



## Short mucin 1 alleles are associated with low virulent *H pylori* strains infection

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### TO THE EDITOR

We read with interest the article published by Nguyen *et al*<sup>[1]</sup> in the World Journal of Gastroenterology, showing an association between short MUC6 alleles and *H pylori* infection. These results, together with previous observations by Vinall *et al*<sup>[2]</sup>, reinforce the role of mucin genes (MUC6 and MUC1) VNTR polymorphisms for the variability in individual susceptibility to *H pylori* infection that cannot be explained by differences in environmental factors.

We conducted a similar analysis based on a previously described<sup>[3]</sup> survey of gastric pathology in shipyard workers at Viana do Castelo, north of Portugal. Briefly, volunteer workers underwent an upper digestive endoscopy, completed symptoms and lifestyle questionnaires, and had a blood sample drawn. *H pylori* infection status was determined by serology and PCR, and typing of *cagA*, *vacA s* and *vacA m* was performed directly in gastric biopsy specimens by multiplex PCR and reverse hybridization<sup>[4]</sup>. The MUC1 gene polymorphisms were evaluated by Southern blot analysis<sup>[5]</sup>.

Information on MUC1 genotypes and *H pylori* infection status was available for 216 subjects (median age: 43 years; 91% males). For analysis, each participant was considered

infected if positive by either serology or PCR ( $n = 172$ , 79.6%), and classified according to MUC1 genotype [long-long (LL), long-short (LS), short-short (SS)]. Data on *H pylori* genotypes were available for 161 participants. The association between MUC1 genotypes and *H pylori* infection was quantified through the calculation of odds ratios (OR) and the respective 95% confidence intervals (CI) by unconditional logistic regression using STATA<sup>®</sup>, version 9.2.

Short MUC1 alleles were associated with *H pylori* infection (SS *vs* LL: OR = 2.7, 95%CI: 1.0-7.1; LS *vs* LL: OR = 1.6, 95% CI: 0.7-3.7). The risk of infection (SS *vs* LL) was increased nearly three-fold for low-virulent strains (*cagA*<sup>+</sup>, *vacA s2* or *vacA m2*) and less than two-fold when considering high-virulent *H pylori* strains (Table 1).

The present study, performed in a population at high risk for gastric cancer, confirms earlier findings on the effect of mucin genes VNTR variability on *H pylori* infection, and adds to previous investigations the evidence of a stronger association between the short mucin alleles and low-virulent strains. However, an increased risk of infection also with high virulence strains cannot be excluded and may be shown in investigations with larger sample sizes, powered enough to disclose an association of this magnitude.

Our results are compatible with previous findings of an increased risk for both intestinal metaplasia<sup>[5]</sup> and gastric carcinoma<sup>[6]</sup> in individuals with short MUC1 mucin alleles, but additional studies should explore the combined effect of *H pylori* genotypes and mucin genes polymorphism on the infection outcome.

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Table 1 Association between MUC1 polymorphisms and *H pylori* infection according to bacterial genotype

	<i>H pylori</i> negative <i>n</i> (%)	<i>H pylori</i> positive											
		<i>cagA</i> genotypes				<i>vacA s</i> genotypes				<i>vacA m</i> genotypes			
		<i>cagA</i> <i>n</i> (%)	OR (95% CI)	<i>cagA</i> <sup>+</sup> <i>n</i> (%)	OR (95% CI)	<i>s</i> <sub>2</sub> (95% CI)	OR (95% CI)	<i>s</i> <sub>1</sub> or <i>s</i> <sub>1</sub> / <i>s</i> <sub>2</sub> <i>n</i> (%)	OR (95% CI)	<i>m</i> <sub>2</sub> <i>n</i> (%)	OR (95% CI)	<i>m</i> <sub>1</sub> or <i>m</i> <sub>1</sub> / <i>m</i> <sub>2</sub> <i>n</i> (%)	OR (95% CI)
MUC1 genotypes													
LL	10 (25.6)	8 (20.5)	1 [reference]	21 (53.8)	1 [reference]	5 (12.8)	1 [reference]	24 (61.6)	1 [reference]	8 (20.5)	1 [reference]	21 (53.9)	1 [reference]
LS	25 (24.5)	30 (29.4)	1.5 (0.5-4.4)	47 (46.1)	0.9 (0.4-2.2)	24 (23.5)	1.9 (0.6-6.4)	53 (52.0)	0.9 (0.4-2.1)	34 (33.3)	1.7 (0.6-4.9)	43 (42.2)	0.8 (0.3-2.0)
SS	9 (14.1)	22 (34.4)	3.1 (0.9-10.2)	33 (51.6)	1.8 (0.6-5.0)	16 (25.0)	3.6 (0.9-13.7)	39 (61.0)	1.8 (0.6-5.1)	23 (35.9)	3.2 (1.0-10.7)	32 (50.0)	1.7 (0.6-4.9)

LL: long-long; LS: long-short; SS: short-short; OR: odds ratio CI: confidence interval.

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