The human PIG-A assay : a new tool for environmental mutagenesis assessment

Pierre Castel*[1], Xavier Carcopino[1], Stéphane Robert[2], and Thierry Orsiere†[1]

[1]Institut méditerranéen de biodiversité et d'écologie marine et continentale (IMBE) – INEE, Université d'Avignon et des Pays de Vaucluse, Institut de recherche pour le développement [IRD] : UMR237, Aix Marseille Université, CNRS : UMR7263, INSB, INSU – Aix Marseille Université, Campus Etoile, Faculté St-Jérôme case 421 Av. . escadrille Normandie-Niemen 13397 MARSEILLE CEDEX 20, France
[2]Vascular Research Center of Marseille - UMRS1076 (VRCM) – Aix-Marseille Université - AMU – Faculté de Pharmacie 27 Bd Jean Moulin 13005 MARSEILLE, France

Abstract

A large number of environmental exposures (solar UV beam, air, food or water pollution, professional or iatrogenic exposure, tobacco or alcohol consumption...) can lead to DNA damage. If this environmental genotoxicity represents the main etiology of an unneglectable number of cancers, health consequences are not related to the level of exposure and vary from one individual to another. This is partly explained by individual susceptibility to a precise genotoxic mode of action, due to polymorphisms in genes involved in DNA repair. Accordingly, planification and personalization of primary or secondary prevention measures are difficult in the absence of a simple, fast, sensitive and cheap biomarker of mutagenic effect, able to detect a vast number of genotoxic modes of action. The frequency of inactivating mutations in PIG-A, an X-linked sentinel gene, is closely related to somatic mutation rate, as such it is a good marker candidate. The PIG-A assay consists in a flow cytometry detection of cells harboring the particular glycosyl-phosphatidyl-inositol deficiency phenotype, consequence of PIG-A inactivating mutation. Due to the high degree of PIG-A interspecies conservation, the cross-species potential is therefore very high. The Biogenotoxicology, Human Health and Environment team (BSHE) develops a new in vivo whole-blood PIG-A assay. We have already set up a new protocol on human granulocytes which results are available within 2 hours after blood collection. We are currently assessing our protocol by testing iterative blood samples from 60 patients undergoing radiation therapy in adjuvant treatment of breast cancer. Preliminary results and cross-species potential will be discussed.

Keywords: environmental mutagenesis, PIG A assay, human, biomarker

*Speaker
†Corresponding author: thierry.orsiere@imbe.fr