丙型肝炎病毒 NS4B（65kDa）抗体

产品货号： mlR4858

英文名称： Hepatitis C Virus RNA-directed RNA polymerase

中文名称： 丙型肝炎病毒 NS4B（65kDa）抗体

别　　名： RNA-directed RNA polymerase; p68; RNA dependent RNA polymerase; NS5B.

研究领域： 细胞生物　细菌及病毒

抗体来源： Rabbit

克隆类型： Polyclonal

交叉反应： HCV

产品应用： WB=1:500-2000 ELISA=1:500-1000 IHC-P=1:400-800 IHC-F=1:400-800 IF=1:50-200 （石蜡切片需做抗原修复）

not yet tested in other applications.

optimal dilutions/concentrations should be determined by the end user.

分 子 量： 65kDa

细胞定位： 细胞浆 细胞膜

性　　状： Lyophilized or Liquid

浓　　度： 1mg/ml

免 疫 原： KLH conjugated synthetic peptide derived from Hepatitis C Virus RNA-directed RNA polymerase:2501-2600/3010

亚　　型： IgG

纯化方法： affinity purified by Protein A

储 存 液： 0.01M TBS(pH7.4) with 1% BSA, 0.03% Proclin300 and 50% Glycerol.

保存条件： Store at -20 ° C for one year. Avoid repeated freeze/thaw cycles. The lyophilized antibody is stable at room temperature for at least one month and for greater than a year when kept at -20° C. When reconstituted in sterile pH 7.4 0.01M PBS or diluent of antibody the antibody is stable for at least two weeks at 2-4 ° C.

PubMed： PubMed

产品介绍 background：

HCV is a positive, single-stranded RNA virus in the Flaviviridae family. The genome is approximately 10,000

nucleotides and encodes a single polyprotein of about 3,000 amino acids. The polyprotein is processed by host cell and viral proteases into three major structural proteins, and several non-structural proteins necessary for viral replication, of which NS5B is one. NS5B RNA-dependant RNA polymerase is responsible for replication of the hepatitis C viral genome, and is currently a principal target for chemotherapeutic inhibition of HCV replication. Hepatitis C virus (HCV) can cause chronic hepatitis, cirrhosis and hepatocellular carcinoma. At present there is no vaccine effective against HCV. Host membrane insertion occurs after processing by the NS3 protease.

Function:

Core protein packages viral RNA to form a viral nucleocapsid, and promotes virion budding. Modulates viral translation initiation by interacting with HCV IRES and 40S ribosomal subunit. Also regulates many host cellular functions such as signaling pathways and apoptosis. Prevents the establishment of cellular antiviral state by blocking the interferon-alpha/beta (IFN-alpha/beta) and IFN-gamma signaling pathways and by inducing human STAT1 degradation. Thought to play a role in virus-mediated cell transformation leading to hepatocellular carcinomas. Interacts with, and activates STAT3 leading to cellular transformation. May repress the promoter of p53, and sequester CREB3 and SP110 isoform 3/Sp110b in the cytoplasm. Also represses cell cycle negative regulating factor CDKN1A, thereby interrupting an important check point of normal cell cycle regulation. Targets transcription factors involved in the regulation of inflammatory responses and in the immune response: suppresses NK-kappaB activation, and activates AP-1. Could mediate apoptotic pathways through association with TNF-type receptors TNFRSF1A and LTBR, although its effect on death receptor-induced apoptosis remains controversial. Enhances TRAIL mediated apoptosis, suggesting that it might play a role in immune-mediated liver cell injury. Seric core protein is able to bind C1QR1 at the T-cell surface, resulting in down-regulation of T-lymphocytes proliferation. May transactivate human MYC, Rous sarcoma virus LTR, and SV40 promoters. May suppress the human FOS and HIV-1 LTR activity. Alters lipid metabolism by interacting with hepatocellular proteins involved in lipid accumulation and storage. Core protein induces up-regulation of FAS promoter activity, and thereby probably contributes to the increased triglyceride accumulation in hepatocytes (steatosis).

E1 and E2 glycoproteins form a heterodimer that is involved in virus attachment to the host cell, virion internalization through clathrin-dependent endocytosis and fusion with host membrane. E1/E2 heterodimer binds to human LDLR, CD81 and SCARB1/SR-BI receptors, but this binding is not sufficient for infection, some additional liver specific cofactors may be needed. The fusion function may possibly be carried by E1. E2 inhibits human EIF2AK2/PKR activation, preventing the establishment of an antiviral state. E2 is a viral ligand for CD209/DC-SIGN and CLEC4M/DC-SIGNR, which are respectively found on dendritic cells (DCs), and on liver sinusoidal endothelial cells and macrophage-like cells of lymph node sinuses. These interactions allow capture of

circulating HCV particles by these cells and subsequent transmission to permissive cells. DCs act as sentinels in various tissues where they entrap pathogens and convey them to local lymphoid tissue or lymph node for establishment of immunity. Capture of circulating HCV particles by these SIGN+ cells may facilitate virus infection of proximal hepatocytes and lymphocyte subpopulations and may be essential for the establishment of persistent infection.

P7 seems to be a heptameric ion channel protein (viroporin) and is inhibited by the antiviral drug amantadine. Also inhibited by long-alkyl-chain iminosugar derivatives. Essential for infectivity.

Protease NS2-3 is a cysteine protease responsible for the autocatalytic cleavage of NS2-NS3. Seems to undergo self-inactivation following maturation.

NS3 displays three enzymatic activities: serine protease, NTPase and RNA helicase. NS3 serine protease, in association with NS4A, is responsible for the cleavages of NS3-NS4A, NS4A-NS4B, NS4B-NS5A and NS5A-NS5B. NS3/NS4A complex also prevents phosphorylation of human IRF3, thus preventing the establishment of dsRNA induced antiviral state. NS3 RNA helicase binds to RNA and unwinds dsRNA in the 3' to 5' direction, and likely RNA stable secondary structure in the template strand. Cleaves and inhibits the host antiviral protein MAVS.

NS4B induces a specific membrane alteration that serves as a scaffold for the virus replication complex. This membrane alteration gives rise to the so-called ER-derived membranous web that contains the replication complex.

NS5A is a component of the replication complex involved in RNA-binding. Its interaction with Human VAPB may target the viral replication complex to vesicles. Down-regulates viral IRES translation initiation. Mediates interferon resistance, presumably by interacting with and inhibiting human EIF2AK2/PKR. Seems to inhibit apoptosis by interacting with BIN1 and FKBP8. The hyperphosphorylated form of NS5A is an inhibitor of viral replication.

NS5B is a RNA-dependent RNA polymerase that plays an essential role in the virus replication.

Subunit:

Core protein is a homomultimer that binds the C-terminal part of E1 and interacts with numerous cellular proteins. Interaction with human STAT1 SH2 domain seems to result in decreased STAT1 phosphorylation, leading to decreased IFN-stimulated gene transcription. In addition to blocking the formation of phosphorylated STAT1, the core protein also promotes ubiquitin-mediated proteasome-dependent degradation of STAT1. Interacts with, and constitutively activates human STAT3. Associates with human LTBR and TNFRSF1A receptors and possibly induces apoptosis. Binds to human SP110 isoform 3/Sp110b, HNRPK, C1QR1, YWHAE, UBE3A/E6AP, DDX3X, APOA2 and RXRA proteins. Interacts with human CREB3 nuclear transcription protein, triggering cell transformation. May interact with human p53. Also binds human cytokeratins KRT8, KRT18, KRT19 and VIM (vimentin). E1 and E2 glycoproteins form a heterodimer that binds to human LDLR, CLDN1, CD81 and SCARB1 receptors. E2 binds and inhibits human EIF2AK2/PKR. Also binds human CD209/DC-SIGN and CLEC4M/DC-SIGNR. p7 forms a homoheptamer in vitro. NS2 forms a homodimer containing a pair of composite active sites at the dimerization interface. NS2 seems to interact with all other non-structural (NS) proteins. NS4A interacts with NS3 serine protease and stabilizes its folding. NS3-NS4A complex is essential for the activation of the latter and allows membrane anchorage of NS3. NS3 interacts with human TANK-binding kinase TBK1 and MAVS. NS4B and NS5A form homodimers and seem to interact with all other non-structural (NS) proteins. NS5A also interacts with human EIF2AK2/PKR, FKBP8, GRB2, BIN1, PIK3R1, SRCAP, VAPB and with most Src-family kinases. NS5B is a homooligomer and interacts with human VAPB, HNRNPA1 and SEPT6.

Subcellular Location:

RNA-directed RNA polymerase: Host endoplasmic reticulum membrane; Single-pass type I membrane protein (Potential). Note=Host membrane insertion occurs after processing by the NS3 protease.

Post-translational modifications:

Specific enzymatic cleavages in vivo yield mature proteins. The structural proteins, core, E1, E2 and p7 are produced by proteolytic processing by host signal peptidases. The core protein is synthesized as a 21 kDa precursor which is retained in the ER membrane through the hydrophobic signal peptide. Cleavage by the signal peptidase releases the 19 kDa mature core protein. The other proteins (p7, NS2-3, NS3, NS4A, NS4B, NS5A and NS5B) are cleaved by the viral proteases.

Envelope E1 and E2 glycoproteins are highly N-glycosylated.

Core protein is phosphorylated by host PKC and PKA.

NS5A is phosphorylated in a basal form termed p56. p58 is an hyperphosphorylated form of p56. p56 and p58 coexist in the cell in roughly equivalent amounts. Hyperphosphorylation is dependent on the presence of NS4A. Human AKT1, RPS6KB1/p70S6K, MAP2K1/MEK1, MAP2K6/MKK6 and CSNK1A1/CKI-alpha kinases may be responsible for NS5A phosphorylation.

NS4B is palmitoylated. This modification may play a role in its polymerization or in protein-protein interactions.

The N-terminus of a fraction of NS4B molecules seems to be relocated post-translationally from the cytoplasm to the ER lumen, with a 5th transmembrane segment. The C-terminus of NS2 may be lumenal with a fourth transmembrane segment.

Core protein is ubiquitinated; mediated by UBE3A and leading to core protein subsequent proteasomal degradation.

Similarity:

Belongs to the hepacivirus polyprotein family.Contains 1 helicase ATP-binding domain.Contains 1 peptidase C18 domain.Contains 1 peptidase S29 domain.Contains 1 RdRp catalytic domain.

SWISS:

P26664

Gene ID:

951475

Important Note:

This product as supplied is intended for research use only, not for use in human, therapeutic or diagnostic applications.

丙型肝炎发病机理仍未十分清楚，当 HCV 在肝细胞内复制引起肝细胞结构和功能改变或干扰肝细胞蛋白合成，可造成肝细胞变性坏死，表明 HCV 直接损害肝脏，导致发病起一定作用。但多数学者认为细胞免疫病理反应可能起重要作用，发现丙肝病毒肝炎与乙型肝炎一样，其组织浸润细胞以 CD3+为主，细胞毒 T 细胞（TC）特异攻击 HCV 感染的靶细胞，可引起肝细胞损伤。