Assessment of *STAT4* variant and risk of Hepatocellular carcinoma in Latin Americans and Europeans

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INTRODUCTION

- Assessment of host genetics by identification of single nucleotide polymorphisms (SNPs) has shown to play a crucial role in identifying individuals at a risk for hepatocellular carcinoma (HCC).
- A point mutation (G for T) in the signal transducer and activator of transcription 4 (STAT4) has been found to increase risk in hepatitis B virus (HBV)-associated HCC.
- However, most studies addressing its risk association have been performed in Asian populations.

METHODS

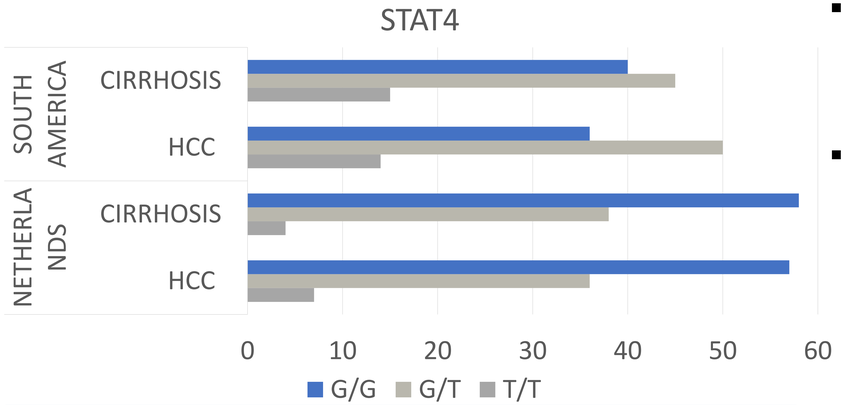
- This is a cross-sectional study performed in Latin American and European individuals through our ESCALON network.
- We analyzed 270 HCC blood samples and 343 cirrhotic controls from Argentina, Chile, Colombia, Ecuador, Peru, and the Netherlands for the variant rs7574865 in STAT4. A mutation in the STAT4 was genotyped using TaqMan-genotyping assay.
- Chi-Squared and Fisher's Exact test were used to evaluate the association between STAT4 and HCC.

RESULTS

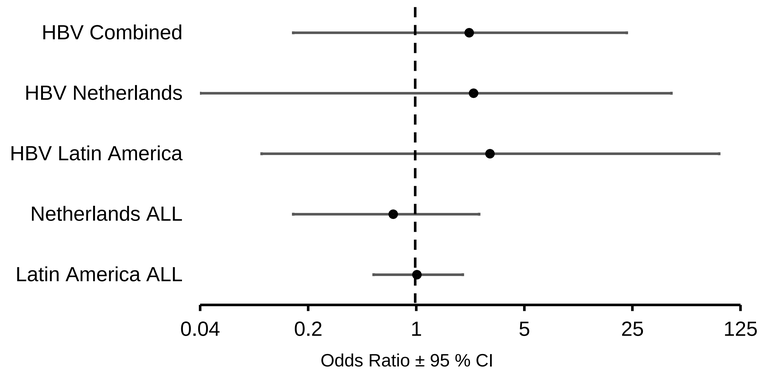
Basic patient characteristics

Characteristics	South America	Netherlands
HCC (n = 270)	n = 117	n=153
Age [median (IQR)] years	68 (62 – 72)	67 (61 – 71)
Male, % (n)	61 (71)	75 (114)
Cause of Liver disease, %(n)		
Hep. B virus (HBV)	4 (5)	16 (25)
Hep. C virus (HCV)	11 (13)	9 (14)
NAFLD/NASH	**49 (57)**	19 (29)
Alcohol	24 (28)	**33 (51)**
Other	12 (14)	22 (34)
Cirrhosis (n =343)	n = 264	n = 79
Age [median (IQR)] years	64 (58 – 70)	61 (53 – 67)
Male, % (n)	52 (137)	68 (54)
Cause of Liver disease, % (n)		
Hep. B virus (HBV)	2 (6)	2 (3)
Hep. C virus (HCV)	6 (17)	**66 (52)**
NAFLD/NASH	**59 (155)**	13 (10)
Alcohol	15 (40)	11 (9)
Other	17 (46)	8 (6)

Proportion of risk genetic variants per region



Odds of HCC comparing carriers of G allele to zero risk allele



- OR for HCC among Latin Americans with risk allele was 1.01 (CI 0.53-2.00), p=1 and among Europeans 0.71 (CI 0.16-2.55), p=0.78
- HBV related HCC – OR of 2.20 (CI 0.16-23.00), p=0.58 in carriers of G mutation for the entire cohort, OR of 3.00 (CI 0.1-90.96), p=1 for Latin Americans and OR of 2.35 (0.04-44.71), p=0.47 among Europeans.

CONCLUSIONS

- STAT4 mutations do not seem to associate with HCC development in Latin American or European populations.
- In those with HBV-related HCC there seems to be an increase OR for presence of G allele, but with a large CI (needing further verification). A larger study (on going) is necessary to confirm these findings.

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