

Assessment of TLL1 variant and risk of hepatocellular carcinoma in Latin Americans

Dhamina Karim¹, Jhon Prieto², Domingo Balderramo³, Javier Diaz Ferrer⁴, Angelo Z. Mattos⁵, Marco Arrese⁶, Enrique Carrera⁷, Manaswita Tappata¹, Zwier M.A. Groothuisink⁸, Jeffrey Oliveira⁸, Andre Boonstra⁸, Jose D. Debes¹

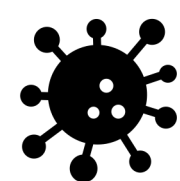
Introduction



Hepatocellular carcinoma (HCC) is an important global health problem accounting for 800,000 deaths per year.



Recently, assessment of host genetics by identification of **single nucleotide polymorphisms (SNPs)** has shown to play a crucial role in identifying those at risk for HCC.



Tolloid like protein 1 (TLL1) is one such SNP found on chromosome 4 which has been mainly shown to increase risk in hepatitis C virus (HCV)-associated HCC.



Most studies addressing its risk-association have been performed in **Asian** populations.

Methods

- A cross-sectional analysis performed in South American and Netherland individuals through the **ESCALON network**.

- We analyzed DNA from 372 HCC patients and 792 controls from Argentina, Chile, Brazil, Colombia, Ecuador, and Peru for the **variant rs1704200** in *TLL1* using TaqMan-genotyping assay.

- Multiple logistic regression was used to evaluate the association between *TLL1* and HCC.



Results

| Characteristics | South American | Netherlands |
|-------------------------------|----------------|-------------|
| HCC (N = 372) | 183 | 189 |
| Age, median (IQR) | 68 (61, 73) | 68 (62, 71) |
| Male, N (%) | 108 (59%) | 145 (77%) |
| Cirrhosis, N (%) | 170 (93%) | 150 (79%) |
| Cause of Liver Disease, N (%) | | |
| Hep B Virus | 6 (3%) | 23 (12%) |
| Hep C Virus | 28 (15%) | 23 (12%) |
| NAFLD/NASH | 87 (48%) | 38 (20%) |
| Alcohol | 51 (28%) | 70 (37%) |
| No HCC (N = 792) | 502 | 290 |
| Age, median (IQR) | 62 (55, 69) | 57 (46, 66) |
| Male, N (%) | 229 (46%) | 184 (63%) |
| Cirrhosis, N (%) | 345 (69%) | 148 (53%) |
| Cause of Liver Disease, N (%) | | |
| Hep B Virus | 16 (3%) | 83 (29%) |
| Hep C Virus | 36 (7%) | 79 (27%) |
| NAFLD/NASH | 263 (53%) | 51 (18%) |
| Alcohol | 77 (15%) | 34 (12%) |

Table 1. Characteristics of patients with HCC and no HCC in South America and Netherlands

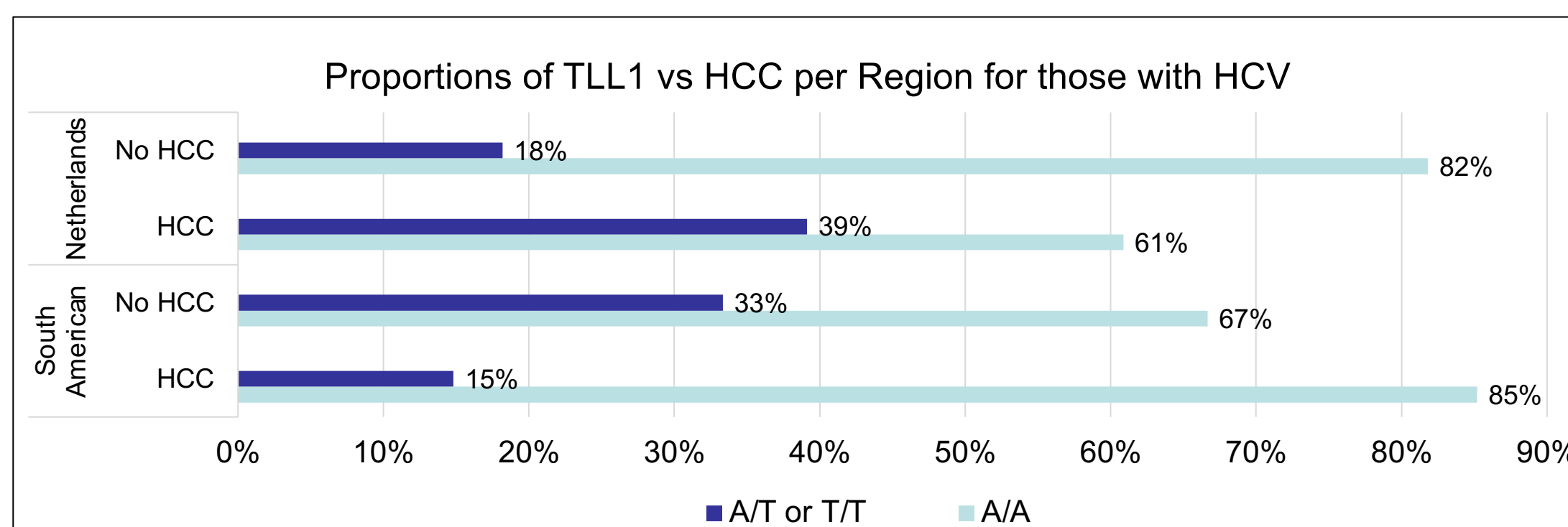


Figure 1. Proportions of TLL1 vs HCC per Region for those with HCV

Results

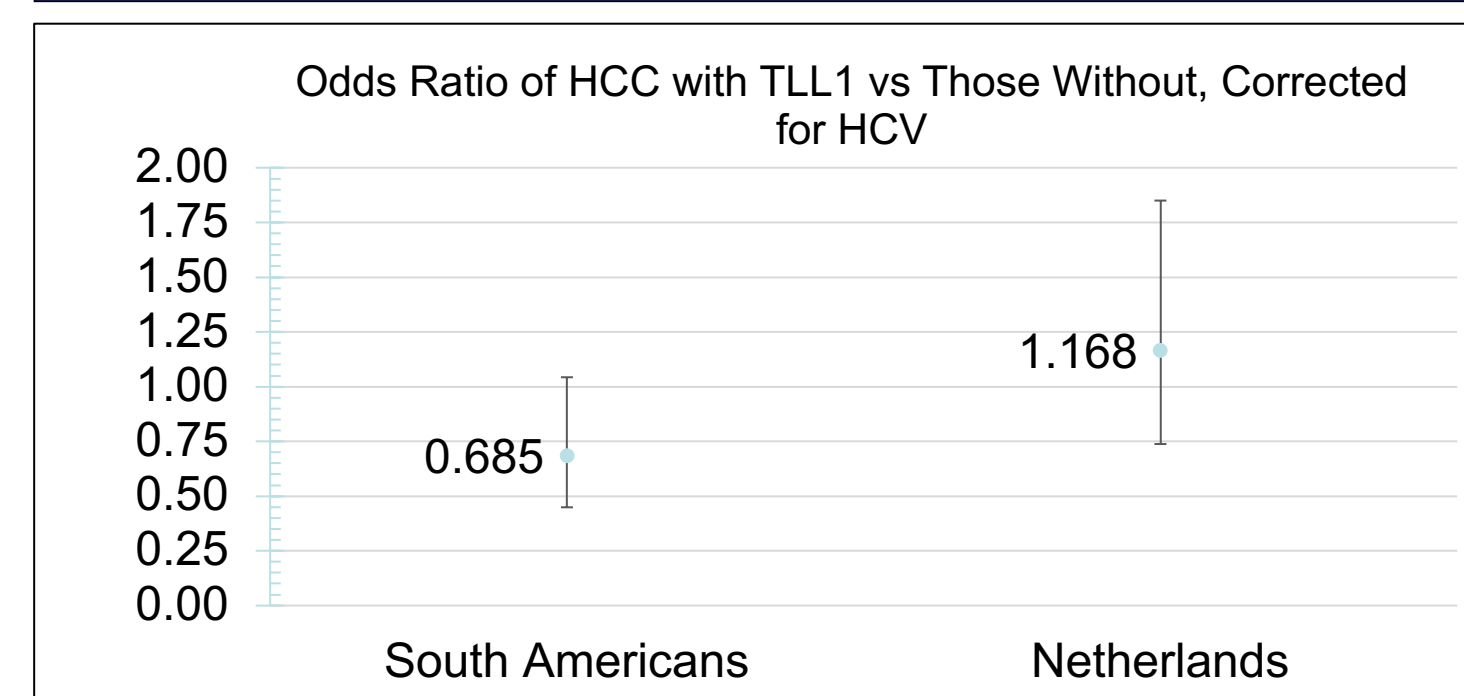


Figure 2. Odds ratio of HCC in those with TLL1 variant versus those without

Conclusions

- The association between *TLL1* mutations do not seem to be significantly associated with HCC development in either population. However, there are **lower odds** of having HCC for those with the *TLL1* variant in the South American population.
- Further GWA studies of HCV related HCC in different ethnicities are required which may serve as a potential marker for screening patients with high risk of HCC.

Affiliations

- University of Minnesota, Minneapolis, MN, USA
- Centro de Enfermedades Hepaticas y Digestivas, Bogotá, Colombia
- Hospital Privado Universitario de Córdoba, Córdoba, Argentina
- Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru
- Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil
- Pontificia Universidad Católica de Chile, Santiago, Chile
- Universidad San Francisco de Quito, Quito, Ecuador
- Erasmus University Rotterdam, Rotterdam, Netherlands