IgG4 (M)

Concentrated and Prediluted Monoclonal Antibody
Control Number: 901-3115-111618

BIOCARE MEDICAL

Catalog Number:	**ACI 3115 A, B**	**API 3115 AA**
Description:	0.1, 0.5 mL, conc.	6.0 mL, RTU
Dilution:	1:100	Ready-to-use
Diluent	Van Gogh Yellow	N/A

Intended Use:
For In Vitro Diagnostic Use
IgG4 (M) [HP6025] is a mouse monoclonal antibody that is intended for laboratory use in the qualitative identification of IgG4 immunoglobulin by immunohistochemistry (IHC) in formalin-fixed paraffin-embedded (FFPE) human tissues. The clinical interpretation of any staining or its absence should be complemented by morphological studies using proper controls and should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.

Summary and Explanation:
IgG4 is an immunoglobulin G subclass of antibody. Mouse monoclonal IgG4 [HP6025] is specific for the Fc region of human IgG4. IgG4 can be helpful in the diagnosis of IgG4 related systemic disease (IgG4-RSD). IgG4-RSD, also known as IgG4-related sclerosing disease, can be found in many different organs and presents itself with such symptoms as lymphoplasmacytic infiltration, mass formation, sclerosis, obliterative phlebitis and increased expression of IgG4+ plasma cells as well as a high IgG4+/IgG+ ratio, typically >30% (1-4).

IgG4 has been shown to be overexpressed in inflammatory pseudotumor (IPT) and under expressed in inflammatory myofibroblastic tumor (IMT). IgG4 may be a useful differential marker in a panel with IgG (IgG4+/ IgG+ plasma cell ratio is higher in IPT) and ALK (positive in IMT) (4,5).

In pulmonary nodular lymphoid hyperplasia (PNLH), there are an increased number of IgG4+ plasma cells as well as a higher ratio of IgG4+ to IgG+ plasma cells as compared to other pulmonary lymphoid proliferations. These characteristics may aid in distinguishing PNLH from low-grade B-cell lymphoma of the bronchus-associated lymphoid tissue (BALT) (6).

Overexpression of IgG4 has been found in 39% of primary cutaneous marginal zone lymphomas, and a localized immunologic (IgG4) pathogenetic involvement at early stages of the disease has been proposed (7). Elevated numbers of IgG4+ plasma cells as well as a higher ratio of IgG4+ plasma cells to IgG+ plasma cells may assist in the diagnosis of autoimmune pancreatitis (AIP, also referred to as IgG4-related sclerosing pancreatitis) versus other mass forming pancreatic lesions, especially invasive ductal carcinoma of the pancreas (8).

In the past, immunofluorescence techniques were used to detect IgGs on formalin-fixed paraffin-embedded tissues. However, immunohistochemical procedures are becoming a more commonly utilized method (1-9).

Principle of Procedure:
Antigen detection in tissues and cells is a multi-step immunohistochemical process. The initial step binds the primary antibody to its specific epitope. After labeling the antigen with a primary antibody, a secondary antibody is added to bind to the primary antibody. An enzyme label is then added to bind to the secondary antibody; this detection of the bound antibody is evidenced by a colorimetric reaction.

Source: Mouse monoclonal
Species Reactivity: Human; others not tested
Clone: HP6025
Isotype: IgG1
Protein Concentration: Call for lot specific Ig concentration.
Epitope/Antigen: Fc region of human IgG4
Cellular Localization: Cytoplasmic
Positive Tissue Control: Spleen
Known Applications:
Immunohistochemistry (formalin-fixed paraffin-embedded tissues)
Supplied As: Buffer with protein carrier and preservative
Storage and Stability:
Store at 2ºC to 8ºC. The product is stable to the expiration date printed on the label, when stored under these conditions. Do not use after expiration date. Diluted reagents should be used promptly; any remaining reagent should be stored at 2ºC to 8ºC.

Protocol Recommendations (intelliPATH FLX® and manual use):
Peroxide Block: Block for 5 minutes with Peroxidazed 1.
Pretreatment: Perform heat retrieval using Diva Decloaker. Refer to the Diva Decloaker product data sheet for specific instructions.
Protein Block (Optional): Incubate for 5-10 minutes at RT with Background Punisher.
Primary Antibody: Incubate for 30 minutes at RT.
Probe: Incubate for 10 minutes at RT with a secondary probe.
Polymer: Incubate for 10-20 minutes at RT with a tertiary polymer.
Chromogen: Incubate for 5 minutes at RT with Biocare's DAB – OR – Incubate for 5-7 minutes at RT with Warp Red.
Counterstain:
Counterstain with hematoxylin. Rinse with deionized water. Apply Tacha's Bluing Solution for 1 minute. Rinse with deionized water.
Technical Note:
This antibody, for intelliPATH FLX and manual use, has been standardized with MACH 4 detection system. Use TBS for washing steps.

Limitations:
The optimum antibody dilution and protocols for a specific application can vary. These include, but are not limited to fixation, heat-retrieval method, incubation times, tissue section thickness and detection kit used. Due to the superior sensitivity of these unique reagents, the recommended incubation times and titers listed are not applicable to other detection systems, as results may vary. The data sheet recommendations and protocols are based on exclusive use of Biocare products. Ultimately, it is the responsibility of the investigator to determine optimal conditions.

Quality Control:
Refer to CLSI Quality Standards for Design and Implementation of Immunohistochemistry Assays; Approved Guideline-Second edition (I/LA28-A2) CLSI Wayne, PA USA (www.clsi.org). 2011

Precautions:
1. This antibody contains less than 0.1% sodium azide. Concentrations less than 0.1% are not reportable hazardous materials according to U.S. 29 CFR 1910.1200, OSHA Hazard communication and EC Directive 91/155/EC. Sodium azide (NaN_3) used as a preservative is toxic if ingested. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal, flush with large volumes of water to prevent azide build-up in plumbing. (Center for Disease Control, 1976, National Institute of Occupational Safety and Health, 1976) (10)

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Precautions Cont'd:
2. Specimens, before and after fixation, and all materials exposed to them should be handled as if capable of transmitting infection and disposed of with proper precautions. Never pipette reagents by mouth and avoid contacting the skin and mucous membranes with reagents and specimens. If reagents or specimens come into contact with sensitive areas, wash with copious amounts of water. (11)
3. Microbial contamination of reagents may result in an increase in nonspecific staining.
4. Incubation times or temperatures other than those specified may give erroneous results. The user must validate any such change.
5. Do not use reagent after the expiration date printed on the vial.
6. The SDS is available upon request and is located at http://biocare.net.

Troubleshooting:
Follow the antibody specific protocol recommendations according to data sheet provided. If atypical results occur, contact Biocare's Technical Support at 1-800-542-2002.

References:
1. Khosroshahi A, *et al.* A clinical overview of IgG4-related systemic disease. Curr Opin Rheumatol. 2011 Jan; 23(1):57-66.
2. Divatia M, Kim S, Ro J. IgG4-related sclerosing disease, an emerging entity: a review of a multi-system disease. Yonsei Med J. 2012 Jan; 53(1):15-34.
3. Sato Y, *et al.* Clinicopathologic analysis of IgG4-related skin disease. Mod Pathol. 2013 Apr; 26(4):523-32.
4. Saab ST, *et al.* IgG4 plasma cells in inflammatory myofibroblastic tumor: inflammatory marker or pathogenic link? Mod Pathol. 2011 Apr; 24(4):606-12.
5. Bhagat P, *et al.* Pulmonary inflammatory myofibroblastic tumor and IgG4-related inflammatory pseudotumor: a diagnostic dilemma. Virchows Arch. 2013 Dec; 463 (6):743-7.
6. Guinee DG Jr, *et al.* Pulmonary nodular lymphoid hyperplasia (pulmonary pseudolymphoma): the significance of increased numbers of IgG4-positive plasma cells. Am J Surg Pathol. 2010 Dec; 34(12):1812-9.
7. Brenner I, *et al.* Primary cutaneous marginal zone lymphomas with plasmacytic differentiation show frequent IgG4 expression. Mod Pathol. 2013 Dec; 26(12):1568-76.
8. Sepehr A, *et al.* IgG4+ to IgG+ plasma cells ratio of ampulla can help differentiate autoimmune pancreatitis from other "mass forming" pancreatic lesions. Am J Surg Pathol. 2008 Dec; 32(12):1770-9.
9. Hamilton RG, *et al.* Epitope mapping of human immunoglobulin-specific murine monoclonal antibodies with domain-switched, deleted and point-mutated chimeric antibodies. J Immunol Methods. 1993 Jan 14; 158(1):107-22.
10. Center for Disease Control Manual. Guide: Safety Management, NO. CDC-22, Atlanta, GA. April 30, 1976 "Decontamination of Laboratory Sink Drains to Remove Azide Salts."
11. Clinical and Laboratory Standards Institute (CLSI). Protection of Laboratory Workers from Occupationally Acquired Infections; Approved guideline-Fourth Edition CLSI document M29-A4 Wayne, PA 2014.

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