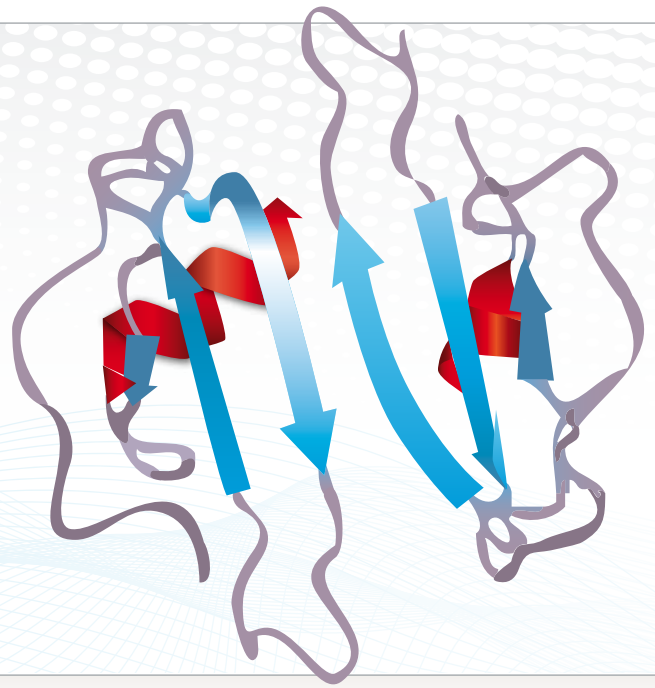


MYRIAD  RBM™

IP-10 MAP

3 PLEX



Myriad RBM's IP-10 MAP 3-plex is a valuable tool for studying chronic inflammatory diseases. Interferon induced protein 10 (IP-10 or CXCL10) is a chemotactic chemokine that attracts T-lymphocytes, natural killer cells, and monocytes¹. The protein exists in multiple forms and in some cases it may antagonize immune system activation depending on its cleavage state. Studies have found IP-10 induction to be involved in many disorders including autoimmune diseases, kidney injury, cancer and infectious diseases such as hepatitis C where measurement of the short and long forms have been used to predict response to therapy²⁻⁶. IP-10 MAP was developed and validated by Myriad RBM in our CLIA-certified lab. The service provided makes use of HuCAL® antibodies licensed by MorphoSys AG. HuCAL® is a registered trademark of MorphoSys AG.

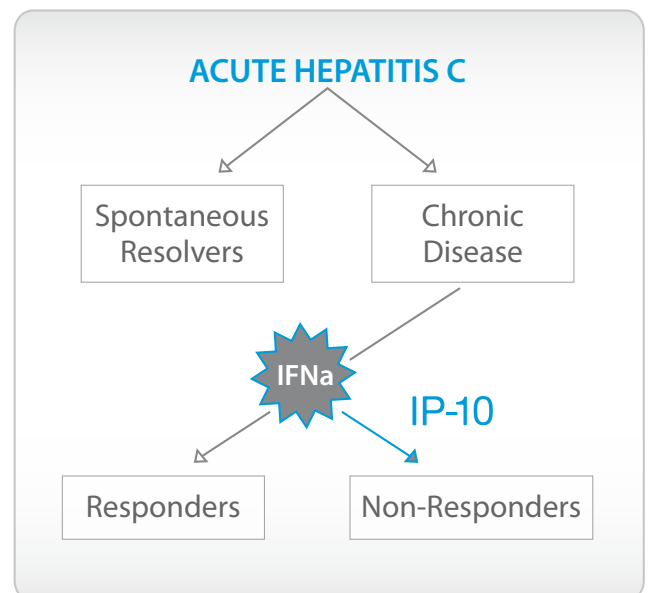
More than 170 million people worldwide suffer from a hepatitis C virus (HCV) infection which if left untreated, results in a greatly increased risk of liver failure and hepatocellular carcinoma (HCC)^{7,8}. One of the greatest difficulties in diagnosing HCV is that the acute stage is often asymptomatic. Spontaneous viral clearance occurs in as many as 45% of infected adults but the majority of cases progress to chronic infection⁹. Eight to twenty percent of chronic infections will develop cirrhosis within 20 years and many are faced with a lifetime risk of HCC¹⁰. The severe consequences resulting from disease progression make it critical that the appropriate therapeutic action is taken to prevent unnecessary liver damage.

The standard of care for patients with HCV is treatment with pegylated-interferon and ribavirin. This therapy is only successful in producing a sustained virologic response for a subset of the infected individuals and there are a number of independent factors that may be responsible for the low success rate of approximately 50%¹¹⁻¹³. As interferon therapy has severe side-effects, it would be beneficial to predetermine those patients who will respond to treatment.

Recently, IP-10 has become a particularly interesting biomarker in the study of HCV. In patients with chronic HCV infections, intrahepatic IP-10 mRNA levels correlate with plasma concentrations of IP-10, indicating that HCV-infected hepatocytes are the primary source of the plasma biomarker¹⁴. Furthermore, it was determined that the pre-treatment plasma levels of IP-10 were greatest in those patients who would become "non-responders" to pegylated interferon (IFN) antiviral therapy (**Figure 1**)². The utility of IP-10 to predict treatment outcome was confirmed in a subsequent study that found IP-10 levels valuable in predicting a sustained viral response to the standard of care in HCV infected individuals with 81% specificity and 95% sensitivity¹².

It is counterintuitive that a chemokine responsible for recruiting activated lymphocytes to the liver, is a negative prognostic marker for response to therapy. One explanation is that alternative forms of the IP-10 protein are interfering with its normal function. We know that the enzyme dipeptidyl peptidase IV (DPP4) has been shown to cleave related chemokines in this chemokine family, resulting in truncated forms of the proteins that exhibit lower biological activity¹⁵. Casrouge et al. proposed that DPP4 cleavage of IP-10 leads to an increased presence of the short form IP-10 protein which could account for the failure of treatment in certain individuals. Indeed, the researchers found that the increase in the levels of total IP-10 in non-responding HCV patients was due to an elevation of the antagonist (short)

Figure 1: HCV Progression



form of the IP-10 protein³ (Figure 2). It appears that the short IP-10 interferes with the chemokine gradient that is required for patients' successful response to therapy. In this example, treatment decisions could be improved dramatically by measuring both forms of the IP-10 protein to make predictions about patient outcome.

Myriad RBM's IP-10 MAP provides the ideal service to quantitatively measure three significant biomarkers that may determine the outcome of treatment for patients with chronic HCV. The levels of these IP-10 proteins can assist in predicting which patients will benefit from pegylated-IFN therapy. In addition, IP-10 MAP may also be useful for studies investigating autoimmune or infectious diseases, two therapy areas for which IP-10 has been shown to play a role. Ultimately, the IP-10 MAP offers a unique 3-plex assay that is well-suited for research on HCV and other chronic inflammatory diseases.

Please see below for acceptable sample types and sample volume requirements.

MAP	Serum or Plasma	Other fluid
IP-10	50 µL*	NA

*Plasma only. Plasma should be collected in BD P700 tubes, specialized vacutainers that are pre-loaded with DPP4V inhibitors, to prevent extra-corporeal cleavage of IP-10.

For more information or to order IP-10 MAP,

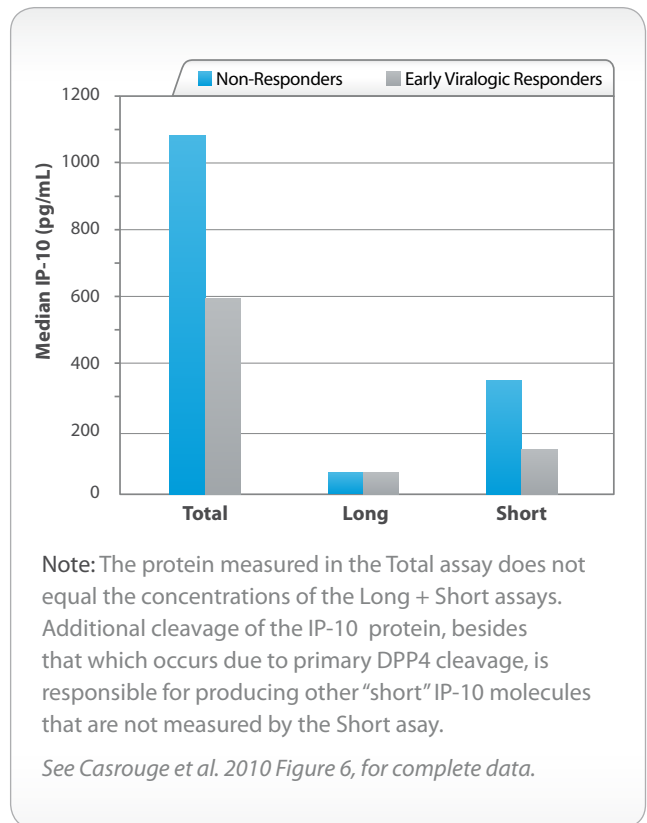
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Figure 2: Measurement of IP-10 in individuals infected with HCV. The antagonist form of IP-10 is predictive of failure to achieve an early viral response.



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