Results A number of peaks were identified in the patients with cirrhosis which were absent or present in significantly different quantities in ten healthy controls. Discriminant analysis allowed the generation of two classification equations using standardised data from 12 peaks to build a predictive model for HE. This model correctly classified all patients from the original population (Abstract P15 figure 1).

Conclusion Analysis of VOCs in breath samples identifies patients with HE with a high degree of accuracy. Future work will validate this classification equation in a new group of patients, while identification of the individual compounds involved will provide insights into the pathogenesis of the syndrome and potential new therapeutic targets.

P15 multiple defects of the immunoregulatory system contribute to the development of autoimmune hepatitis

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Introduction Concordance for autoimmune hepatitis (AIH) is rare within families, though non-hepatic autoimmune disorders are frequent among first degree relatives (FDR) of AIH patients. While a defect in immunoregulation has been demonstrated in AIH patients, the mechanism preventing the development of AIH in FDR, who share genetic background, remains to be elucidated.

Aim To investigate multiple immunoregulatory systems in AIH patients and their FDR.

Method 44 children with AIH (3 AIH-1 and 11 AIH-2, median age 13.5 yrs, 23 females), 65 FDR from 34 families [23 fathers, 47 yrs (38–58); 28 mothers, 44 yrs (24–55) and 14 siblings, 7 females, 15 yrs (5–24)] and 42 healthy subjects [HS, 36 yrs (22–54), 37 females] were studied. Frequency of conventional CD4posCD25neg regulatory T-cells (T-regs), CD4posCD25high regulatory T-cells (Tregs), CD4posCD25posCD127neg cells, CD3negCD56pos natural killer (NK) cells, CD5posTCRva24pos/TCRvb11pos invariant NKT cells (iNKT) was defined by flowcytometry. Tregs and CD4posCD1pos cells were purified from PBMCs using immunomagnetic beads. CD25neg and PD-1neg cells (responders) were co-cultured for 5 days with cells with regulatory potential and their proliferation was measured by 3H-thymidine incorporation.

Results Conventional Tregs were lower in patients (10.5%±1.1) than FDR (15.9%±1.1, p=0.001) and HS (14.7%±1.7, p=0.04), while ‘True’ Tregs were similar in all (6.0%±0.6, 6.3%±0.4 and 6.2%±0.5). CD4posPD-1pos T-cells were lower in patients (17.0%±2.0) and in FDR (19.6%±2.1) than in HS (30.5%±2.0, p=0.0001 for patients and p=0.0007 for FDR). NK cells were lower in patients (8.6%±1.2) than in FDR (15.8%±1.2, p=0.0004) and HS (12.3%±0.9, p=0.02). CD8posCD25neg T cells in patients tended to be lower (8.8%±1.46) than in FDR (12.4%±1.56, p=0.18) and HS (13.1%±1.62, p=0.11). The frequency of iNKT cells was similar in all groups. ‘True’ Tregs decreased CD25neg cell proliferation by 15.8% in patients, 28.2% (p=0.007) in FDR and 56.9% (p<0.0001) in HS, while CD4posPD-1pos T cells decreased similarly PD-1neg cell proliferation in patients (25.4%), FDR (22.5%) and HS (26.8%).

Conclusion A numerical impairment of CD4posPD-1neg T cells in patients and their FDR suggests that these defects are genetically determined and account for family clustering of autoimmune disorders. A numerical impairment of conventional Tregs and functional impairment of CD4posCD25posCD127neg ‘True’ Tregs, confined to patients with AIH, may be crucial to loss of liver tolerance.