ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE LISBOA

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CENTRO DE INVESTIGAÇÃO E ESTUDOS EM SAÚDE PÚBLICA

The Eighth International Symposium on Biological Monitoring in Occupational and Environmental Health – ISBM 2010

Interaction of formaldehyde and tobacco smoking in the frequency of micronucleus and the XRCC3 Thr241Met polymorphism

Carina Ladeira, Manuel C. Gomes, Miguel Brito

Finland, 6 September 2010

Introduction

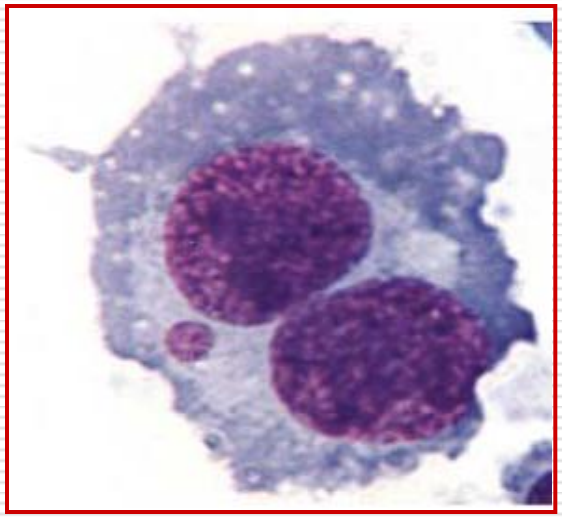
- **Formaldehyde** is classified by IARC as carcinogenic to humans (nasopharyngeal cancer)

- **Tobacco smoke** has been epidemiologically associated to a higher risk of development of cancer, especially in the oral cavity, larynx and lungs, as these are places of direct contact with many carcinogenic tobacco's compounds

- **XRCC3** is involved in homologous recombination repair of cross-links and chromosomal double-strand breaks (**Thr241Met polymorphism**)

Aim of the study

- Determine whether there is an *in vivo* association between genetic polymorphism of the gene XRCC3 and the frequency of **genotoxicity biomarkers** in subjects exposed or not to formaldehyde and with or without tobacco consumption



Fenech et al., 2003

Micronucleus

-Chromosome damage

-Genetic endpoint for detection of FA induced genotoxicity

Study developed

- The study was carried out in Portugal in pathology anatomy laboratories
- Cases: 56 workers occupationally exposed to FA
- Controls: 85 non-exposed subjects
- Both groups were asked about their smoking habits (null, light, moderate and heavy)

Study developed

Genotoxic effects

- CBMN in peripheral blood lymphocytes taken by venipuncture

XRCC3 Thr241Met polymorphism

- *iCycler iQ® Multicolor Real-Time PCR Detection System* (BIO-RAD)
- dbSNP no.rs861539, Applied Biosystems

Results

	Exposed group	**Control group**
Number of subjects	56	85
Gender Females Males	 37 (66%) 19 (34%)	 54 (64%) 31 (36%)
Age **(mean std. dev., in years)** Range	 39.45 11.5 20-61	 32.42 8.1 20-53
Tobacco consumption Non-smokers Smokers	 45 (80,4%) 11 (19,6%)	 60 (70,6%) 25 (29, 4%)

Results

Exposure to FA

	Mean, MN lymphocytes S.E. (range)
Controls	0.81 0.172 (0-7)
Exposed	3.96 0.525 (0-14)

OR = 9.665

CI 95% 3.81-24.52

p<0.001, Mann-Whiteny test

Results

Tobacco smoke

Tobacco	N	Mean, MN ± S.E. (range)
Controls		
Non-smokers	60	0.77±0.201 (0-6)
Smokers	25	0.92±0.336 (0-7)
Exposed		
Non-smokers	45	4.31±0.591 (0-14)
Smokers	11	2.55±1.082 (0-12)

OR=0.155

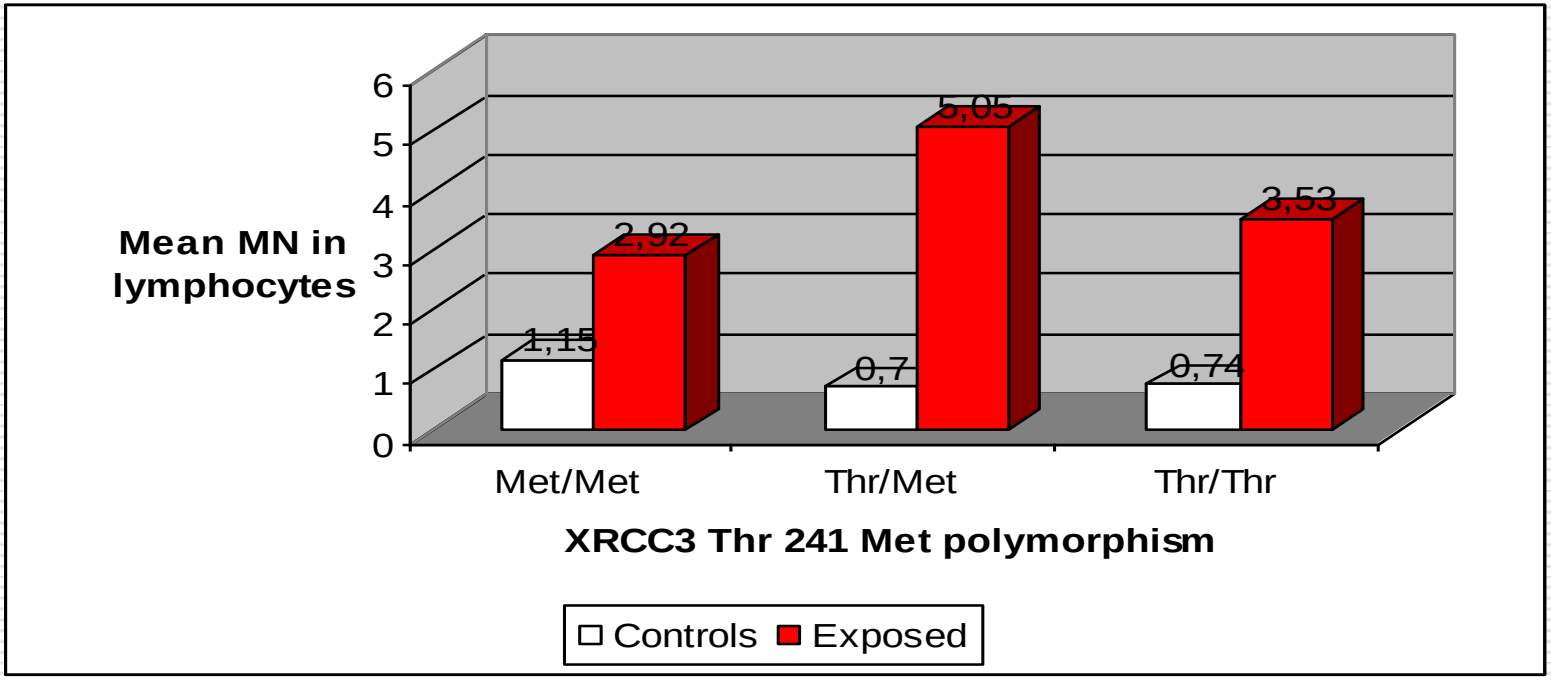
95% CI 0.036-0.662

OR=0.167

95% CI 0.034-0.816

Results

XRCC3 Thr241Met polymorphism



Results

Interaction between exposure, tobacco and XRCC3 polymorphism

		XRCC3 polymorphism Mean MN lymphocytes	S.E.				
Groups	**Smoking status**	**Met/Met**		**Met/Thr**		**Thr/Thr**	
Exposed	**Non smokers**	3.50	1.13	5.89	1.10	3.13	0.77
	Smokers	1.00	1.00	1.25	0.48	5.00	2.61
Controls	**Non smokers**	0.82	0.55	0.64	0.34	0.92	0.31
	Smokers	1.56	0.78	1.00	0.63	0.36	0.28

Conclusions

- Binary logistic regression showed that only the exposure is significative ($p<0.0001$)
- The analysis of the polymorphisms of XRCC3 did not found significant results, however the presence of the Thr allele was found to be associated with the higher frequencies of MN (4 to 14 MN) in exposed
- A biomonitoring study is complex and is important to consider individual susceptibility and factors inherent to lifestyle such as tobacco
- The preponderant factor in the increase of MN in lymphocytes is the occupational exposure to FA

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