



DIAGNOSTICS BY CANCER TYPE

Lymphomas

Diagnostic pathway: specimen, morphology, IHC, FISH and molecular testing

FOR PATIENTS

A clear guide to confirming the diagnosis and selecting a test.

FOR CLINICIANS

Specimen, testing sequence and key clinical questions.

Core principle

First establish the morphologic diagnosis. Additional IHC, FISH/ISH, PCR and NGS are selected according to tumor type, stage, available specimen and a defined clinical question. No single test replaces the entire diagnostic pathway.

Educational material. It does not establish a diagnosis, prescribe treatment or replace decisions by an oncologist, hematologist, pathologist or molecular tumor board.

Lymphomas

Lymphomas are neoplasms of the lymphoid system. Accurate classification generally combines morphology, immunophenotype, flow cytometry and genetic testing.

Why morphology comes first

CT, MRI, PET/CT and ultrasound define location and extent, but in most solid tumors the final type is established from cells and tissue. The pathologist evaluates architecture, cytology, invasion and grade, then selects ancillary studies. Broad molecular testing should not precede an adequate morphologic diagnosis.

Diagnostic pathway

1. Obtain specimen	Prefer excisional/incisional node biopsy; fresh tissue for flow cytometry plus FFPE; core biopsy when excision is not feasible
2. Morphologic confirmation	Architecture and cytology distinguish Hodgkin and diverse non-Hodgkin entities
3. Refining biomarkers	Lineage and classification panel such as CD20/PAX5, CD3, CD30, ALK, BCL2, BCL6, MYC and Ki-67
4. Molecular stage	FISH for MYC/BCL2/BCL6 or entity-specific rearrangements; clonality and targeted DNA/RNA NGS in selected cases

IHC and special methods

IHC detects proteins in tumor cells. It can establish lineage, distinguish morphologic mimics, refine subtype and determine selected predictive biomarkers. The panel should follow a morphologic hypothesis: indiscriminate large panels consume tissue and can complicate interpretation.

2. Morphologic confirmation

Architecture and cytology distinguish Hodgkin and diverse non-Hodgkin entities

What immunohistochemistry adds

Lineage and classification panel such as CD20/PAX5, CD3, CD30, ALK, BCL2, BCL6, MYC and Ki-67

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Molecular testing

Molecular testing

FISH for MYC/BCL2/BCL6 or entity-specific rearrangements; clonality and targeted DNA/RNA NGS in selected cases

When FISH / ISH is useful

FISH/ISH is used to confirm a defined amplification, deletion or rearrangement. It is not a universal substitute for NGS; it is particularly useful when a specific diagnostic or predictive target is known.

What NGS can provide

NGS can interrogate many genes simultaneously and, depending on assay design, detect SNVs, small insertions/deletions, copy-number changes and gene fusions. Panel value depends on relevance to the tumor, specimen and clinical question rather than gene count alone.

Somatic and germline alterations are different

Somatic alterations arise in the tumor during life. Germline variants are present from birth and may matter to relatives. Tumor NGS may reveal a variant suspicious for hereditary risk, but confirmation requires a dedicated germline assay on an appropriate specimen with genetic counseling.

Most testing is somatic; germline predisposition assessment is reserved for selected patients

How to select a test

Diagnosis is not yet confirmed	Start with morphology: histology, cytology, or blood/bone marrow examination depending on the disease.
Origin or subtype needs clarification	The pathologist selects a focused IHC panel. A large marker set should not be ordered without a morphologic hypothesis.
The result may alter treatment	Discuss a validated single-gene assay, FISH/ISH or an appropriate NGS panel. Selection depends on current clinical guidelines.
Young age or relevant family history	Consider genetic counseling and germline testing. A blood germline test is not the same as tumor profiling.

How to select an NGS panel

- Define the clinical question first: diagnosis, prognosis, biomarker selection or resistance.
- Confirm morphologic type and stage; one panel does not fit every tumor.
- Check which variant classes are required: SNV/indel, CNV, fusion and others.
- Assess tumor content and specimen quality; prioritize tests before tissue is exhausted.
- A broad panel is most useful when its result can change further evaluation or treatment discussion.

Required specimen

Required specimen

Prefer excisional/incisional node biopsy; fresh tissue for flow cytometry plus FFPE; core biopsy when excision is not feasible

Why specimen quality matters

Fixation, decalcification, tumor-cell percentage, necrosis and tissue amount directly affect IHC and molecular assays. Before NGS, a pathologist selects the best block and assesses tumor content. RNA/fusion assays are particularly sensitive to nucleic-acid preservation.

When tissue is limited

Do not simply run every test in sequence. The laboratory and clinician should prioritize morphologic confirmation and mandatory biomarkers before broader profiling. In some cases, a repeat biopsy is more informative than multiple unreliable tests from an exhausted block.

- Pathology report and all previous test results
- Paraffin block and stained/unstained slides, or another agreed specimen
- Clinical diagnosis, site, stage and previous therapy

FOR CLINICIANS

Questions the clinician should include on the referral

- Which diagnosis or tumor origin needs confirmation?
- What are the stage, primary site and biopsy site?
- What treatment has already been given and is there progression or recurrence?
- Which IHC, FISH, PCR or NGS studies have already been performed?
- Which result could potentially change the next clinical decision?

FOR PATIENTS

Useful points for patients

- Do not order the “largest panel” without discussion with your clinician and laboratory.
- Keep copies of pathology and molecular reports.
- Know where the paraffin block is stored and whether it contains sufficient tumor.
- A tumor test and a hereditary germline test are different studies.
- Biomarkers are interpreted together with stage, patient status and previous treatment.

Core principle

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Tests to discuss with the treating clinician

These are CELL DIGITAL LABORATORY catalog options relevant to this disease pathway. They are not automatic orders: final selection depends on morphology, stage, prior therapy, specimen and the defined clinical question.

I0097	IHC Extended Panel Comprehensive diagnostic IHC with an extended antibody selection to verify the histologic diagnosis and determine tumor histogenesis when indicated. It does not imply that every antibody is required for every patient.
F0228	High-grade lymphoma FISH panel Targeted FISH to confirm a specific amplification/rearrangement in the appropriate morphologic setting.
F0227	MYC rearrangement FISH - paraffin Targeted FISH to confirm a specific amplification/rearrangement in the appropriate morphologic setting.
F0030	BCL2 rearrangement FISH - paraffin Targeted FISH to confirm a specific amplification/rearrangement in the appropriate morphologic setting.
F0031	BCL6 rearrangement FISH - paraffin Targeted FISH to confirm a specific amplification/rearrangement in the appropriate morphologic setting.
F0029 / F0224	CCND1(BCL1)::IGH t(11;14) FISH Targeted FISH to confirm a specific amplification/rearrangement in the appropriate morphologic setting.

How to select PD-L1

CELL DIGITAL offers 22C3, 28-8, SP142 and SP263. The clone must be stated on the request because internal codes I0032 and P0151 each cover more than one clone option. Assay, scoring system (TPS/CPS/TC/IC) and cut-off must match the intended drug, tumor type, treatment line and current local labeling. Clones/scoring systems are not automatically interchangeable.

Important: NGS008 and NGS009 do not mean every patient needs 161 or 546 genes. Use a broad panel when it can answer a defined clinical question.

Before contacting the laboratory

- Pathology report and all previous test results
- Paraffin block and stained/unstained slides, or another agreed specimen
- Clinical diagnosis, site, stage and previous therapy
- A defined question: establish origin, determine a biomarker or select a molecular panel

Core principle

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Key sources

- National Cancer Institute: <https://www.cancer.gov/types/lymphoma>
- NCI, Biomarker Testing for Cancer Treatment: <https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment>
- College of American Pathologists, Current Cancer Protocols: <https://www.cap.org/protocols-and-guidelines/cancer-protocols/current-cancer-protocols/>
- ASCO Guidelines: <https://www.asco.org/guidelines>
- ASCO/CAP, MMR/MSI Testing Guideline Endorsement: <https://ascopubs.org/doi/10.1200/JCO.22.02462>
- FDA, Cleared or Approved Companion Diagnostic Devices: <https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools>
- WHO Classification of Tumours: <https://tumourclassification.iarc.who.int/>

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