

SUPPLEMENTARY INFORMATION

Supplementary Table 1: Genotype frequency of *TM6SF2* rs58542926 in Discovery Cohort NAFLD patients vs. the 1000 Genomes European Caucasian population sample.

<i>TM6SF2</i> Genotypes	NAFLD N=349 (%)	EUR Pop. N=379 (%)	OR (95% CI)	P-value
CC	271 (77.6%)	328 (86.5%)	-	-
CT	70 (20%)	49 (12.9%)	OR 1.72 (1.16-2.57)	0.008
TT	8 (2.3%)	2 (0.5%)	OR 4.84 (1.01-22.9)	0.049

ChiSq for trend $p=0.0008$ ($X^2=11.34$, $df=1$).

1000 Genomes MAF (EUR) = 0.07 (<http://browser.1000genomes.org>).

Supplementary Table 2: Genotype frequency of *PNPLA3* rs738409 in Discovery Cohort NAFLD patients vs. the 1000 Genomes European Caucasian population sample.

<i>PNPLA3</i> Genotypes	NAFLD N=349 (%)	EUR Pop. N=379 (%)	OR (95% CI)	P-value
CC	152 (43.5%)	233 (61.5%)	-	-
CG	148 (42.4%)	128 (33.8%)	OR 1.77 (1.29-2.42)	0.0003
GG	49 (14%)	18 (4.7%)	OR 4.17 (2.34-7.43)	3.04 x10⁻⁷

ChiSq for trend $p<0.0001$ ($X^2=31.29$, $df=1$).

1000 Genomes MAF (EUR) = 0.22 (<http://browser.1000genomes.org>).

Supplementary Table 3: Comparison of the FLIP SAF Score and the NAFLD CRN (Kleiner) Score for the histological grading and staging of NAFLD/NASH.

SAF Score ^{1,2}			Kleiner Score ³		
Histological Feature	Category Definition		Histological Feature	Category Definition	
Steatosis	0	<5%	Steatosis	0	<5%
	1	5-33%		1	5-33%
	2	34-66%		2	34-66%
	3	>66%		3	>66%
(S) Steatosis Score 0-3			PLUS		
Hepatocyte Ballooning	0	None	Hepatocyte Ballooning	0	None
	1	Clusters of hepatocytes with rounded shape and pale cytoplasm		1	Few
	2	Same as grade 1 with enlarged hepatocytes (>2x normal size)		2	Many
PLUS			PLUS		
Inflammation	0	None	Inflammation	0	None
	1	< 2 foci per 20x field		1	1-2 foci per x20 field
	2	> 2 foci per 20x field		2	2-4 foci per x20 field
(A) Total = Activity Score 0-4				(NAS) Total = NAFLD Activity Score 0-8	
Fibrosis	0	No fibrosis	Fibrosis	0	No fibrosis
	1a	Zone 3 mild perisinusoidal fibrosis		1a	Zone 3 mild perisinusoidal fibrosis
	1b	Zone 3 moderate perisinusoidal fibrosis		1b	Zone 3 moderate perisinusoidal fibrosis
	1c	Periportal/portal fibrosis only		1c	Periportal/portal fibrosis only
	2	Zone 3 plus portal/periportal fibrosis		2	Zone 3 plus portal/periportal fibrosis
	3	Bridging fibrosis		3	Bridging fibrosis
	4	Cirrhosis		4	Cirrhosis
(F) Fibrosis Stage 0-4			Fibrosis Stage 0-4		

Table modified from (Dyson et al, 2013⁴) with permission.

SUPPLEMENTARY REFERENCES

1. Bedossa P, *et al.* Histopathological algorithm and scoring system for evaluation of liver lesions in morbidly obese patients. *Hepatology* **56**, 1751-1759 (2012).
2. Bedossa P, *et al.* Utility and appropriateness of the FLIP algorithm and SAF score in the evaluation of biopsies of nonalcoholic fatty liver disease. *Hepatology*, (2014).
3. Kleiner DE, *et al.* Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* **41**, 1313-1321 (2005).
4. Dyson JK, McPherson S, Anstee QM. Non-alcoholic fatty liver disease: non-invasive investigation and risk stratification. *Journal of clinical pathology* **66**, 1033-1045 (2013).