

Rabbit Anti-Hepatitis C Virus NS4B antibody

SL4857R

Product Name:	Hepatitis C Virus NS4B
Chinese Name:	丙型肝炎病毒NS4B抗体
Alias:	HCV; HCV NS4B; Non structural protein 4B; NS4B; p27; Non-structural protein 4B
Organism Species:	Rabbit
Clonality:	Polyclonal
React Species:	HCV
Applications:	WB=1:500-2000ELISA=1:500-1000IHC-P=1:400-800IHC-F=1:400-800IF=1:50-
	200 (Paraffin sections need antigen repair)
	not yet tested in other applications.
	optimal dilutions/concentrations should be determined by the end user.
Molecular weight:	29kDa
Cellular localization:	cytoplasmicThe cell membrane
Form:	Lyophilized or Liquid
Concentration:	1mg/ml
immunogen:	KLH conjugated synthetic peptide derived from Hepatitis C Virus NS4B:1712-
	1820/3010
Lsotype:	IgG
Purification:	affinity purified by Protein A
Storage Buffer:	0.01M TBS(pH7.4) with 1% BSA, 0.03% Proclin300 and 50% Glycerol.
Storage:	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:	<u>PubMed</u>
Product Detail:	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 protein necessary for viral
	replication. Several different genotypes of HCV with slightly different genomic
	sequences have since been identified that correlate with differences in response to

treatment with interferon alpha.

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 virusmediated 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 NKkappaB 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 C1OR1 at the T-cell surface, resulting in downregulation 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:

Non-structural protein 4B: Host endoplasmic reticulum membrane; Multi-pass membrane protein.

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

Database links:

Entrez Gene: 951475 Hepatitis C Virus genotype 1a

SwissProt: P26664 Hepatitis C Virus genotype 1a

SwissProt: P26663 Hepatitis C Virus genotype 1a

Important Note:

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

