



Domanda di partecipazione alle Giornate **CUIA 2014** in Argentina (3-15 aprile 2014)

Dati del referente italiano partecipante

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Specificare l'ambito tematico in cui si inserisce l'iniziativa:

- Studi europei ed integrazione regionale
- Patrimonio culturale
- Scienze e Tecnologie
- Bioscienze e biotecnologie

Titolo dell'iniziativa

Value of polymorphisms and DNA methylation for the expression of CYP2E1 enzyme: implications in pharmacogenomics



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Abstract

Different individuals possess slightly different genetic information and show genetically-determined differences in several enzyme activities due to genetic variability. Following an integrated approach, we studied the polymorphisms and DNA methylation of the 5' flanking region of the metabolizing enzyme CYP2E1 in correlation to its expression in both tumor and non-neoplastic liver cell lines, since to date little is known about the influence of these (epi)genetic elements in basal conditions and under induction by the specific inductor and a demethylating agent. In treated cells, reduced DNA methylation, assessed both at genomic and gene level, was not consistently associated with the increase of enzyme expression. Interestingly, the Rsa/Pst haplotype differentially influenced CYP2E1 enzyme expression. In addition, regarding the Variable Number of Tandem Repeats polymorphism, cells with A4/A4 genotype showed a greater expression inhibition (ranging from 20% to 30%) compared with others carrying the A2/A2 one, while those cells bringing A2/A3 genotype showed an increase of expression (of 25%, about). Finally, we demonstrated for the first time that the A2 and A3 CYP2E1 alleles play a more important role in the expression of the enzyme, compared with other (epi)genetic factors, since they are binding sites for trans-acting proteins. In conclusion our data contributes to define a hypothetical model of regulation of the expression of this enzyme. Clarifying the complex regulation of CYP2E1 enzyme expression, either by genetic or epigenetic elements, will give useful topics in pharmacogenomics, for typing people regarding its metabolizing capability and therapy response.

Breve biografia / curriculum del coordinatore del programma

University Degree in Biological Sciences 110/110 with maximum honours. PhD in Cellular and Developmental Biology, Specialist in Clinical Pathology, Permanent researcher of Genetics, University of Palermo. Permanent teacher of Evolutionary Genetics, Genetics of populations, Molecular Genetics, Plant Genetics, Human genetics and cytogenetics, at University of Palermo.

Excellent experience in Cytogenetics, molecular cytogenetics, genotyping of genic polymorphisms, DNA methylation status technics, RT-PCR with taqman chemistry.

Editorial Board member of "Journal of Carcinogenesis & Mutagenesis" (IF: 5,4).

(Co)Author of 22 ISI papers, 2 Italian national papers ISSN, 2 book chapter ISBN, 3 book ISBN, 6 international abstracts ISI published and 41 (inter)national abstracts no-ISI.