Technical Bulletin

A Novel Pulmo panel of Napsin A, TTF-1, p40 (ΔNp63) and Cytokeratins 5, 6, 5/6, & 7 for more precise differential diagnosis of Lung Cancer

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Lung cancer is the deadliest form of cancer worldwide and is a leading cancer killer for both men and women in the United States. Lung cancer causes 28% of all cancer mortality. During 2012, an estimated 226,160 new cases of lung cancer were expected to be diagnosed, representing 14% of all cancer diagnoses. In 2012, an estimated 160,340 Americans were expected to die from lung cancer.

Immunohistochemistry (IHC) is now considered a valuable adjunct to histo-pathological diagnosis, particularly for poorly differentiated tumors. IHC is often utilized in differential diagnosis of various human cancers and is frequently helpful in the reliable distinction of Lung Adenocarcinomas (LADCs) from Squamous Cell Carcinomas (SqCCs) or different types of large cell carcinomas. Multiplex IHC further facilitates simultaneous testing of two or more analytes thus immensely increasing diagnostic accuracy in differential tumor diagnosis.

Several histotypes of lung cancer exist, including small cell lung cancer. With the advent of new potential diagnostic antibodies, more precise differentiation of subtypes of lung cancer is possible which is vital for targeted therapies. The emergence of new cancer biomarkers viz. Napsin A and p40 in combination with some of the more traditional markers such as TTF-1, CK 5, 6, 5/6 and 7 facilitate increased sensitivity and specificity in the precise identification of LADCs and SqCCs using multiplex IHC.

To date, p63 has been commonly used as an aid in differentiation of LADCs vs SqCCs. Although this marker offers sensitivity approaching 100% for SqCC, its utility is limited because p63 is also expressed in 16% to 65% of all cases of LADC as well as the majority of large cell lymphomas, which can mimic the histomorphological characteristics of Non-Small Cell Lung Carcinoma (NSCLC).

p40 is a relatively new antibody that recognizes ΔNp63 – a p63 isoform suggested to be highly specific for squamous/basal cells. The p40 protein, an N-terminal truncated form of p63 protein (ΔNp63), seems to be more firmly associated with SqCCs than p63. p40 staining is equivalent to p63 in sensitivity for SqCC but shows a considerably higher specificity.

Napsin A is a pepsin-like aspartic proteinase which plays a vital role in the maturation of pulmonary surfactant proteins. It is commonly expressed in type II pneumocytes and adenocarcinomas of the lung and kidney. TTF-1 is a nuclear protein originally identified in thyroid epithelial cells, a known mediator of thyroid specific gene transcription and activator of the transcription of thyroglobulin and thyroperoxidase. Its role has also been shown in the developing fetal lung, where it is localized to the nuclei of developing airways. TTF-1 is selectively expressed by type II alveolar epithelial cells and a subset of bronchiolar epithelial cells in the mature lung.

Napsin A has been demonstrated to be a more sensitive and specific marker of adenocarcinoma than TTF-1, with 74% to 87% sensitivity and probable 100% specificity. Expression of TTF-1 is retained in thyroid carcinomas (80%) and in up to 75% of pulmonary adenocarcinomas, but is not expressed in adenocarcinomas from other sites. In addition to the expression of TTF-1 in LADC, TTF-1 is also expressed in small cell carcinoma of the lung, which may mimic the histomorphological characteristics of NSCLC when poorly differentiated. Although the sensitivity and specificity of different clones of Napsin A and TTF-1 can affect the accurate diagnosis, TTF-1 and Napsin A are a dynamic pair that can help in differential diagnosis of lung cancer.
Cytokeratins 5, 6, and 5/6 (CK 5, 6, 5/6) are also very useful antibodies in diagnostic pathology. These antibodies characteristically stain SqCCs strongly, but generally stain adenocarcinomas focally, weakly, or not at all. As such, CK 5, 6, and 5/6 antibodies can be used as markers of squamous differentiation when trying to assess the nature of poorly differentiated carcinomas. A cocktail of TTF-1 and CK 5 can increase sensitivity and diagnostic utility in differential diagnosis of the tumor. Cytokeratin 7 (CK 7) expression is restricted to most glandular and transitional epithelia of lung, breast, urinary bladder and female genital tract and their adenocarcinoma. CK 7 is typically not observed in gastrointestinal epithelium, prostate, hepatocyte and squamous epithelium.

Napsin A and p40 (ΔNp63) are excellent emerging markers for lung carcinomas that when used in combination with more traditional markers such as TTF-1, CK 5, 6, 5/6 and 7, may help achieve a more precise differential diagnosis.

References:

Products

Continuing with our firm belief that high quality reagents can be produced and delivered at reasonable pricing. ScyTek Laboratories offers the following panel of markers for Lung Cancer. Each item is available in both Ready-To-Use and Concentrated format. All have undergone extensive in-house validation to provide consistent, high intensity results with virtually no lot-to-lot variability.

<table>
<thead>
<tr>
<th>Catalog Number</th>
<th>Description</th>
<th>Clone(s)</th>
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<tbody>
<tr>
<td>A00112</td>
<td>p40 (ΔNp63)</td>
<td>Polyclonal</td>
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<td>A00139</td>
<td>Cytokeratin 5</td>
<td>EP42</td>
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<td>Cytokeratin 6</td>
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<td>TTF-1</td>
<td>8G7G3/1</td>
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<tr>
<td>A00145</td>
<td>TTF-1 &amp; Cytokeratin 5 Cocktail</td>
<td>8G7G3/1 &amp; EP42</td>
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</tbody>
</table>
Product Reference Images

Antibody A00112
p40 (ΔNp63); Polyclonal
Rabbit Polyclonal
Human Lung Squamous Cell Carcinoma
(Original Magnification x200)

Antibody A00139
Cytokeratin 5; Clone EP42
Rabbit Monoclonal
Human Lung Squamous Cell Carcinoma
(x200)

Antibody A00140
Cytokeratin 6; Clone EP67
Rabbit Monoclonal
Human Lung Squamous Cell Carcinoma
(x200)

Antibody A00141
Cytokeratin 5/6 Cocktail; Clones EP42 & EP67
Rabbit Monoclonal Cocktail
Human Lung Squamous Cell Carcinoma
(x200)
Antibody A00142
Cytokeratin 7; Clone OV-TL12/30
Mouse Monoclonal
Human Lung Squamous Cell Carcinoma
(x200)

Antibody A00143
Napsin A; Clone EP205
Rabbit Monoclonal
Human Lung Adenocarcinoma
(x200)

Antibody A00144
TTF-1; Clone 8G7G3/1
Mouse Monoclonal
Human Lung Adenocarcinoma
(x400)

Antibody A00145
TTF-1 & Cytokeratin 5 Multiplex Cocktail; Clones 8G7G3/1 & EP42
Rabbit & Mouse Monoclonal Cocktail
Human Lung Squamous Cell Carcinoma
(x400)

All antibodies visualized using ScyTek’s UltraTek reagents and counterstained with hematoxylin