

# Advances in theranostic biomarkers for lung cancer from clinical to molecular pathology

In 2018, lung cancer is the first cause of death by cancer in the world (1). So, it is mandatory to continue to look for more effective treatments, targeting precisely the biological characteristics of tumors. In this context, the rapid discovery and, then, the use in daily practice of biomarkers of the efficacy of therapy is essential to thoracic oncology (2,3). Currently, the detection of a number of theranostic biomarkers is necessary to administer effective therapy to patients with advanced stage or metastatic lung cancer (4). A minimum of five analyses/tests is required to evaluate the status of PD-L1, ROS1, ALK, BRAF and EGFR in metastatic lung adenocarcinoma patients (4). The increase in the number of therapeutic molecules targeting genomic alterations combined with the accelerated development of molecules of immunotherapy has transformed suddenly the activity of clinical and molecular pathology laboratories. Within this context, the number of immunohistochemical and in situ hybridization analyses as well as molecular analyses has dramatically increased and it is now necessary to coordinate the best practices to obtain all the results at one time, with a good turnaround time (5). Moreover, the analytical methods must be now adapted to liquids (in particular blood), cytological and/or tissue samples. The laboratories are thus faced with several challenges. The first is to master the pre-analytical phase for optimal treatment of the biological samples and to decrease the number of false negative or positive results (5-7). Poor management (inadequate fixation or inappropriate buffers for examples) and an insufficient amount of the samples and long delays in their transfer from the clinical departments to the laboratories can directly influence the quality of the results (5,6). In this regard, the clinician and pathologist need to consider the choice of sample, either blood, cells and/or tissue, according to the clinical situation (8,9). The second challenge involves setting up adequate algorithms for the tests to be performed based in particular on the amount and type of available biological material (tissue micro biopsy, cytological samples, blood and/or other fluids). In some situation it can be difficult to perform from the same sample, all the immunohistochemical analyses for diagnosis, to look for theranostic biomarkers and to extract a minimal quantity of nucleic acids for molecular approaches such as next generation sequencing (10). Depending on the type of technique under consideration, the organization of the care and the proximity of the laboratory must be taken into account (11). The economic impact of investigating the more and more numerous theranostic biomarkers can also influence the strategy of the laboratory by initially looking for a minimal number of biomarkers and adopting targeted methods. Irrespective of the different strategies under consideration, the theranostic tests must be performed in a laboratory that masters perfectly the methods employed using technical platforms accredited according to international norms. The continual development of diagnostic methods, of techniques, of the type (origin) and, in particular, of the volume of the samples sent to the laboratory as well as the different targeted therapy, require laboratories to adapt and innovate by rapidly transferring knowledge from research laboratories to daily practice (3,12).

This special issue gives an update on the most recent advances in the domain of thoracic oncology and discusses in particular the new diagnostic approaches as well as theranostic biomarkers to look for both today and probably in the near future.

## Acknowledgements

The author thanks le cancéropole PACA, le conseil départemental des alpes maritimes et le comité départemental 06 de lutte contre le cancer.

#### References

- 1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
- Ettinger DS, Aisner DL, Wood DE, et al. NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 5.2018. J Natl Compr Canc Netw 2018;16:807-21.
- 3. VanderLaan PA, Rangachari D, Majid A, et al. Tumor biomarker testing in non-small-cell lung cancer: A decade of change. Lung Cancer 2018;116:90-5.

#### Hofman. Predictive biomarkers and lung cancers

- 4. Lindeman NI, Cagle PT, Aisner DL, et al. Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors: Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. J Thorac Oncol 2018;13:323-58.
- 5. VanderLaan PA, Chen Y, DiStasio M, et al. Molecular Testing Turnaround Time in Non-Small-Cell Lung Cancer: Monitoring a Moving Target. Clin Lung Cancer 2018;19:e589-90.
- 6. Engel KB, Moore HM. Effects of preanalytical variables on the detection of proteins by immunohistochemistry in formalinfixed, paraffin-embedded tissue. Arch Pathol Lab Med 2011;135:537-43.
- 7. Ilie M, Hofman P. Pitfalls in lung cancer molecular pathology: how to limit them in routine practice? Curr Med Chem 2012;19:2638-51.
- 8. Ilié M, Hofman P. Pros: Can tissue biopsy be replaced by liquid biopsy? Transl Lung Cancer Res 2016;5:420-3.
- 9. Mino-Kenudson M. Cons: Can liquid biopsy replace tissue biopsy?-the US experience. Transl Lung Cancer Res 2016;5:424-7.
- 10. Hofman V, Lassalle S, Bence C, et al. Any Place for Immunohistochemistry within the Predictive Biomarkers of Treatment in Lung Cancer Patients? Cancers (Basel) 2018;10.
- 11. Sheikine Y, Kuo FC, Lindeman NI. Clinical and Technical Aspects of Genomic Diagnostics for Precision Oncology. J Clin Oncol 2017;35:929-33.
- 12. VanderLaan PA, Rangachari D, Costa DB. Lung cancer with a high tumor mutational burden. N Engl J Med 2018;379:1093.



Paul Hofman

# Paul Hofman<sup>1,2,3</sup>

<sup>1</sup>Université Côte d'Azur; CHU Nice, FHU OncoAge, Laboratory of Clinical and Experimental Pathology, Pasteur Hospital, Nice, France; <sup>2</sup>Université Côte d'Azur; CNRS, INSERM, IRCAN, FHU OncoAge, Team 4, Nice, France; <sup>3</sup>Université Côte d'Azur; CHU Nice, FHU OncoAge, Hospital-Integrated Biobank (BB-0033-00025), Nice, France. (Email: hofman.p@chu-nice.fr) doi: 10.21037/jtd.2018.10.28 Conflicts of Interest: P Hofman declares receiving honoraria from pharmaceutical (Astrazeneca, Roche, Novartis, Bristol Myers Squibb, MSD) and biotechnology (Qiagen, Biocartis, Thermofisher) companies for attendance at advisory board meetings. **View this article at:** http://dx.doi.org/10.21037/jtd.2018.10.28

**Cite this article as:** Hofman P. Advances in theranostic biomarkers for lung cancer from clinical to molecular pathology. J Thorac Dis 2019;11(Suppl 1):S1-S2. doi: 10.21037/jtd.2018.10.28

© Journal of Thoracic Disease. All rights reserved.

### S2