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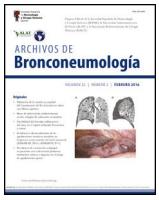

Editorial

The use of non-tumor-related liquid biopsy in respiratory medicine☆

Biopsia líquida no tumoral: aplicación en neumología

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The use of biomarkers for the assessment of respiratory diseases is yet another step on the path towards what is known as precision medicine.[1] This approach, in which each patient receives individualized treatment based on the characteristics of their disease, is applicable not only at the time of diagnosis but also during the entire clinical course of the disease. In the field of respiratory diseases, the use of biomarkers is especially helpful for assessing and selecting the best treatment in many diseases, such as bronchial asthma,[2,3] diffuse interstitial lung diseases,[4] and various infectious processes.[5]

To give an example of personalized medicine in pulmonology, various biomarkers in the field of bronchial asthma, such as eosinophil counts in peripheral blood or the measurement of nitric oxide in exhaled air (FeNO), have been associated with underlying biological processes and the future risk of unfavorable outcomes or response to certain treatments.[6] This evidence has led to these biomarkers being included in clinical practice guidelines for the diagnosis and evaluation of patients with bronchial asthma.[7]

For years, biomarkers have been studied in most depth in the analysis of body fluids to assist clinical decision-making in the diagnosis, prognosis, and treatment of certain diseases. The use of biomarkers in pulmonology is logical, given that in a large number of respiratory diseases, it is unfeasible to determine biological processes by analyzing pathological lung tissue.[8]

The concept of liquid biopsy involves taking a body fluid (mainly peripheral blood, but also urine, bronchoalveolar lavage, and other body fluids) and using it to isolate cells from epithelial tissues or other derived material, such as circulating tumor cells (CTC), circulating tumor-derived factors (ctDNA), or cell-free tumor DNA.[9] Liquid biopsy has probably been studied more closely in the field of medical oncology. Currently, the detection of CTCs by liquid biopsy in medical oncology offers an individualized patient-specific molecular study as an alternative to invasive tumor detection procedures.[10] However, it seems logical that in certain circumstances or in diseases which involve the destruction or alteration of tissue by non-tumor-related processes, other cells or substances may also be released[11] that can be detected by liquid biopsy. This has already been demonstrated in the field of liver diseases, where similar results to those observed in tumor diseases are emerging.[12]

In non-tumor-related respiratory diseases, the need to find new biomarkers is guiding lines of basic research in all areas, including interstitial lung disease, bronchial asthma, and chronic obstructive pulmonary disease (COPD),[13–15] driven in part by the low specificity of the biomarkers available to date and the need for more information on the course of respiratory diseases. In this context, the use of biomarkers from liquid biopsy could be a way of obtaining samples of lung parenchyma (without the use of invasive techniques, such as bronchoscopy or lung biopsy), facilitating, moreover, monitoring of the disease through repeated sampling. Furthermore, if we combine this information with data obtained from other techniques such as radiological imaging,[16] we will have taken the first steps towards personalized respiratory medicine.[17]

The first application of liquid biopsy in the field of a non-tumor-related respiratory disease, COPD, has been recently reported.[18] This liquid biopsy technique is based on the positive selection of epithelial cells using antibodies against epithelial markers (cytokeratin), combined with an antibody directed against a specific marker of type II pneumocytes in lung epithelial tissue (cd44v6). This study found that by isolating cell material using liquid biopsy,

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circulating pulmonary cells (CPC) can be identified in the peripheral blood of up to 40% of patients with COPD, and that the isolation of these CPCs is associated with more severe disease, suggesting their role as a highly specific biomarker that is potentially useful in both the diagnosis and prognostic assessment of COPD.

This, of course, is a first step, and more in-depth knowledge will be needed to determine the usefulness of peripheral blood in liquid biopsy and its diagnostic and prognostic applications. It may even be useful for predicting response to different treatments in non-tumor-related lung diseases, especially in those that involve destruction or alteration of the pulmonary parenchyma, such as cystic fibrosis, alpha 1-antitrypsin deficiency, or idiopathic pulmonary fibrosis. We hope that the results of new projects already underway[19] can help determine whether this 21st century technique will be able to respond to the needs of 21st century patients.

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Conflict of interests

Dr Alcázar-Navarrete states that he has received personal funding, grants for research projects, and non-financial assistance in the last 5 years from GSK, Novartis AG, Boehringer Ingelheim, Chiesi, Laboratorios Menarini, and Astra-Zeneca, unrelated to this article. Dr Alcázar-Navarrete has also registered Patent No. P201730724. Dr Romero Palacios states that he has received personal funding, grants for research projects, and non-financial assistance in the last 5 years from GSK, Novartis AG, Boehringer Ingelheim, Chiesi, and Esteve, unrelated to this article. Dr Romero Palacios has also registered Patent No. P201730724.

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