Supplemental Material to:

Aloysious Aravinthan, George Mells, Michael Allison,
Julian Leathart, Anna Kotronen, Hannele Yki-Jarvinen,
Ann K Daly, Christopher P Day, Quentin M Anstee,
and Graeme Alexander

Gene polymorphisms of cellular senescence marker p21
and disease progression in non-alcohol-related fatty liver
disease

Supplementary Tables

Supplementary table 1A: Covariate analysis of rs762623 and rs2395655

SNP	OR (L95–U95)	p-value
rs762623	1.968 (1.007–3.846)	0.048
rs2395655	1.418 (0.947–2.123)	0.090

Supplementary table 1B: Covariate analysis of rs762623 and rs3176329

SNP	OR (L95–U95)	p-value
rs762623	2.207 (1.213–4.014)	0.009
rs3176329	0.630 (0.369–1.075)	0.090

Results of logistic regression analysis of rs2395655 conditioned on rs762623 (supplementary table 4A), and rs3176329 conditioned on rs762623 (supplementary table 4B). Note that in the analyses conditioned on rs762623, association with rs2395655 and rs3176329 is no longer significant, reflecting linkage disequilibrium between these SNPs and showing that their effects are not completely independent. OR, odds ratio; L95, lower 95% confidence interval of the OR; U95, upper 95% confidence interval of the OR.

Supplementary table 2A: Covariate analysis of rs762623 (*CDKN1A*) and rs738409 (*PNPLA3*) in the UK cohort

SNP	OR (L95–U95)	p-value
rs762623	2.335 (1.285–4.244)	0.005
rs738409	1.715 (1.195–2.460)	0.003

Results of logistic regression analysis of rs738409 conditioned on rs762623. OR, odds ratio; L95, lower 95% confidence interval of the OR; U95, upper 95% confidence interval of the OR.

Supplementary table 2B: Covariate analysis of rs762623 (*CDKN1A*) and rs738409 (*PNPLA3*) in the Finnish cohort

SNP	OR (L95–U95)	p-value
rs762623	2.410 (1.149–5.056)	0.019
rs738409	2.429 (1.289–4.577)	0.006

Results of logistic regression analysis of rs738409 conditioned on rs762623. OR, odds ratio; L95, lower 95% confidence interval of the OR; U95, upper 95% confidence interval of the OR.

Supplementary table 3: Multivariate analysis of rs762623 in the UK cohort (n=304)

Variable	OR (L95–U95)	p-value
Male sex	1.280 (0.729–2.250)	0.390
Age (years)	1.021 (1.000–1.042)	0.046
BMI	1.077 (1.022–1.135)	0.005
DM	2.302 (1.346–3.936)	0.002

rs762623-A	2.195 (1.179–4.084)	0.013

Results from multivariate logistic regression analysis of rs762623 and clinical covariates in the UK cohort. Note that in this analysis, association with rs762623 remained significant at p<0.05, indicating that the effect of the SNP is independent of clinical variables included in the model. OR, odds ratio; L95, lower 95% confidence interval of the OR; U95, upper 95% confidence interval of the OR; BMI, body mass index; DM, diabetes mellitus

Supplementary table 4: Multivariate analysis of rs762623 in the Finnish cohort (n=121)

Variable	OR (L95–U95)	P-value
Male sex	0.945 (0.406–2.199)	0.8949
Age (years)	1.024 (0.978–1.072)	0.3152
BMI	1.022 (0.976–1.070)	0.3509
DM	3.172 (1.272–7.912)	0.0133
rs762623-A	2.546 (1.170–5.540)	0.0184

Results from multivariate logistic regression analysis of rs762623 and clinical covariates in the Finnish cohort. Note that in this analysis, association with rs762623 remained significant at p<0.05, indicating that the effect of the SNP is independent of clinical variables included in the model. OR, odds ratio; L95, lower 95% confidence interval of the OR; U95, upper 95% confidence interval of the OR; BMI, body mass index; DM, diabetes mellitus

Supplementary table 5: Multivariate analysis of rs762623 in the combined UK and Finnish cohort

Variable	OR (L95–U95)	P-value
Male sex	1.144 (0.716–1.829)	0.566
Age (years)	1.020 (1.001–1.040)	0.030
BMI	1.046 (1.011–1.082)	0.008
DM	2.500 (1.570–3.981)	0.0001
UK ethnicity	5.056 (2.829–9.036)	2.37E-08
rs762623-A	2.444 (1.487–4.017)	0.0003

Logistic regression to determine the effect of rs762623 on fibrosis in the combined UK and Finnish Cohort, with ethnicity, sex, age, DM and BMI included as covariates. Controls are patients with steatosis but no fibrosis on liver biopsy (fibrosis stage = 0). Cases are patients with steatosis and ANY fibrosis on liver biopsy (fibrosis stage ≥1). A log-additive genetic model is assumed. OR odds ratio; L95 lower 95% confidence interval of the odds ratio; U95 upper 95% confidence interval of the odds ratio.

Supplementary table 6: Multinomial logistic regression analysis of diabetes mellitus with nationality included as a covariate

Fibrosis	OR (L95–U95)	p-value
Stage 0 versus stage 1	2.314 (1.393–3.842)	0.0012
Stage 0 versus stage 2	1.902 (0.981–3.685)	0.0568
Stage 0 versus stage 3	5.633 (2.935–10.81)	2.01E-07
Stage 0 versus stage 4	7.491 (3.248–17.27)	2.32E-06
Stage 1 versus stage 2	0.822 (0.416–1.623)	0.5723

Stage 1 versus stage 3	2.435 (1.248–4.750)	0.0091
Stage 1 versus stage 4	3.238 (1.388–7.550)	0.0065
Stage 2 versus stage 3	2.962 (1.367–6.417)	0.0059
Stage 2 versus stage 4	3.939 (1.555–9.978)	0.0038
Stage 3 versus stage 4	1.330 (0.532–3.324)	0.5420

Multinomial logistic regression to determine the effect of diabetes mellitus on the development of different stages of fibrosis in the combined UK and Finnish Cohort, with nationality included as a covariate. The reference level of fibrosis ranges from fibrosis stage 0 to 4.