



DIAGNOSTICS BY CANCER TYPE

Liver cancer

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.

Liver cancer

Primary liver tumors must be distinguished from metastases. Diagnosis integrates clinical data, imaging and morphology when biopsy is indicated.

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	Core biopsy or resection FFPE; ensure non-necrotic tumor and paired clinical/imaging context
2. Morphologic confirmation	Hepatocellular carcinoma, cholangiocarcinoma or metastasis
3. Refining biomarkers	Arginase-1, HepPar-1, glypican-3; CK7/CK19 and site-specific markers as indicated
4. Molecular stage	Selected advanced cases: FGFR2/IDH1 for intrahepatic cholangiocarcinoma; NTRK, MSI and broad NGS; HCC profiling is selective

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

Hepatocellular carcinoma, cholangiocarcinoma or metastasis

What immunohistochemistry adds

Arginase-1, HepPar-1, glypican-3; CK7/CK19 and site-specific markers as indicated

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Molecular testing

Molecular testing

Selected advanced cases: FGFR2/IDH1 for intrahepatic cholangiocarcinoma; NTRK, MSI and broad NGS; HCC profiling is selective

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.

Germline testing is not routine for HCC; consider according to syndrome or family history

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

Core biopsy or resection FFPE; ensure non-necrotic tumor and paired clinical/imaging context

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.
NGS008	161-gene OCAV3 Broad molecular profiling when results may alter downstream clinical management.
NGS009 I0032	546-gene OCA Plus + MSI/TMB/HRR + PD-L1 Most comprehensive profiling for a justified clinical question; not mandatory for every patient.
NGS010	Oncomine Tumor Mutation Load (TMB) Tumor mutational burden for selected indications; TMB does not replace other required biomarkers.

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/liver>
- 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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