ΠΡΟΣΚΕΚΛΗΜΕΝΕΣ ΞΕΝΟΓΛΩΣΣΕΣ ΑΝΑΚΟΙΝΩΣΕΙΣ ΕΛΛΗΝΩΝ ΕΡΕΥΝΗΤΩΝ

● META-ANALYSIS ON THE RELATIONSHIPS BETWEEN *H. pylori* INFECTION AND COLON CANCER

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H. pylori is an important causative factor in gastric carcinogenesis. However its role in colon cancer is controversial.

Aim: The main aim of this study was to explore the relationship between *H. pylori* infection and this malignancy by meta-analyzing all relevant cohort and case-control studies. Secondary aims were to investigate the possible sources of heterogeneity between studies and to look for the existence of publication bias.

Methods: Extensive Medline English language medical literature searches for human studies were performed through March 2010, using suitable keywords. Pooled estimates were obtained using fixed or random-effects models as appropriate. Heterogeneity between studies was evaluated with the Cochran Q test whereas the likelihood of publication bias was assessed by constructing funnel plots. Their symmetry was estimated by the Begg and Mazumdar adjusted rank correlation test and by the Egger's regression test.

Results: For colon cancer the pooled odds ratio (OR) with 95% confidence intervals (CI) were 1. 44 (1.02–2.02), test for overall effect $Z = 2$, $p = 0.038$. The heterogeneity Q value was 10.5, $I^2 = 52.3$, $p = 0.062$. There was no publication bias (Begg and Mazumdar adjusted rank correlation test p two tailed value 0.7, Egger's regression test p value 0.09).

Conclusion: The results of this study showed a statistically significant relationship between *H. pylori* infection and colon cancer.

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● RISK FACTORS FOR *H. pylori (Hp)* INFECTION: A PROSPECTIVE CASE-CONTROL STUDY

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Background: *Hp* infection consists a significant health-related issue worldwide but few data are available regarding predisposing risk factors for infection acquisition.

Aim: To calculate prospectively several predefined risk factors for acquisition of *Hp* infection.

Patients and Methods: Cases (*Hp*+) and controls (*Hp*-) were matched only to the number. Predefined risk factors studied were: age, sex, nationality, education and socioeconomic status, diabetes mellitus, arterial hypertension, hyperlipidemia, thyroid disease, number of kids, smoke or alcohol abuse, and the use of NSAIDs. Statistical analysis was performed with logistic regression analysis.

Results: 50 consequetive cases and 50 controls were studied. 31 (62%) females - 19 (38%) males (cases) and 29 (58%) females - 21 (42%) males (controls). Mean age was 57.22 y and 52.7 y for cases and controls respectively. 86% of cases and 90% of controls were of Greek origin. Of the cases 44% had primary education and from the controls 48% had secondary education. Low income had 48% of the cases and 26% of the controls. Figures for diabetes mellitus were 16%, hypertension 38%, hyperlipidemia 19%, thyroid disease 18%, high alcohol consumption 3%, smoking 44% and NSAIDs use 16% of cases. Respective figures were 12%, 17%, 13%, 11%, 7%, 42% and 4% for the controls. Logistic regression analysis showed that low-income patients were most likely (58%) to be *Hp*(+) compared with high-income controls (48%) (95% CI). High-income individuals had a 92% less probability for being *Hp*+.

Conclusion: In the cohort studied, low income was the only statistically significant risk factor for *Hp* infection acquisition.

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● ACCURACY OF A TRIPLE MOLECULAR GENETIC TEST FOR *H. pylori (Hp)* INFECTION AND ITS RESISTANCE TO FLUOROQUINOLONES AND CLARITHROMYCIN: PRELIMINARY RESULTS

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Background: Diagnosis and treatment of *Hp* infection consists a very frequent and important task in routine clinical practice.

Aim: To assess the applicability, efficacy and accuracy of a triple molecular genetic test for identification of *Hp* infection and its resistance to fluoroquinolones and/or clarithromycin.

Patients and Methods: Thirty-six consecutive patients undergone upper GI endoscopy due to various upper GI tract symptoms. *Hp* infection was assessed by a RUT test (CLO), histology of gastric biopsies (2 antral and 2 corpus specimens) and the GenoType Helico DR [based on the DNA strip technology for the identification of *Hp* and its resistance to fluoroquinolones and/or clarithromycin through the detection of the most significant mutations of the gyrA gene (codons 87 and 91) for fluoroquinolones and the examination of 23S gene (positions 2146 and 2147) for clarithromycin]. The biopsy samples for the GenoType Helico DR were analyzed into three steps which included DNA extraction, amplification and hybridization.

Results: Endoscopic biopsies were processed with the three *Hp* detection methods. There was concordance of the three detection methods in 28/36 (78%) patients. In 4 patients histology was negative for *Hp*, while both CLO test and GenoType Helico DR were positive and in another 4 patients CLO test was positive while histology and GenoType Helico DR were negative. Resistance to clarithromycin was detected in 4/24 (16,5%) and to fluoroquinolones in 4/24 (16,5%) of *Hp*+ patients.

Conclusions: The triple molecular genetic test looks promising for both the detection of *Hp* infection and its resistance to fluoroquinolones and/or clarithromycin.

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● PYK2 INTERACTION WITH CagA PROTEIN IS CONCOMITANT WITH PYK2 INCREASED TYROSINE PHOSPHORYLATION AND REDUCED PAXILLIN EXPRESSION IN *H. pylori*-INFECTED GASTRIC EPITHELIAL CELLS

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The calcium-dependent proline-rich tyrosine kinase-2 (Pyk2/CAKβ/RAFTK), closely related to FAK, has been recently implicated with cytoskeletal remodeling, proliferation and motility of epithelial cells and fibroblasts. Our aim was to investigate whether PYK2 may be implicated in CagA-induced alterations of signalling involved in cytoskeletal homeostasis.

Gastric epithelial cells (AGS) were infected with isogenic CagA-positive strains harbouring variable number of EPIYA-C motifs and the respective Δ*cagA* strains in the presence or absence of serum. Potential physical interactions of CagA with FAK, PYK2, p130Cas, Paxillin, Crk-L, SHP2, c-Src were investigated following immunoprecipitation with anti-CagA antibody and western blot analysis. Tyrosine phosphorylation levels of all proteins were detected in total cell lysates following anti-phosphotyrosine immunoprecipitation. Intracellular localization was investigated utilizing confocal laser scanning microscopy.

We observed an interaction between CagA and PYK2 with maximum levels at 60 min post infection, under our experimental conditions. Total PYK2 tyrosine phosphorylation levels were increased, with a concomitant reduction in tyrosine phosphorylated FAK, although PYK2 or FAK expression remained unchanged. Paxillin expression was reduced in a CagA-dependent manner, whereas p130Cas, Crk-L and SHP2 levels remained unaffected. In serum deprived cells, increased expression of PYK2 was observed only in loosely attached cells at earlier time points, upon infection with strains harbouring more EPIYA-C repeats in CagA.

Our data suggest a CagA-PYK2 interaction that may depend on the number of EPIYA-C repeats and is accompanied by increased levels of PYK2 tyrosine phosphorylation and concomitant reduction of tyrosine phosphorylated FAK along with perturbation of Paxillin expression in *H. pylori*-infected cells.

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● VARIABILITY IN LEWIS ANTIGEN EXPRESSION IN *H. pylori*-INFECTED GREEK CHILDREN: PREPONDERANCE OF NONTYPEABLE AND TYPE 1 LEWIS B ANTIGEN-POSITIVE STRAINS

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H. pylori infection is acquired in childhood and can persist for life. Previous studies in adult patients from North America and Europe have shown that *H. pylori* lipopolysaccharides (LPSs) express predominantly type 2 Lewis x (Le^x) and Le^y epitopes, while LPSs from Asian strains have the capacity to express type 1 Le^a and Le^b structures.

In order to understand the influence of environmental and host factors on the expression of Le antigens we analyzed 49 Greek *H. pylori* isolates from symptomatic children. Both CagA-positive and -negative strains were evaluated. The isolates were characterized by whole-cell indirect enzymelinked immunosorbent assay, gel electrophoresis and immunoblotting. It was found that pediatric isolates had the propensity to express type 1 Le^b blood group antigen, a feature relatively uncommon in *H. pylori* isolates from adult population. Additionally, one-third of the isolates were nontypeable. Combined chemical and mass spectrometric analyses carried out directly on bacterial cells revealed that the majority of nontypeable strains expressed the O-chain composed of partially fucosylated *N*-acetyllactosamine polysaccharide chains. This suggests that LPS of *H. pylori* is involved in host adaption of the bacterium and that fucosylation of the Ochain might be host-induced.

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● CHARACTERIZATION OF VIRULENCE FACTORS CagA, VacA AND LEWIS ANTIGENS IN *H. pylori* STRAINS ISOLATED FROM CHILDREN AND LACK OF CORRELATION WITH THE SEVERITY OF HISTOLOGICAL FINDINGS

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Our aim was to characterize Lewis antigens and virulence factors CagA and vacA in *H. pylori* clinical strains isolated from children and correlate with histopathology.

Lewis antigens Le^x, Le^y, Le^a and Le^b were determined by whole cell ELISA in 49 clinical isolates from symptomatic children (10.4 ± 2.9 yo) of Greek origin. Presence of CagA EPIYA motifs and the vacA s, i, m isotypes were determined by PCR. Functionality of type IV secretion system (TFSS) was verified by detection of phosphorylated CagA protein. Histology was evaluated with the updated Sydney System. Non-parametric analysis and logistic regression were utilized for statistical analysis.

Type 2 (Le^x, Le^y) antigens were observed in the majority of strains. The predominant type was Le^y (35/49, 71%), with concomitant presence of Le^x in 24 isolates (49%). Le^b were observed in 11 (22%) cases, out of which 4 (8%) expressed Le^y as well as Le^x. Only one strain expressed Le^a. Simultaneous presence of Le^x and Le^y antigens with a functional TFSS and *vacA*s1 allele (OR: 4.433, 95%CI: 1.269–15.489) was observed. No correlation with the presence of increased numbers of EPIYA motifs in CagA was evident. Moreover a lack of correlation between all the aforementioned bacterial virulence characteristics with the histopathological observations was observed. We established that there is simultaneous presence of Le^x and Le^y antigens, a functional TFSS and VacAs1 allele in *H. pylori* isolates from symptomatic children, which is however, not correlated with the severity of histopathological lesions, but may confer advantageous conditions for the establishment of persistent infection.

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● IN VITRO EFFECTS OF HUMAN BETA-DEFENSINS ON PLANKTONIC CELLS, BACTERIAL ADHESION AND BIOFILM FORMATION OF THE TWO SEQUENCED STRAINS OF *H. pylori*

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Objectives: (a) Investigate the bactericidal potential of the human beta defensins (hbDs) 1,2,3 and 4 against planktonic *H. pylori* (*Hp*) cells and (b) examine their ability to influence initial bacterial adhesion and subsequent development of a biofilm providing thus, some insights into the bacterium's adaptation mechanisms in the gastric niche.

Materials & Methods: *Hp* strains 26695 and J99 were grown planktonically and as adherent to rectangular thermanox® cover slips to determine the effect of the biofilm phenotype on the level of susceptibility following short exposure to various concentrations of recombinant hbDs. Transmission electron microscopy was engaged to demonstrate possible structural changes. *Hp* cells pre-exposed to sub-inhibitory concentrations of the above peptides, were tested for their capacity to form a biofilm.

Results: In planktonic cells hbDs were highly susceptible over a 30 min period, however a significant decrease in the bactericidal effect of all four hbDs was evident for cells in biofilms indicating the presence of certain persister cells. Interestingly, sub-lethal concentrations of hbDs appear to induce the bacterium's ability to biofilm formation favoring mainly adherence.

Conclusion: This study provides evidence of the activities of hbDs against *Hp* biofilms and supports the hypothesis that the biofilm phenotype significantly affects the level of resistance to those peptides facilitating *H. pylori* persistence and survival.

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