

BACKGROUND

MUM1 (multiple myeloma 1)/IRF4 (also known as LSIRF, Pip, and ICSAT) is a member of the IRF family of transcriptional factors. It is considered to be a key regulator of several steps in lymphoid, myeloid, and dendritic cell differentiation and maturation. It is also an established marker of plasma cell differentiation. MUM1/IRF4 is normally expressed in plasma cells, a small percentage of germinal center (GC) B cells mainly located in the *light zone*, and activated T cells.¹ Unlike other IRF-family members, MUM1/IRF4 is not induced by interferon, but rather by diverse mitogenic stimuli, including antigen receptor engagement, lipopolysaccharides, and CD40 signaling. These stimuli all activate the NF- κ B pathway, which leads to MUM1/IRF4 promoter activation by NF- κ B heterodimers. In addition, MUM1/IRF4 transcription can be activated by IL-4, implicating the STAT6 in its activation. The abundance of MUM1/IRF4 varies within the hematopoietic system in a lineage- and stage-specific manner. In mature B cells, MUM1/IRF4 expression is repressed by the *Mitf* transcription factor. In addition, MUM1/IRF4 is strongly expressed in multiple myeloma and several other lymphomas. Gene microarray analysis has further shown that the MUM1/IRF4 gene is preferentially clustered within the gene expression profile exhibited by activated B-like DLBCL, a subset of DLBCL associated with a worse prognosis. These studies implicate a significant role for MUM1/IRF4 in tumorigenesis and immune regulation. MUM1/IRF4 may be a promising target for the treatment of some of these neoplasms.²

For many genes, MUM1/IRF4 functions as a positive regulator of transcription, using its C-terminal transactivation domain. However, MUM1/IRF4 can repress the expression of some interferon-inducible genes by binding to interferon-stimulated response elements (ISREs) in their promoters, displacing the interferon-responsive IRF factors *Irf1* and *Irf2*. MUM1/IRF4 can also repress other genes, such as *BCL6*, through as yet undefined mechanisms. Alone, MUM1/IRF4 binds DNA weakly due to its C-terminal autoinhibitory domain. However, MUM1/IRF4 can bind with high avidity to the 3' enhancers of both κ and λ immunoglobulin light chains in conjunction with the ETS-family transcription factor *PU.1* and the closely related factor *SPIB*. Moreover, additional protein-protein interactions between MUM1/IRF4 and other regulatory factors modulate its DNA-binding properties and/or transactivation potential. MUM1/IRF4 is an essential regulator at multiple steps in B-cell differentiation and plays a critical role in the adaptive immune responses of mature B cells. MUM1/IRF4 is also required for immunoglobulin class switch recombination (CSR). IRF4-deficient B cells fail to upregulate *AID*, the critical enzyme that mediates CSR. Outside the B-cell lineage, MUM1/IRF4 is essential for several stages of T-cell and myeloid-cell differentiation.

IRF4 is emerging as a critical regulator of T-helper-cell differentiation, playing a required role in both Th2 and Th17 development by controlling cytokine expression and apoptosis. Mice deficient in MUM1/IRF4 exhibit impaired B- and T-cell function, absence of plasma cells with a drastic reduction in serum immunoglobulins, and an abrogated response to B-cell activation.³ However, MUM1/IRF4-deficient mice have no apparent phenotypes outside of the lymphoid and myeloid lineages, in keeping with the restricted expression of MUM1/IRF4 in these cell types. Therefore, potential therapies aimed at MUM1/IRF4 would have restricted and potentially manageable on-target toxicities within the hematopoietic system.⁴

References:

- Gualco, G. et al: *Appl. Immunohistochem. Mol. Morphol.* 18:301-10, 2010
- Lu, R.: *Trends Immunol.* 29:487-92, 2008
- Shaffer, A.L. et al: *Clin. Cancer Res.* 15:2954-61, 2009
- Mudter, J. et al: *J. Clin. Invest.* 118:2415-26, 2008

TECHNICAL INFORMATION

Source:

IRF4/MUM1 Antibody is a mouse monoclonal antibody raised against recombinant human IRF4/MUM1 fragments expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous IRF4/MUM1 proteins without cross-reactivity with other family members.

Storage Buffer: PBS and 30% glycerol

Storage:

Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

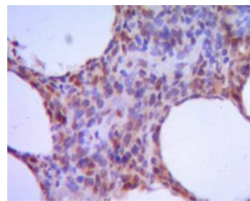
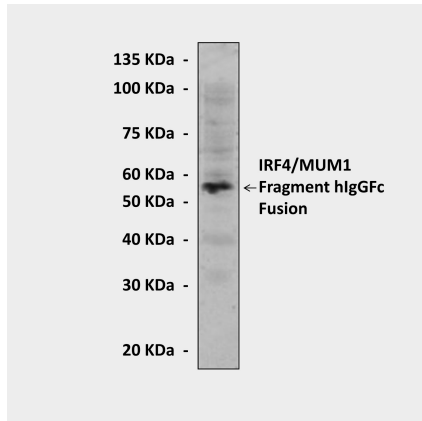
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	1:50-200
ICC	n/d
FACS	n/d

**Optimal dilutions must be determined by end user.*



QUALITY CONTROL DATA



Top: Western Blot detection of IRF4/MUM1 proteins in cell lysate from 293 cell transfected with human IRF4 fragment-hlgGfc fusion expressing vectors using IRF4/MUM1 Antibody. **Bottom:** This antibody stains paraffin-embedded human non-Hodgkin's lymphoma tissue in immunohistochemical analysis.

