IDENTIFICATION OF A RECEPTOR INVOLVED IN THE CHRONIC DELETEROUS EFFECTS OF TWO ENVIRONMENTAL POLLUTANTS IN A PRECANCEROUS BREAST CELL LINE

CF Donini1,2,3, M El Helou4,5, E Grisard1,2, E Maguer-Satta2, A Escande2, ML Bayle1, C Casellas5, B Combroujeu7, L Lachuer1,2, T Philip1,3, S Ghayad1, M Diab-Assa1, V Cavailles5, B Fervers3 and PA Cohen1,2,3

1Université Lyon 1, Lyon, France; 2CRCL-Inserm U1052-CNRS U5286, Lyon, France; 3Département Cancer et Environnement, Centre Léon Bérard, Lyon, France; 4Lebanese University, Beirut, Lebanon; 5Inserm U896, Montpellier, France; 6UMR5569 (UM UMI IRD CNRS), Montpellier, France; 7Plateforme de Recherche en Toxicologie Environnementale et Ecotoxicologie de ROVALTAIR, Valence, France. *Equal contributors
(corresponding author: pascale.cohen@univ-lyon1.fr)

INTRODUCTION

Growing evidence indicates that exposure to environmental carcinogens may increase the risk of sporadic breast cancers, so it is of most importance to decipher the role of environmental pollutants in the chronic carcinogenesis of human breast epithelia and their contribution in the development of this cancer. In this study we first characterized the MCF10 breast tumour progression model, which mimics progression from benign to premalignant or fully malignant phenotype [1]. Two environmental factors possessing distinct mechanisms of toxicity were chosen for chronic and low doses exposure of the MCF10AT1 precancerous breast cell line of the tumour progression model. Cells were exposed to low-doses of an endocrine disruptor, ED, or a genotoxic compound, GT, or both of them for 60 days. We characterized the cellular and molecular phenotypes developed by the exposed cells, and investigated the candidate role of a specific receptor X (RX), in mediating their deleterious effects.

METHODS

Establishment of the chronically exposed cellular model: MCF10AT1 cells were chronically exposed to the indicated concentration of chemicals during 60 days in phenol red-free DMEM/Ham's F12 medium supplemented with 5% steroids-depleted, dextran-coated and charcoal-treated horse serum and 100 ng/ml cholaerteroxin, 10 mg/ml insulin, 0.5 mg/ml hydrocortisol, 20 ng/ml epidermal growth factor. Media and treatment were changed every 2 days. Unexposed MCF10C1A.c1 were used as control.

Characterization of the cellular and molecular phenotypes developed by the exposed cells: RTO-PCR, Western Blot analysis, Anchorage independent growth and Mammospheres formation efficiency assays were performed.

1. The increasing malignant potential of the MCF10 model is associated with increased anchorage-independent growth and mammospheres formation efficiency

2. Long-term and low-doses exposure of environmental factors affects the aggressiveness of the precancerous cell line MCF10AT1

3. The deleterious effects of the environmental factors are directly or indirectly mediated by the receptor RX

4. The use of a specific antagonist for the receptor RX is sufficient to prevent the chronic deleterious effects of the environmental pollutants in the precancerous cells

CONCLUSION

This study highlights that:
- Chronic and low-doses exposure of environmental factors affects the aggressiveness of the precancerous cell line MCF10AT1
- The RX receptor is directly or indirectly involved in mediating the deleterious effects of the environmental pollutants in the precancerous cell line MCF10AT1
- Blocking the receptor RX with a specific antagonist is sufficient to prevent the deleterious effects of the chronic and low-dose exposure to the environmental factors

References: