



▶ **Primary Biliary Cirrhosis Panel**

Anti-Nuclear Ab by IFA

Anti-Mitochondrial Ab by IFA

Anti-Mitochondrial M2 EP (MIT3) Abs by ELISA

Anti-gp210 Ab by ELISA

Anti-sp100 Ab by ELISA

Primary biliary cirrhosis (PBC) is an organ-specific autoimmune disease characterized by chronic progressive destruction of small intrahepatic bile ducts with portal inflammation and ultimately fibrosis. PBC affects women more than men (female:male ratio of 9:1) and typically occurs between the ages of 30 and 65. The prevalence range of PBC in first-degree relatives of PBC patients is from 1.3 to 6.4%.

Serologic assays are important aids to the recognition and diagnosis of PBC, since many antibodies associated with PBC are present before symptoms become evident.

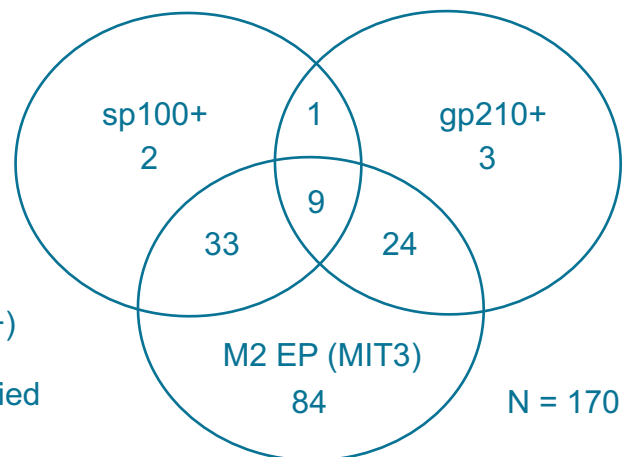
- ▶ PBC patients frequently are positive for ANA, especially multiple (1-20) nuclear dots (containing sp100 antigen) and nuclear membrane with nuclear rim (containing gp210 antigen) patterns in the HEp-2 ANA staining.
- ▶ The pattern of anti-mitochondrial antibody (AMA) detected by IFA on kidney/liver/-stomach (KLS) substrate shows coarse granular filamentous staining extending throughout the cytoplasm. **The detection of AMA was reported in up to 95% of PBC patients.**
- ▶ Anti-mitochondrial 2 (M2) specific antigens were identified as the E2 subunits of the pyruvate dehydrogenase complex (PDC-E2). First generation anti-M2 ELISA tests utilized PDC-E2 as the primary substrate to detect PBC-specific antibodies. While 80-90% of histologically proven patients have anti-PDC-E2 antibodies, about 10% of PBC patients only react to branched-chain 2-oxo-acid dehydrogenase complex (BCOADC-E2) and/or 2-oxo glutarate dehydrogenase complex (OGDC-E2). Identification of these antigens permitted the development of the new M2 ELISA. ELISA tests have been shown to be more specific than IFA.

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- ▶ **The new M2 (MIT3-based ELISA)** was shown to have enhanced performance over IFA or conventional PDC-E2- based ELISA tests and detected AMA in over two-thirds of the sera from “AMA-negative” (by IFA) PBC patients. The new anti-M2 reactivity has the high specificity (95%) with high sensitivity (88%).
- ▶ Anti-gp210 and/or sp100 antibodies can be detected in approximately 25% of all PBC patients and 30% of AMA-negative PBC patients. The gp210 and sp100 antibodies have a relatively low sensitivity, but the specificity is greater than 99%. Additionally, these antibodies may identify a subgroup of patients with a more severe disease course. The gp210 and sp100 ELISA will provide clinicians with additional serological markers for the detection of PBC and may help earlier identification, diagnosis, and treatment of patients negative for conventional markers of PBC. **Combined testing for the three markers (M2, gp210 and sp100) identifies 92% of PBC patients.**

Overlap of PBC-specific Markers in PBC Patients.

- ▶ 11.8% (20/170) of the total cohort of definite PBC specimens were AMA (MIT3) negative
- ▶ 30% (6/20) of the AMA (MIT3) negative PBC patients were positive for gp210 and/or sp100 antibodies (3 pts gp210+, 2 pts sp100+, 1 pt both gp210 and sp100+)
- ▶ Combined testing for the 3 markers identified 91.8% (156/170) of the PBC patients



Panel Code#: 1600

CPT Codes: 86038, 86256, 83516 X 3

Specimen Requirement: 2 mL serum, ambient, refrigerated or frozen (Minimum 1 mL)

Methodology: IFA, EIA

Turnaround time: 3 - 5 days

Reference:

Norman G, Lee L, Shums Z, Bogdanos D, Worman H, Krawitt E, Leung P, Aoki C, Vergani D, Gershwin M, INOVA Diagnostics, Institute of Liver Studies, Kings College Hospital, Columbia University, University of Vermont, UC Davis: Enhanced Detection and Characterization of Primary Biliary Cirrhosis Patients with New M2 EP(MIT3), gp210 and sp100 Elisa Assays. Presented at Annual Meeting of Association of Medical Laboratory Immunologists, August 2005.