

Tissue-Tek Genie®

anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098]

REF 8364-C010

Instructions for use

For *in vitro* diagnostic use.

Intended purpose

Intended use: The Tissue-Tek Genie® anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] is designed to qualitatively detect Cadherin 17 protein in formalin-fixed, paraffin-embedded (FFPE) human tissue specimen sections by immunohistochemistry (IHC) staining on the automated Tissue-Tek Genie® Advanced Staining System.

This device functions as an aid for diagnosis and shall be used by a qualified pathologist with a panel of other antibodies to identify colorectal, gastric, and pancreatic carcinoma.

Limitations

The Tissue-Tek Genie® anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] has been optimized for use with the Tissue-Tek Genie® Advanced Staining System, Tissue-Tek Genie® reagents, and FFPE specimen sections. Staining quality may be diminished when used with other systems and/or reagents.

The clinical interpretation must be made in conjunction with histological examination, relevant clinical information, a panel of other antibodies, other diagnostic tests, and proper controls by a qualified pathologist.

Staining quality may be diminished by improper or incomplete removal of the paraffin.

The sensitivity of this antibody to identify the Cadherin 17 protein may be affected by improper specimen handling. This may alter antigenicity, weaken detection, and may generate false negative results.

Special processing of tissues such as decalcification of bone marrow tissues may lead to inconsistent staining.

Positively charged slides are recommended to obtain optimal staining with the Tissue-Tek Genie Advanced Staining System.

Dot-like nucleolar positivity may be seen in testicular germ cells, but it is not regarded as a positive result.

Summary and principle

Immunohistochemistry (IHC) staining is an established *in vitro* diagnostic method to visualize the presence of specific proteins expressed within a tissue section to study the microscopic features.

IHC staining is accomplished in two steps:

1) a primary antibody recognizes a particular target protein expressed on a specific cell compartment of a specific cell type on various tissues, and

2) a secondary and tertiary antibody conjugated to a chromogenic enzyme bind with the primary antibody for the detection of the antibody-antigen interaction. In chromogenic detection under a light microscope, an enzyme conjugated to the antibody cleaves a substrate to produce a colored precipitate at the location of the protein.

Cadherin 17 (CDH17), also known as liver-intestinal cadherin (LI-cadherin), is a transmembrane glycoprotein involved in cell adhesion.¹⁻³ CDH17 is expressed in normal intestinal epithelium (e.g., colon including appendix and small intestine).^{1,2,4} It is also expressed in pancreatic excretory ducts and is occasionally observed focally in gallbladder epithelium and intrahepatic bile ducts.² In addition, CDH17 expression can be seen in rare inflammatory cells within or near epithelial cell layers (e.g., tonsillar epithelium).² CDH17 is not expressed in liver hepatocytes.^{1,2,4} CDH17 is also not expressed in other normal tissues, including lung, breast, kidney, stomach, placenta, thymus, adrenal gland, prostate, skeletal muscle, heart, cerebrum, cerebellum, testis, and salivary gland.^{1,2}

In recent studies, CDH17 has been used to identify carcinomas of colorectal, gastric, and pancreatic origin.^{1,2,4,5} CDH17 is detected in 96-100% of colorectal carcinomas, 43-90% of gastric carcinomas, and 39-82% of pancreatic ductal carcinomas.^{1,2,4-6} CDH17 has shown superior sensitivity when compared to CDX2 or CK20 in detecting colorectal, gastric, and pancreatic carcinomas.^{4,5,7} Similarly, studies have shown that CDH17 expression is present in

neuroendocrine neoplasms, with increased immunoreactivity from upper to lower gastrointestinal tract.⁸ Cadherin 17 expression is absent in 100% of breast carcinomas^{1,2,4,5}, 90-100% of prostate carcinomas^{1,2,4,5}, and 99-100% of urothelial carcinomas^{2,4,5}.

Anti-Cadherin 17 antibody labels Cadherin 17 protein in both normal and neoplastic cells and has a predominantly membranous staining pattern.

The Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] is a primary antibody against the human Cadherin 17 protein and is provided in buffered saline containing 1% bovine serum albumin and 0.09% sodium azide. FFPE specimen sections are placed on positively charged slides and the paraffin is removed using the Tissue-Tek Genie® Dewax Solution (REF 8865-G001), after which heat-induced epitope retrieval is performed using the Tissue-Tek Genie® High pH Antigen Retrieval Solution (REF 8744-G001).

IHC demonstration of Cadherin 17 protein in FFPE specimen sections is achieved through the use of the Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] and the Tissue-Tek Genie® PRO Detection Kit, DAB (REF 8826-K250). This procedure entails the sequential application of antibody and kit components as follows:

- Tissue-Tek Genie® Protein Block
- Tissue-Tek Genie® anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098]
- Tissue-Tek Genie® Peroxidase Block
- Tissue-Tek Genie® Link (binds to the primary antibody)
- Tissue-Tek Genie® Poly HRP-Conjugate (binds to the Link)
- Tissue-Tek Genie® DAB (visualizes the detected protein)
- Tissue-Tek Genie® DAB Intensifier

Tissue-Tek Genie® Hematoxylin (REF 8830-M250) is then used to visualize the nuclei of cells. The IHC stained slide is coverslipped and reviewed using a light microscope.

Expected results

Cellular staining pattern: predominantly membranous

Positive control tissue: appendix, pancreas, or colorectal carcinoma

The specificity and intended use of this antibody were validated by performing IHC staining on the Tissue-Tek Genie Advanced Staining System using normal and neoplastic FFPE tissue sections as follows.

Analytical sensitivity/specificity: A total of 33 types and 119 specimens of normal FFPE tissues were tested. Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] exhibited moderate to strong membranous staining of columnar epithelial cells in appendix/colon (11/11) and small intestine (3/3). In pancreas, at least moderate membranous staining in excretory ducts was observed (12/12). Positive CDH17 staining was also observed in inflammatory cells adjacent to epithelial layers in tonsil (3/8) and rare positivity in lymphocytes of spleen (1/2). In liver, rare to focal

membranous positivity was observed in biliary ductal cells (2/6) but all hepatocytes were negative for CDH17 (0/6). CDH17 was also not observed in other normal tissues (0/77), including lung (0/4), breast (0/3), kidney (0/7), stomach (0/5), placenta (0/4), thymus (0/1), adrenal gland (0/5), prostate (0/9), skeletal muscle (0/3), heart (0/1), cerebrum (0/4), cerebellum (0/1), testis (0/5), and salivary gland (0/1).

Precision studies for Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] lots were completed. FFPE tissue sections of appendix or colon were used. Studies were conducted to demonstrate reproducibility in lot-to-lot (minimum of 2 lots), run-to-run (minimum of 2 Genie runs), instrument-to-instrument (2 Genies), station-to-station (minimum of 2 stations), and operator-to-operator (2 operators). The results were compared and met their acceptance criteria: In appendix or colon, moderate to strong membranous staining of columnar epithelial cells; no staining in other cell types.

These results demonstrate precision of the Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098], which was consistent across lots, runs, instruments, stations, and operators. Precision studies for reproducibility in lot-to-lot (a minimum of 2 lots) will be conducted.

Diagnostic sensitivity/specificity: A total of 29 types and 214 specimens of neoplastic FFPE tissues were tested. Cadherin 17 was detected in neoplastic cells of colorectal carcinoma (32/32, 100%), gastric carcinoma (17/20, 85%), and pancreatic carcinoma (14/21, 67%). Membranous positivity for neuroendocrine neoplasms (NENs) were also observed (4/4, 100%). Cadherin 17 was absent in carcinomas of the breast (27/27, 100%), prostate (22/22, 100%), and urothelium (22/22, 100%). In addition, no staining was seen in neoplastic cells of thyroid carcinoma (0/5), lung squamous cell carcinoma (0/2), small cell lung carcinoma (0/3), hepatocellular carcinoma (0/3), melanoma (0/5), Hodgkin lymphoma (0/2), non-Hodgkin B-cell lymphoma (0/6), and T-cell lymphoma (0/2).

Clinical performance:

The Tissue-Tek Genie anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098] demonstrated conformity with the expected clinical performance through analytical studies and assessments of diagnostic performance in conjunction with established scientific validity (summarized in the "Summary and principle" section above with data from the references at the end of this IFU) based on information on other IVD medical devices with the same antibody, textbooks, and available peer-reviewed literature.

Tissue specimen	Established validity	Tissue specimen tested
Colon, appendix, small intestine	CDH17 is expressed in normal intestinal epithelium (e.g., colon including appendix and small intestine). ^{1,2,4}	Moderate to strong membranous staining was observed in columnar epithelial cells of the appendix/colon (11/11) and small intestine (3/3).
Pancreas	CDH17 is expressed in	At least moderate membranous staining

	pancreatic excretory ducts. ²	of pancreatic excretory ducts was observed (12/12).
Liver	CDH17 is not expressed in liver hepatocytes. ^{1,2,4}	No staining was detected in liver hepatocytes (0/6).
Other normal tissue specimens	CDH17 is also not expressed in other normal tissues, including lung, breast, kidney, stomach, placenta, thymus, adrenal gland, prostate, skeletal muscle, heart, cerebrum, cerebellum, testis, and salivary gland. ^{1,2}	CDH17 was also not observed in other normal tissues (0/77), including lung (0/4), breast (0/3), kidney (0/7), stomach (0/5), placenta (0/4), thymus (0/1), adrenal gland (0/5), prostate (0/9), skeletal muscle (0/3), heart (0/1), cerebrum (0/4), cerebellum (0/1), testis (0/5), and salivary gland (0/1).
Colorectal carcinoma	CDH17 is detected in 96-100% of colorectal carcinomas. ^{1,2,4,5}	Membranous staining was observed in 100% of colorectal carcinoma (32/32).
Gastric carcinoma	CDH17 is detected in 43-90% of gastric carcinomas. ^{1,2,4,5}	Membranous staining was observed in 85% of gastric carcinoma (17/20).
Pancreatic carcinoma	CDH17 is detected 39-82% of pancreatic ductal carcinomas. ^{1,2,4-6}	Membranous staining was observed in 67% of pancreatic carcinoma (14/21).
Breast carcinoma	Cadherin 17 expression is absent in 100% of breast carcinomas. ^{1,2,4,5}	No staining was observed in all breast carcinomas tested (27/27, 100%).
Prostate carcinoma	No staining was observed in all prostate carcinoma tested (22/22, 100%).	No staining was observed in all prostate carcinoma tested (22/22, 100%).
Urothelial carcinoma	Cadherin 17 expression is absent in 99-100% of urothelial carcinomas. ^{2,4,5}	No staining was observed in all urothelial carcinoma tested (22/22, 100%).

Together, this information is sufficient to demonstrate conformity with relevant essential principles without the need for additional clinical performance data.

Cautions and warnings

For professional use only.

Take reasonable precautions when handling. Avoid contact of reagents with eyes, skin, and mucous membranes. Wear protective gloves, protective clothing, and eye protection.

The product should not be exposed to temperatures outside of the storage conditions.

Capsules filled with ready-to-use, pre-diluted, antibody are for single use only. The in-use stability of each capsule is approximately 72 hours when used outside the storage conditions. Do not attempt to refill or add additional reagent. Discard capsule after use.

It is recommended to include appropriate controls on each specimen slide to help in identifying any deviation that might occur during the staining process.

All disposal practices must be in compliance with all Federal, State/Provincial and local laws and regulations. Refer to the SDS for further information.

Specimen collection and preparation for analysis

Routinely processed, formalin-fixed, paraffin-embedded tissues are suitable for use with this reagent when used with Tissue-Tek Genie reagents and a Tissue-Tek Genie Advanced Staining System (see section "Material required but not supplied"). The recommended fixation is performed using 10% (v/v) neutral buffered formalin for 24-72 hours.⁹ Variable results may occur because of prolonged fixation or special processes such as decalcification of bone marrow preparations. Each cut section should be 3-5 µm in thickness and placed on a positively charged glass slide. Slides containing the tissue section may be baked for at least 30 minutes to overnight (typically up to 16 hours) in a 58-60°C oven.⁹

Storage conditions

Store this product at 2-8°C. Do not freeze. Return unused capsules to 2-8°C.

For the date of expiration, refer to the label on the product.

The reagent will be stable until its expiration date when stored and handled properly. Do not use the reagent beyond its assigned expiration date. Storage conditions other than those specified above must be verified by the user.

Do not use when precipitate is visible in the reagent container.

Instructions for use

Tissue-Tek Genie® anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098], RTU, 10 capsules/pack (REF 8364-C010):

1. Place the Tissue-Tek Genie® Reagent Dispensing Area Tag (RDA-Tag) attached to the capsule into the RDA.
2. Push the capsule into the RDA with foil side down and click the attached RDA-Tag down into place on the RDA.
3. Place the RDA on the desired station of the Tissue-Tek Genie Advanced Staining System.

- Place the slide with the specimen section on the same station, specimen section side down.
- Assign protocol 8364 to the same station.
- Initiate execution of protocol 8364.
- The RDA-Tag 8364 will be scanned and registered automatically when the staining process is initiated.
- During the primary antibody application step, the antibody will be released from the capsule into the RDA and onto the specimen section on the slide.
- The staining protocol continues to the end.

Material required but not supplied

- Tissue-Tek Genie® Advanced Staining System (REF 8200)
- Positive and negative tissue controls
- Drying oven capable of maintaining a temperature of 58-60°C
- Tissue-Tek Genie® Dewax Solution (REF 8865-G001)
- Tissue-Tek Genie® Wash Buffer Solution (REF 8874-G004)
- Tissue-Tek Genie® High pH Antigen Retrieval Solution (REF 8744-G001)
- Tissue-Tek Genie® Non-Immune Rabbit Ig Antibody, Negative Control (REF 8605-C010)
- Tissue-Tek Genie® PRO Detection Kit, DAB (REF 8826-K250)
- Tissue-Tek Genie® Hematoxylin (REF 8830-M250)
- Tissue-Tek Genie® Reagent Dispense Area [RDA] (REF 8616-G090)

Further information can be found on the Sakura Finetek USA website at www.sakuraus.com/Genie

Troubleshooting

Testing run should include proper reagent and tissue controls.

- If the positive control exhibits negative, or weaker, or stronger staining, or more background staining than expected, other positive controls on the same instrument run should be examined to determine if this is due to the antibody, other reagents, software, instrumentation, or the processing and fixation of tissue specimen(s).
- If the paraffin has not been removed completely, the deparaffinization procedure should be verified.
- If tissue sections have washed off, slides should be examined to ensure they are positively charged, and the specimen should be examined for possible inadequate processing or fixation.
- Refer to the Tissue-Tek Genie Advanced Staining System operating manual or contact your Sakura Finetek Technical support representative for information or assistance.

Order information / product provided

Product code, product name and quantity

REF 8364-C010 Tissue-Tek Genie® anti-Cadherin 17 Rabbit Monoclonal Antibody [QR098]; RTU, 10 capsules/pack.

NOTE: The Safety Data Sheet (SDS) is available online on the Sakura Finetek USA website at www.sakuraus.com/SDS.html

The Summary of Safety and Performance (SSP) is available online via EUDAMED.

References

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Contact

If located within the United States, contact Sakura Finetek USA, Inc. by calling toll free 1-800-725-8723 or contact your Sakura Finetek representative or authorized distributor.

In countries other than the United States, contact the nearest authorized Sakura Finetek instrument distributor or representative. Contact details may be found at www.sakura.com

Any incident should be reported to the manufacturer. In the European Union, any serious incident that has occurred in relation to the device shall be reported to the manufacturer, authorized representative, and the competent authority of the appropriate Member State in which the user and/or the patient is established.

Symbols

-  Catalog number
-  Batch code
-  *in vitro* diagnostic medical device
-  Temperature limitation
-  Use by
-  Manufacturer
-  Consult instructions for use
-  European Conformity
-  Authorized representative in the European Community
-  Do not re-use (applies to capsule format only)

  Please see product label for lot and expiration date information and if available the date of manufacture

Storage: 2°C  8°C

  


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