

Product Focus : Proliferation Markers

Zeta designs and develops tumor-specific biomarkers using cutting edge technology to uniquely select the immunogens for our famed RAbMono™ (Rabbit Monoclonal) and MonoMab™ (Monospecific monoclonal antibodies). Zeta's MonoMab™ Antibodies are produced through the hybridoma and recombinant technologies.

Zeta offers over 375 individual primary antibodies of high-quality and IVD certified for Pathology/IHC. Primary antibodies include Mouse Monoclonals, Rabbit Monoclonals, and Rabbit Polyclonals. These antibodies are carefully chosen and developed to consistently produce staining on formalin-fixed paraffin-embedded tissue (FFPE) sections.

Ki-67 Mouse Monoclonal Antibody

IVD

Anti-mouse: Clone ZM67, Cat # Z2377

Diagnostic Value

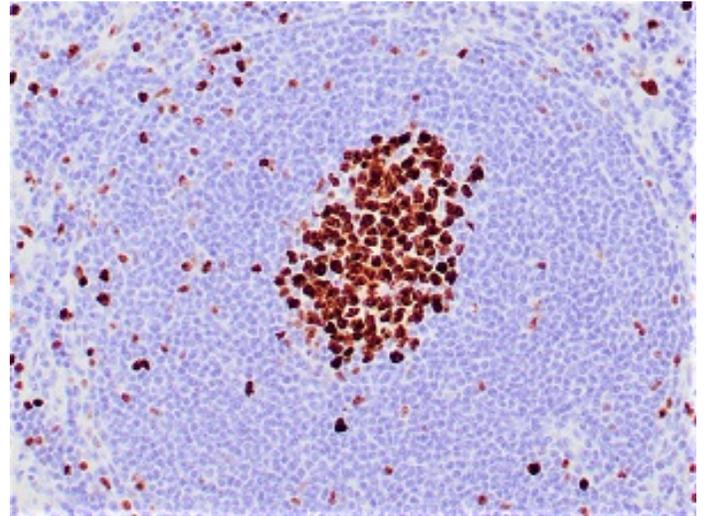
In lymphomas, Ki-67 may be useful for obtaining an overall estimate of the lymphoma grade, which generally parallels the percentage of Ki-67-positive cells. Burkitt or Burkitt-like lymphoma should show near 100% Ki-67 expression. A highly proliferative DLBCL should have at least 80% Ki-67 expression. The Hodgkin cells and variants of the classical Hodgkin lymphoma are also Ki-67 positive, despite their relatively low mitotic activity.

In addition, Ki-67 has been studied as a marker for HPV infection by virtue of its altered expression in HPV-infected epithelium. In normal and atrophic squamous epithelium without HPV infection, Ki-67 only stains basal/parabasal cells, whereas in HPV infection, Ki-67 staining extends above parabasal cells. In severe dysplasia, there is positive nuclear staining throughout the full epithelial thickness. The proportion of Ki-67-positivity increases in parallel with the increasing p16 intensity. The positive predictive value of Ki-67 for HPV is 82%, and the negative predictive value is 92%.

Prognostic value

Ki-67 protein is expressed during the proliferative cell cycle (G1, S, G2, and M phases) and is absent in the resting (G₀) phase. Histone H3 protein is maximally phosphorylated during the mitotic phase of the cell cycle, making it a specific marker for mitosis. Ki-67 and phosphohistone H3 (PHH3) have been shown to be useful in assessing proliferative and mitotic activities in melanocytic lesions in distinguishing between melanocytic nevi and malignant melanoma. The immunohistochemical expression of Ki-67 is an independent prognostic factor for disease-free survival. A progressive increase in Ki-67 expression is correlated with tumor thickness, Clark level of invasion, distant metastasis, and shorter survival.

Ki-67 antigen is a nuclear, non-histone protein that is present in all stages of the cell cycle except G0. This characteristic makes Ki-67 an excellent marker for proliferating cells and is commonly used as one of the prognostic factors in cancer studies. A correlation has been demonstrated between Ki-67 index and the histo-pathological grade of neoplasms. Assessment of Ki-67 expression in breast and neuroendocrine tumors shows a correlation between tumor proliferation and disease progression, thus making it possible to differentiate high-risk patients. Ki-67 expression may also prove to be important for distinguishing between malignant and benign peripheral nerve sheath tumors. Ki-67 labeling index has been shown to be a prognostic marker in a number of neoplasms including neuroendocrine tumor and breast carcinoma. In general, Ki-67 is a good marker of proliferating cell populations.



Human lymph node stained with anti-Ki-67 antibody (Clone ZM67)

1. Ki-67 stain is widely used as a prognostic marker for breast carcinoma. Carcinomas with $\geq 15\%$ of Ki-67 index have a worse prognosis than $< 15\%$ of Ki-67 index.
2. Ki-67 stain is used to classify neuroendocrine tumor (NET) as low grade G1 ($\leq 3\%$ Ki-67 index) and G2 ($> 3\% - 20\%$ Ki-67 index), and high grade G3 ($> 20\%$ Ki-67 index).
3. In lymphomas, Ki-67 may be useful for obtaining an overall estimate of the lymphoma grade, which generally parallels the percentage of Ki-67-positive cells. Burkitt or Burkitt-like lymphoma should show near 100% Ki-67 expression. A highly proliferative DLBCL should have at least 80% Ki-67 expression. The Hodgkin cells and variants of the classical Hodgkin lymphoma are also Ki-67 positive, despite their relatively low mitotic activity.

*References

1. McKeever P, et al. J Neuropathol Exp Neurol. 1998; 57:931-6.
2. Allegra CJ, et al. J Clin Oncol. 2003; 21:241-50.
3. Pathmanathan N, et al. J Clin Pathol. 2013; 66:512-6.

All of our antibodies work on formalin-fixed paraffin embedded (FFPE) tissue sections. As an ISO 13485:2016 certified biomedical company, all our antibody clones are scientifically selected to fit the need of clinical immunohistochemical laboratories. Our primary antibodies are manufactured by FDA-certified GMP facilities in the USA and purified by affinity chromatography with $> 99\%$ purity.

All antibodies are offered in different formats and sizes with the Suffix after the Catalog #s; "L", "S" & "T" for Concentrated antibodies in 1.0 ml, 0.5 ml & 0.1 ml sizes and Suffix "P" for Ready To Use (RTU) in 7 ml.

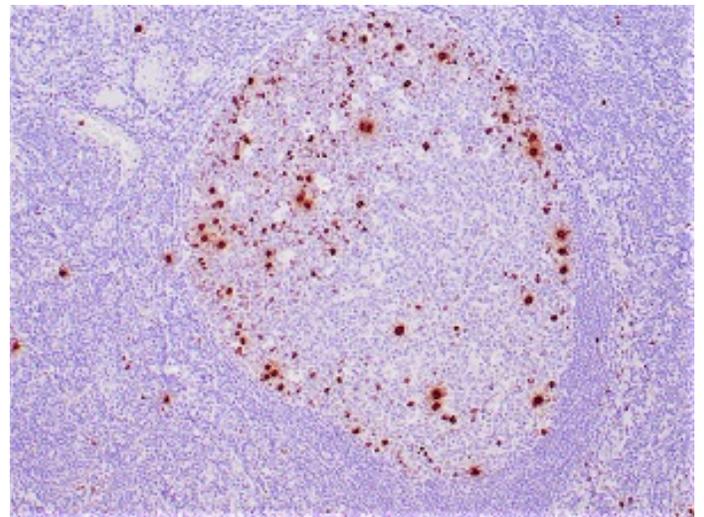
PHH3 Rabbit Monoclonal Antibody

IVD

Anti-rabbit: Clone ZR285, Cat # Z2600

Phosphohistone H3 (PHH3) is a marker specific for cells undergoing mitosis. Serine 10 of Histone H3 is phosphorylated in association with mitotic chromatin condensation in late G2 and M phase of the cell cycle and thus, PHH3 can distinguish mitosis from apoptotic nuclei. The range of percentage PHH3 positive tumor nuclei are from 0.0 to 6.6% (median value 0.8%). Increased expression of PHH3 was significantly associated with tumor thickness ($p = 0.031$), presence of tumor ulceration ($p = 0.041$) and tumor necrosis ($p = 0.027$), but not with Clark's level of invasion. High levels of PHH3 is associated with increased mitotic count ($p = 0.003$) and high Ki-67 expression ($p = 0.002$). For central nervous system tumors, melanoma, soft tissue tumors, GIST, etc., PHH3 mAb is helpful for tumor pathological classification and prognosis.

Phosphohistone-H3 (PHH3) is a core histone protein, which together with other histones forms the major protein constituents of the chromatin in eukaryotic cells. In mammalian cells, phosphohistone H3 is negligible during interphase but reaches a maximum for chromatin condensation during mitosis. Immunohistochemical studies showed anti-PHH3 detected specifically the core protein histone H3 only when phosphorylated at serine 10 or serine 28. Studies have also revealed no phosphorylation on the histone H3 during apoptosis. Therefore, PHH3 can serve as a mitotic marker to separate mitotic figures from apoptotic bodies and karyorrhectic debris, which may be a very useful tool in diagnosis of tumor grades, especially in CNS, skin, Gyn., Soft tissue, and GIST.



Human tonsil stained with anti-PHH3 antibody (Clone ZR285)

References

1. Colman H, et al. Am J Surg Pathol. 2006; 30:657-64.
2. Nasr MR, et al. Am J Dermatopathol. 2008; 30:117-22.
3. Kim YJ, et al. Am J Clin Pathol. 2007; 128:118-25.