non-synonymous polymorphism in exon 4 of the Tapasin gene causing an arginine to threonine change that could affect tapasin function. We have investigated the effect of this SNP in resolving hepatitis C virus (HCV) infection in a cohort of 336 patients from the UK.

**Aim:** We have investigated the effect of the SNP rs2071888 in resolving hepatitis C virus (HCV) infection in a cohort of 336 patients from the UK.

**Method:** Genomic DNA from 216 chronically infected individuals and 120 spontaneous resolvers of HCV was genotyped with an allele specific PCR designed to identify the G/C SNP in exon 4 of the Tapasin gene. Individuals were also typed for HLA-A, -B and -C.

**Results:** Overall the G allele of tapasin was associated with protection against chronic HCV infection (p = 0.018, OR = 1.99, 95% CI 1.14 to 3.46). Interestingly, in combination with heterozygosity at the HLA-B locus, heterozygosity at the tapasin locus was also protective (Abstract OP04 figure 1, p trend = 0.005). Furthermore, we identified specific HLA-B alleles associated with protection in the context of the Tapasin G, but not Tapasin C allele. Specifically the G allele was most protective in the context of B*0702 (p = 0.029, OR = 4.56, 95% CI 1.2 to 17.27), and B*5701 (p = 0.029, OR = 12, 95% CI 1.2 to 120). Tapasin has been shown to bind specifically to amino acids 114 and 116 of HLA class I. Consistent with this functional interaction we found that aspartate at position 114 and serine at 116 were most beneficial in the context of both the G allele (D114/TapG, p < 0.0001, OR = 3.3, 95% CI 1.83 to 5.98; S116/TapG, p < 0.0001, OR = 2.73, 95% CI 1.57 to 4.76).

**Conclusion:** The G allele of tapasin was associated with protection from chronic HCV infection, both alone and in combination with specific HLA class I alleles. Individuals who are heterozygous for both tapasin and HLA-B are relatively protected from chronic HCV infection. This heterozygosity may allow them to present a broader range of peptides to CTL and thus mount a more effective anti-HCV immune response.

**Basic science**

**OP06** MATERNAL OBESITY PROGRAMS OFFSPRING INNATE IMMUNE DYSREGULATION IN NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** Obesity induced, non-alcoholic fatty liver disease (NAFLD), is the major cause of chronic liver dysfunction. In tandem, obesity and NAFLD rates in reproductive age women are rising. We have previously reported increased susceptibility to NAFLD in offspring exposed to maternal obesity via programming.

**Aim:** Our aim is to investigate the effects of maternal obesity on hepatic innate immune function in a more physiologically relevant model of NAFLD.

**Method:** Female mice were fed standard or obeseogenic chow, before, throughout pregnancy and in lactation. Offspring were then weaned onto either standard or obeseogenic chow and studied at 5, 6 and 12 months. Read-outs included biochemical and histological indicators of NAFLD and fibrosis, hepatic triglycerides, gene expression analysis of pro-fibrotic pathways, FACS analysis of liver innate immune cells and flow cytometric detection of ROS.

**Results:** Offspring only exposed to a post-weaning hyper-caloric diet (Group 2) exhibited raised leptin, ALT and hepatic triglycerides, gene expression analysis of pro-fibrotic pathways, FACS analysis of liver innate immune cells and flow cytometric detection of ROS.

**Conclusion:** We demonstrate that comorbidities significantly impact on the outcome of patients with chronic liver disease at TA, on wait-list and post LT survival. Adding CCI to known liver prognostic models may improve their prediction ability.