancer according to the 2015 WHO classification of lung tumors (PMID: 26291008). Therefore, we would like to keep this term.

Comment 6: In the paragraph "ROS1" page 5 the Authors should discuss the possibility that despite ROS1 protein is basically absent in normal human lung tissue, its IHC expression may be observed in reactive alveolar type II pneumocytes and macrophages.

Response to comment 6:

We thank for this comment and added the following sentence to our manuscript: 'Although ROS1 protein is basically absent in normal human lung tissue, its IHC expression may be observed in reactive alveolar type II pneumocytes and macrophages.'

Comment 7: Page 7 lines 202 and 227, the Authors should adopt only the acronyms FISH and RT-PCR.

Response to comment 7:

We agree with reviewer 1 and added the acronyms for FISH and RT-PCR.