13:45～14:35 Program (1)-1

Thirteen-year follow up of a PBC patient with hepatocellular carcinoma

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In 1982, a 48 year old woman was referred to our hospital to investigate her abnormal liver function tests found on an annual health check. Her medical history and family history were negative. Physical examination was unremarkable. At that time the patient's laboratory tests were as follows: total bilirubin 0.8mg/dL, AST 87KU, ALT 97KU, ALP 832IU (normal 70-260), IgG 1960mg/dL, IgM 804mg/dL. Anti-mitochondrial antibody (AMA) was positive, and viral hepatitis markers were all negative (HBsAg, anti-HBc and HCV-RNA; confirmed later by stored sera). A liver biopsy was performed laparoscopically. Laparoscopy showed a smooth liver surface with a reddish patch. The biopsy showed stage II～III PBC. She was diagnosed as having asymptomatic PBC. Two years later, at the age of 50, the patient developed intractable pruritus, and her bilirubin gradually increased. At the age of 53, she developed icterus. Nine years after the diagnosis of PBC, esophageal varices were diagnosed and ascites developed. At the age of 59, follow-up ultrasonography revealed a liver tumor with characteristic features of hepatocellular carcinoma (HCC) in segment 7 (25 mm in diameter). CT and arteriography confirmed this diagnosis. The HCC was treated several times by transarterial embolization and percutaneous ethanol injection. Two years after the diagnosis of HCC, the patient died as a result of liver dysfunction due to PBC. Though it would appear that asymptomatic PBC rarely progresses to symptomatic PBC, the long-term follow up of this patient showed the whole spectrum of disease - from asymptomatic PBC to cirrhosis and finally HCC.

13:45～14:35 Program (1)-2

Eighty four-year-old female with autoimmune cholangiopathy-like manifestations at her first presentation but revealed liver histology of autoimmune hepatitis.

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Eighty four-year-old female had a past history of gastrectomy at 50 in her age. Slight elevation of γ-GTP (106 IU/L) among other blood biochemical parameters was the only finding in a clinic in February 2000. There she had taken verapamil hydrochloride 120 mg/day for the treatment of tachycardial arrhythmia, carbocisteine 750 mg/day and ambroxol hydrochloride 45 mg/day for chronic bronchitis and ifenprodil tartrate 30 mg/day for the sequellae of cerebral infarction. She suffered from herpes zoster at her right face in January 16, 2004, thus had a medication for it in a dermatologist nearby. She was referred to our outpatient clinic for further examination of her generalized itching and liver dysfunction in March 2004. The results of blood biochemical analysis were as follows: AST/ALT=89/58 IU/L, ALP/γ-GTP=1,172/664 IU/L, T.B.=1.5 (D.B.=1.0) mg/dl, T.P.=8.3 g/dl, Albumin=3.55 g/dl, γ-gl=3.34 g/dl, IgG=3,089 mg/dl, IgA=375 mg/dl, IgM=229 mg/dl, ANA (+); 160 fold, speckled type, ASMA (+); 40 fold, AMA (-); <20 fold, anti-PDC E2 (-); <5.0 Index. PSC was excluded by using MRCP. Echo-guided liver biopsy was performed in April 2004. Liver histology revealed fibrously enlarged portal tracts with lymphoplasmocytic infiltration. Ductpenia of interlobular bile ducts and lymphocytic infiltration into remaining interlobular bile epithelial linings were other findings. Marginal ductular proliferation was noted reflecting the presence of interface hepatitis. Central zonal necrosis with marked plasma cell infiltration was seen. Focal necroses were numerous and diffuse lymphoplasmocytic infiltration in hepatic lobules was locally conspicuous. Based on these histological findings, she was diagnosed to have autoimmune hepatitis (AIH). To aviod unfavorable effects of adrenocorticosteroids including osteoporosis in such a high-aged woman, ursodeoxycholic acid (300 mg/day) was administered for the treatment of AIH from April 17, 2004. Since then, liver function tests dramatically improved early in April 30 as follows: AST/ALT=29/14 IU/L, ALP/γ-GTP=337/152 IU/L, T.B.=0.8 mg/dl.

13:45～14:35 Program (1)-3

Effective treatment with Bezafibrate administration in a case of patient with primary biliary cirrhosis and autoimmune hepatitis overlap syndrome

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A 55-year-old woman was admitted to our hospital because of fatigue, appetite loss and body weight loss. She was found to have anemia(hemoglobin level, 8.8g per deciliter) and rapid erythrocyte sedimentation rate, 114 mm/hr. Other laboratory data are as follows. Total bilirubin(T.Bil) 0.47 mg/dl, Alkaline phosphatase(ALP), 1079 IU/l, AST, 121 IU/l, ALT 99 IU/l, γ-GTP 401 IU/l. Both HBs Antigen and HCV Antibody were negative. Elevated immunoglobulin level(IgG, 5571 mg/dl, IgA, 958 mg/dl, IgM 1193 mg/dl)was observed. The diagnosis of primary biliary cirrhosis and autoimmune hepatitis was supported by the findings of markedly elevated serum level of auto-antibodies(anti-nuclear antibody, x160, positive anti-centromere antibody, anti-mitochondrial antibody, M2, x1650, anti-smooth muscle antibody, x80). Laparoscopic and histological findings will be shown. The patient was treated with Predonisolone 30 mg a day and the abnormalities of liver function tests resolved markedly, but serum level of ALP was gradually elevated several months later. After addition of Bezafibrate to Predonisolone, marked immprovment of serum level of ALP was observed. This clinical observation suggests that Bezafibrate administration could be effective for primary biliary cirrhosis especially overlap syndrome.

13:45～14:35 Program (1)-4

Randomized double blind control trial of reverse transcriptase inhibitor for UDCA-resistant PBC

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***Backgrounds*:** Currently, ursodeoxycholic acid (UDCA) is the only proven therapy to prolong the time for liver transplantation, especially in stage I and II patients with PBC. However, the presence of UDCA resistant cases is well known, and for these subpopulation of the patients with PBC has no means to prevent liver failure. The pathogenesis of PBC has been enigma although there have been lines of evidences that this condition is the results of immune-mediated destruction of intrahepatic bile ducts. Recently, Mason et al reported the involvement of retrovirus infection in the pathogenesis of PBC. Moreover, the antiviral therapy using reverse transcriptase inhibitor has been reported to be effective by the same authors.

***Aim*:** Thus, the aim of this study is to evaluate the efficacy of anti-reverse transcriptase inhibitor (Lamivudine) in the UDCA-resistant Japanese patients with PBC.

***Patients and methods*:** Total of 20 patients with PBC were enrolled in the study. The diagnosis of PBC was made by both well established criteria (liver enzyme profile and positive anti-mitochondrial antibody) and liver biopsy. The inclusion criteria are: 1) elevated liver enzyme (GGT, ALP) in spite of UDCA administration more than 6 month, 2) age between 20 to 70 years old, 3) normal renal function, 4) normal CPK, 5) no past history of administration of anti-retroviral agents, 6) obtainment of written informed consent. Exclusion criteria include: 1) normal liver enzyme, 2) patients with abnormal renal function, 3) presence of other cause of liver injury (HBV, HCV, alcoholic, AIH), 4) use of corticosteroids. Finally, 20 patients (4 male, 16 female) were randomly grouped into Lamivudine group and placebo group. Each patients were given either 100mg/day of lamivudine or lactose in power form for 3 month. These 20 patients were monitored monthly.

***Results*:** Each group of patients has completed the study. Lamivudine was well tolerated by patients with PBC. There was no significant difference between symptomatic adverse effects (ex. headache, abdominal pain, deteriorating renal function), although certain portion of lamivudine treated patients exhibited the elevation of serum CPK and amylase levels. As for liver enzymes, there are no significant improvements between two patients group, similar to changes of anti-mitochondrial antibodies' titer. However, some patients in Lamivudine group have demonstrated the improvement of liver enzymes as well as the decrease of AMA titer.

***Conclusion*:** Lamivudine is well tolerated in patients with PBC. Although its short term effects have not been significant, some patients have demonstrated the improvements. Long term effects need to be monitored to draw conclusion about its efficacy.

14:35～15:25 Program (2)-5

Prevalence of anti-mitochondrial antibody in Japanese population.

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Purpose: We studied the prevalence of anti-mitochondrial antibody (AMA) in a Japanese population with a modified enzyme-linked immunosorbent assay (ELISA) to measure serum anti-M2. We used an immunoblot (IB) method as gold standard and studied the diagnostic performance of the ELISA method and determined the most accurate cut-off value.

Subjects: We studied 1,467 (486 males and 981 females, mean age 68.5 ± 9.9 years) general population in Shodo island of Kagawa prefecture in Shikoku.

Methods: Serum anti-M2 was measured by MESACUP-2 test and Mitochondria M2 with a cut-off value of seven according to the attached manual. Anti-M2-positive samples were re-examined with indirect immunofluorescence (IF) and IB methods.

Results: Anti-M2 was positive in 58 people (4.0%, 95% CI 3.0-5.0%). Eight of these positive cases were positive with IF and 10 were positive with IB. Using IB method as the gold standard, the pre-test probability of AMA was estimated to be 0.68%. The positive predictive value (PPV) of the ELISA method was 17.2% and the accuracy was 96.7%. With the receiver operating characteristic analysis, we found that the optimal cut-off value was 55 when the ELISA method was applied to general population. With this cut-off value, the PPV was 100% and the accuracy was 99.9%. Ten out of 58 people (17%) with positive anti-M2 and five out of 10 people (50%) with positive IB, were found to have abnormal results of liver function tests. Two of these people had elevations of alkaline phosphatase and immunoglobulin M, which suggested primary biliary cirrhosis (PBC). The prevalence of AMA in the Japanese general population was estimated to be 0.5% (0.2-0.9%) with IF method, 0.7% (0.3-1.1%) with IB method, and the prevalence of PBC was estimated to be 0.1% (0-0.3%). These results were consistent with those of our previous study conducted in Kanto area.

Conclusion: The modified ELISA produces many false positive results when applied to the general population whose pre-test probability is low. Therefore, the cut-off value should be set at a higher level. The prevalence of AMA is approximately 0.5% in the east as well as in the west Japan and there was no regional difference.

14:35～15:25 Program (2)-6

High frequency of the cross-reactivity against *E. coli* derived-pyruvate dehydrogenase complex-E2 in sera from patients with other than PBC

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Antimitochondrial antibodies are a serological hallmark of primary biliary cirrhosis (PBC). Pyruvate dehydrogenase complex-E2 (PDC-E2), a member of the 2-oxo dehydrogenase enzyme complex family, is the primary autoantigen of antimitochondrial antibodies. The PDC-E2 molecule contains antigenic inner lipoyl domains that are highly conserved among various species including bacteria. Human anti-PDC-E2 in PBC patients' sera cross-reacts with *E. coli* PDC-E2 based on molecular mimicry of the common antigenic site. However, the frequency and potency of reactivity with *E. coli* PDC-E2 in sera other than from PBC individuals have not been clarified. In the present study, we investigated immunoreactivity against *E. coli* lysate with sera other than from PBC individuals and compared the frequency and reactive potency of sera from PBC patients. Lysate derived from *E. coli* DH5 alpha was developed with SDS-PAGE and then immunoblotted onto a nitrocellulose membrane. Seventy-seven serum samples from 24 PBC patients and 53 non-PBC individuals (autoimmune hepatitis: 16, primary sclerosing cholangitis: 10, and normal control: 27) were examined for the reactivity against *E. coli* lysate by immunoblotting. The specificity for anti-PDC-E2 of two bands visible at 74-kDa and 52-kDa was confirmed using mouse anti-human monoclonal PDC-E2 antibody (C355.1). The bands were visible for all PBC patient sera by immunoblotting. The same reactivity was also observed in 20-38% of non-PBC sera. However, based on dilution tests, the overall potency was one-hundredth lower than that of PBC sera. Such non-PBC sera cross-reacted with the synthetic peptide derived from *E. coli* PDC-E2. Taken together, using the *E. coli* unique buffer, we succeeded in reducing the optical density values of non-PBC sera for an enzyme-linked immunosorbent assay with recombinant proteins as the antigen for antimitochondrial antibodies. Since weak cross-reactivity with *E. coli* PDC-E2 occurred in sera other than from PBC patients at a high frequency, this was taken to be the cause of the non-specific reaction of non-PBC sera in the recombinant assay.

14:35～15:25 Program (2)-7

Anti-p95c antibody from patients with primary biliary cirrhosis inhibits *in vitro* nuclear envelope assembly and may be identical to p97/VCP

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We have reported previously that p95c, a novel 95-kDa cytosolic protein, was the target of autoantibodies in sera of patients with autoimmune hepatic diseases. We studied 30 sera that were shown previously to immunoprecipitate a 95-kDa protein from [^{35}S]-methionine-labelled HeLa lysates and had a specific precipitin band in immunodiffusion. Thirteen sera were available to test the ability of p95c antibodies to inhibit nuclear envelope assembly in an *in vitro* in which confocal fluorescence microscopy was also used to identify the stages at which nuclear assembly was inhibited. The percentage inhibition of nuclear envelope assembly of the 13 sera ranged from 7% to 99% and nuclear envelope assembly and the swelling of nucleus was inhibited at several stages. The percentage inhibition of nuclear envelope assembly was correlated with the titer of anti-p95c as determined by immunodiffusion. To confirm the identity of this autoantigen, we used a full-length cDNA of the p97/valosin-containing protein (VCP) to produce a radiolabelled recombinant protein that was then used in an immunoprecipitation assay. Our study demonstrated that 12 of the 13 (93%) human sera with antibodies to p95c immunoprecipitated recombinant p97/VCP. Because p95c and p97 have similar molecular masses and cell localization, and because the majority of sera bind recombinant p97/VCP and anti-p95 antibodies inhibit nuclear assembly, this is compelling evidence that p95 and p97/VCP are identical.

14:35～15:25 Program (2)-8

Treatment of PBC by modulating antigen-specific immune response via CD4 T cells

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New therapy with antibodies targeting costimulatory molecules has been identified in autoimmune diseases. Previously it was cleared that activation of CD40 on BEC using recombinant CD40L induce apoptosis. Then it's hypothesized that blocking CD40L from T cells may prevent BEC from apoptosis in PBC. We have established cytotoxic assay of PDC-E2 reactive T cell clones (TCC) to PDC-E2 pulsed BEC. This cytotoxic assay may reflect the bile duct lesions in PBC. To assess the effect of antibody targeting CD40L, this antibody was used in this assay.

In the CTL assay, anti-CD40L antibody had prevented TCC from killing BEC. In the immunohistochemistry, CD40L positive T cells from PBC existed around BEC, on the contrary CD40L positive T cells from other liver diseases did not. The stimulation from TLRs directly influenced the aquired immunity in the CTL assay. New therapy with anti-CD40L antibody has possibility to control the inflammation around BEC in PBC.

15:45～16:35 Program (3)-9

Enhanced- expression of type I IFN and Toll- like receptor- 3, - 4 mRNAs in the liver of primary biliary cirrhosis

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Background and Aims: It is generally believed that primary biliary cirrhosis (PBC) is an autoimmune liver disease. However, there are several reports that microbial agents are involved in the etiology of PBC. To address the pathophysiology of PBC, we examined the expression of messages for various cytokines and toll- like receptors (TLRs) in portal tract and liver parenchyma of PBC.

Methods: Using laser captured microdissection, 18 portal tracts and 9 liver parenchymas were captured from 9 liver biopsy specimens of PBC patients. As a control, 12 portal tracts and 4 parenchymas were captured from 4 specimens of autoimmune hepatitis (AIH) patients, and 6 portal tracts and 3 parenchymas were captured from 3 specimens of chronic hepatitis C (CHC) patients. Total RNA was extracted from these samples. The mRNAs of cytokines (IFN- α, -β, -γ, IL- 1β, -6, -10), and TLRs (-2, -3, -4, -7, -9) were measured by quantitative reverse- transcription polymerase chain reaction. To study the *in situ* localization of type I IFN and TLR-3 proteins, immunostaining was also done using the same specimens.

Results: While almost all mRNAs of cytokines, except IL-10, were detectable in the portal tract, IFN- α and -β (type I IFN) were the only cytokines which were detectable in liver parenchyma. TLRs were all detectable in both portal tract and liver parenchyma. Interestingly, there were positive correlation between TLR-3, 4 and type I IFN in both areas. In addition, the mean values of TLR- 3, - 4 and type I IFN were significantly higher in PBC of both portal tracts and parenchyma than those in AIH and CHC. By immunohistochemistry, TLR-3 was detected in hepatocytes and histiocytes in portal tracts. IFN- α was detected in histiocytes and plasma cells in portal tracts and IFN- β was detected in hepatocytes and histiocytes in portal tracts.

Conclusions: These data indicate that as yet unknown ligands for TLR- 3 and/ or -4 exist in the portal tracts and parenchyma, and that the stimulation by these ligands leads to the sustained production of type I IFN in PBC.

15:45～16:35 Program (3)-10

Intraepithelial lymphocytes of intrahepatic bile ducts: Physiologic distribution and phenotypes and pathologic alterations

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Background and Aims: Mucosa of the luminal tract such as the intestine is equipped with a developed lymphoid tissue, and harbor intraepithelial lymphocytes (IEL). They are known to be involved in the innate immunity and to relate to the pathogenesis of intestinal diseases. So far, there have been no reports on such system along the intrahepatic bile ducts. The present study was aimed to examine the presence of IEL and their presumed roles in the normal and pathologic intrahepatic bile ducts.

Methods:Intraepithelial lymphocytes of intrahepatic bile ducts were surveyed immunohistochemically at the different anatomical levels in four "histologically normal" autopsy livers and in the surgically resected and wedge biopsied liver specimens as "histologically normal" livers, chronic viral hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, extrahepatic biliary obstruction, and hepatolithiatic livers. Immunostaining of leukocyte common antigen (LCA), CD3, CD4, CD8, CD20, and CD57 was done to identify intraepithelial lymphoid cells. CD4 and CD28 double stain was also done.

Results: There were lymphoid cells positive for LCA within the biliary epithelial layer of the intrahepatic bile ducts. They were regarded as biliary intraepithelial lymphocytes (*b*IEL). LCA^+ *b*IEL /1,000 biliary epithelial cells were 11.6 ± 1.9 (mean ± S.D.) at interlobular bile ducts, and their number increased along with the increased size of the intrahepatic biliary tree (33.3 ± 3.8 and 40.5 ± 6.8 at septal and large bile ducts, respectively). A majority of them were positive for CD3 and CD8, and some positive for CD57. In primary biliary cirrhosis, there were significant increase of LCA^+ *b*IEL (205.7 ± 186.3) at the interlobular bile ducts, and an increase of $CD4^+$, $CD8^+$ and $CD20^+$ cells were also evident. About 48 % of $CD4^+$ *b*IEL were negative for CD28 in primary biliary cirrhosis, but not so rich in normal liver (18%), extrahepatic biliary obstruction (30%), and chronic viral hepatitis (25%). In hepatolithiasis, an increase of LCA^+ *b*IEL (81.5 ± 14.6), particularly $CD3^+$ and $CD8^+$ ones, were evident at the intrahepatic large bile ducts. In other diseases, the density and phenotypes of *b*IEL were not different from those of normal livers.

Conclusions: IEL physiologically present in the intrahepatic bile ducts belong to $CD8^+$ T cells or $CD57^+$ cells, similar to IEL of the intestine, though their number were very small, suggesting their limited roles as innate immunity in normal states. Markedly increased $CD8^+$, $CD20^+$ and $CD4^+$, especially $CD4^+CD28^-$ *b*IEL at the interlobular bile ducts of primary biliary cirrhosis and increased $CD8^+$ *b*IEL at the large bile duct in hepatolithiasis seem to be involved in the immunopathogenesis of these diseases.

15:45～16:35 Program (3)-11

FAS-L$^+$CD56$^+$CD3$^+$ cells significantly increase in the liver of patients with late stage primary biliary cirrhosis (PBC) compared with early sitage PBC: possible involvement in the disease progression.

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Backgrounds: Primary biliary cirrhosis (PBC) is an autoimmune cholestatic liver disease characterized by immunological destruction of intrahepatic biliary epithelial cells. Although its pathogenesis has not been clearly elucidated, growing evidence suggests a major role for T cells. However, the liver contains a large population of natural killer (NK) and natural killer T (NKT) cells, and their roles in the pathogenesis of PBC are still unknown.
Aim: To investigate intrahepatic lymphocytes, especially NK and NKT cells, in patients with early and late stage PBC, and to elucidate their roles in the pathogenesis of PBC.
Methods: Liver tissues and heparinized venous blood were obtained from 15 patients with PBC and 7 donors for LDLT as control with written informed consent from each individual. Eight asymptomatic patients who underwent needle liver biopsy were diagnosed as stage I or II (early stage PBC), and 7 patients underwent LDLT (late stage PBC). Mononuclear cells (MNCs) were separated by Ficoll-gradient from peripheral blood and liver tissues, and then various surface markers, including CD3, CD4, CD8, CD25, CD16, CD56, CD57, CD161, CD28, CD152 (CTLA-4), and CD95 ligand (FasL), were analyzed by FACScan. We also investigated the distribution of FasL$^+$ cells in the liver with PBC by immunohistochemical staining according to the avidin-biotin- peroxidase complex method.
Results: The total cell numbers of intrahepatic MNCs were higher in PBC patients than donors. The proportion of CD3$^+$CD56$^+$ NKT cells in the liver of early stage PBC patients was significantly lower than donors (p<0.05), but in late stage patients the proportion of CD3$^+$CD56$^+$ NKT cells in the liver was significantly higher than those in early stage (p<0.05). CD3$^+$CD57$^+$ NKT cells in the liver also constituted significant high proportion in late stage PBC compared with donors (p<0.05). Conventional CD3$^+$CD56$^-$ T cells in the liver constituted significant high proportions in early stage PBC compared with donors (p<0.05), but decreased in late stage PBC. Most of CD3$^+$CD56$^+$ NKT cells in the liver and peripheral blood expressed CD28 in control, but intrahepatic CD3$^+$CD56$^+$ NKT cells in patients with both early and late stage PBC significantly decreased (p<0.01). The expressions of CTLA-4 and FasL on CD3$^+$CD56$^+$ NKT cells in the liver increased with the progression of disease, and were significantly higher in late stage PBC than those in control (p<0.01 and p<0.05, respectively). The increased expression of FasL on the cytoplasm of MNCs infiltrating around the injured bile duct in late stage PBC was confirmed by immunohistochemical staining. Furthermore, we investigated both biopsy samples diagnosed Stage I or II (early stage) and removed liver (late stage) from the same patients who underwent LDLT, and less expression of FasL on MNCs in the liver of early stage than late stage was also confirmed by immunohistochemical staining.
Conclusion: We revealed that activated FasL$^+$ NKT cells constituted significant high proportion in the liver of late stage PBC patients compared with early stage PBC patients and normal donors. NKT cells may play an important role in the progression of bile duct and hepatocyte injury in PBC through Fas/FasL interaction.

15:45～16:35 Program (3)-12

Genome wide analysis of the SNPs that relates to susceptibility to primary biliary cirrhosis in Japanese population

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***Aim*:** The aim of this study is to investigate whether gene polymorphism of CTLA-4, which was reported to associate with the susceptibility to PBC in Caucasian, and IFN-γ that is thought to participate in the pathogenesis of autoimmune disease relate to disease susceptibility to PBC in Japanese. In addition we tried to identify new disease related SNPs by genome wide analysis.

***Patients and Methods*:** 90 PBC patients and 84 controls were studied. The CTLA-4 exon 1 position 49 AG polymorphism was typed by RFLP. The IFN-γ position 874 AT polymorphism was defined by ARMS PCR. The genome wide analysis of SNPs was performed by using GeneChip HuSNP Mapping Array.

***Results*:** Both CTLA-4 GG genotype and IFN-γ TA genotype were significantly over repressed in patients compared to controls (57.3% vs. 40.4%, OR=1.97, 95%CI:1.1-3.6, $p<0.04$), (34.4% vs. 19.0%, OR=2.23, 95%CI:1.1-4.4, $p<0.03$). The risk for PBC of individuals carrying both CTLA-4 GG and IFN-γ TA (OR=5.23) was higher compared with CTLA-4 GG or IFN-γ TA alone (OR=2.34, 2.95), indicating the effect of both genotypes on susceptibility to PBC was additive. The CTLA-4 GG and IFN-γ TA positive patients were resistance to UDCA treatment compared to other patients. Genotypes of 172 known SNPs, which existed on almost every chromosome, were different between CTLA-4 GG positive patients and control.

***Conclusion*:** Genetic polymorphisms of CTLA-4 and IFN-γ related to susceptibility to PBC in Japanese additively and associated with clinical features. In addition, many CTLA-4 relevant SNPs may relate to susceptibility to PBC in Japanese.

16:35～17:25 **Special Lecture**

The Molecular Basis of Primary Biliary Cirrhosis

Professor, Division of Rheumatology, Allergy and Clinical Immunology
University of California at Davis
M.E. Gershwin