



# Molecular Subtypes of Lymphoma: Diagnostic Approaches and Implications

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identify these subtypes, including histopathology, immunohistochemistry, cytogenetics, molecular genetics, next-generation sequencing (NGS), and prognostication are also discussed. By integrating molecular and traditional diagnostic methods, clinicians can

## Keywords:

## Introduction

Lymphoma is a group of hematologic malignancies characterized by the proliferation of lymphocytes. The disease is classified into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL is further divided into B-cell and T-cell lymphomas. The most common B-cell lymphomas are diffuse large B-cell lymphoma (DLBCL) and follicle lymphoma (FL). DLBCL is the most common type of NHL, accounting for approximately 30% of all lymphomas. FL is the most common type of indolent NHL, accounting for approximately 25% of all lymphomas. The pathogenesis of lymphoma is complex and involves a combination of genetic and environmental factors. The identification of molecular subtypes of lymphoma is crucial for accurate diagnosis and prognostication. This review discusses the molecular subtypes of lymphoma and the diagnostic approaches used to identify them.

### Mantle cell lymphoma (MCL):

Mantle cell lymphoma (MCL) is a type of B-cell lymphoma that typically presents as a localized disease. It is characterized by the presence of a t(11;14) translocation, which results in the overexpression of the cyclin D1 gene. MCL is often diagnosed in the advanced stages of the disease, and it has a poor prognosis. The median overall survival is approximately 5 years. The diagnosis of MCL is based on histopathology, immunohistochemistry, and cytogenetics. The presence of the t(11;14) translocation is a key diagnostic feature of MCL.

### Chronic lymphocytic leukemia (CLL):

Chronic lymphocytic leukemia (CLL) is a type of B-cell lymphoma that is characterized by the presence of a large number of lymphocytes in the peripheral blood. It is a chronic disease that typically progresses slowly. The pathogenesis of CLL is complex and involves a combination of genetic and environmental factors. The identification of molecular subtypes of CLL is crucial for accurate diagnosis and prognostication. This review discusses the molecular subtypes of CLL and the diagnostic approaches used to identify them.

### Primary mediastinal large b-cell lymphoma (PMBL):

Primary mediastinal large b-cell lymphoma (PMBL) is a type of B-cell lymphoma that is characterized by the presence of large B-cells in the mediastinum. It is a rare disease that typically presents as a localized disease. The pathogenesis of PMBL is complex and involves a combination of genetic and environmental factors. The identification of molecular subtypes of PMBL is crucial for accurate diagnosis and prognostication. This review discusses the molecular subtypes of PMBL and the diagnostic approaches used to identify them.

## Diagnostic approaches

### Histopathology:

Histopathology is the study of the microscopic changes in tissues. It is a key diagnostic approach for lymphoma. The identification of the characteristic morphology of the lymphoma cells is crucial for accurate diagnosis. Histopathology is often used in conjunction with other diagnostic approaches, such as immunohistochemistry and cytogenetics.

### Immunohistochemistry (IHC):

Immunohistochemistry (IHC) is a technique used to detect the presence of specific proteins in tissues. It is a key diagnostic approach for lymphoma. The identification of the characteristic immunophenotype of the lymphoma cells is crucial for accurate diagnosis. IHC is often used in conjunction with other diagnostic approaches, such as histopathology and cytogenetics.

### Cytogenetics:

Cytogenetics is the study of the chromosomes. It is a key diagnostic approach for lymphoma. The identification of the characteristic chromosomal abnormalities of the lymphoma cells is crucial for accurate diagnosis. Cytogenetics is often used in conjunction with other diagnostic approaches, such as histopathology and immunohistochemistry.

### Molecular genetics:

Molecular genetics is the study of the genes. It is a key diagnostic approach for lymphoma. The identification of the characteristic genetic mutations of the lymphoma cells is crucial for accurate diagnosis. Molecular genetics is often used in conjunction with other diagnostic approaches, such as histopathology, immunohistochemistry, and cytogenetics.

### Next-generation sequencing (NGS):

Next-generation sequencing (NGS) is a high-throughput sequencing technology. It is a key diagnostic approach for lymphoma. The identification of the characteristic genetic mutations of the lymphoma cells is crucial for accurate diagnosis. NGS is often used in conjunction with other diagnostic approaches, such as histopathology, immunohistochemistry, and cytogenetics.

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**Flow cytometry:**

Flow cytometry is a powerful tool for identifying and characterizing lymphoma subtypes. It allows for the simultaneous analysis of multiple parameters, such as cell surface markers and intracellular proteins, on individual cells. This technique is particularly useful for distinguishing between different types of lymphoma and for identifying specific subgroups within a population of cells.

**Implications for treatment and prognosis**

The identification of molecular subtypes of lymphoma has significant implications for both treatment and prognosis. Different subtypes may respond differently to various therapeutic approaches, and the presence of certain molecular markers can be associated with specific clinical outcomes.

**Treatment tailoring:**

Treatment tailoring involves customizing therapy based on the molecular characteristics of a patient's lymphoma. This approach aims to improve response rates and reduce side effects by targeting specific molecular pathways or markers. For example, the use of targeted therapies like monoclonal antibodies or small molecule inhibitors is often guided by the presence of specific genetic alterations.

**Prognostic indicators:**

Prognostic indicators are molecular markers that provide information about the likely course of a disease and the patient's overall survival. In lymphoma, certain genetic alterations, such as chromosomal translocations or mutations in specific genes, are known to be associated with either favorable or unfavorable prognoses. These indicators help clinicians in risk stratification and in selecting the most appropriate treatment strategy.

**Monitoring and follow-up:**

Monitoring and follow-up are essential components of lymphoma management. Regular clinical and laboratory assessments, including imaging and flow cytometry, are used to evaluate treatment response and detect any relapse or progression of the disease. Molecular markers can also be used for monitoring, as changes in their levels over time may indicate disease activity.

**Discussion**

The identification of molecular subtypes of lymphoma represents a significant advancement in the field of oncology. It provides a more precise understanding of the disease's biology and opens up new avenues for targeted therapy. However, several challenges remain, including the need for larger clinical trials to validate the prognostic and therapeutic implications of these subtypes.

One of the key challenges is the heterogeneity of lymphoma, which can lead to complex interactions between different molecular markers. Additionally, the development of resistance to targeted therapies is a common occurrence, necessitating the discovery of novel therapeutic targets and combination strategies. The integration of molecular data with clinical information is crucial for optimizing patient care and improving long-term outcomes.

Future research should focus on refining the diagnostic and prognostic utility of molecular markers and exploring the potential of personalized medicine in lymphoma. Collaborative efforts between basic scientists, clinicians, and regulatory agencies are essential to accelerate the translation of these findings into clinical practice. The ultimate goal is to provide each patient with the most effective and least toxic treatment based on their unique molecular profile.

In conclusion, the identification of molecular subtypes of lymphoma is a promising area of research that holds the potential to revolutionize the way we diagnose and treat these diseases. Continued investment in research and clinical trials is needed to fully realize the benefits of this approach for patients.

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