

Cadmium elicits alterations in mitochondrial morphology and functionality in C3H10T1/2Cl8 mouse fibroblast cell

Monica Oldani,¹ Chiara Milani,¹ Federico Gaboardi,² Marta Manzoni,³ Anna M. Villa,¹ Federico M. Stefanini,⁴ Pasquale Melchiorretto,² Eugenio Monti,³ Matilde Forcella,¹ Chiara Urani,^{2,5} Paola Fusi^{1,5}

¹Dipartimento di Biotecnologie e Bioscienze, Università degli Studi di Milano-Bicocca, Milano; ²Dipartimento di Scienze dell'Ambiente e della Terra, Università degli Studi di Milano-Bicocca, Milano; ³Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, Brescia; ⁴Dipartimento di Statistica, Informatica, Applicazioni, Università degli Studi di Firenze, Firenze; ⁵Integrated Models for Prevention and Protection in Environmental and Occupational Health (MISTRAL) University Research Center, Pisa, Italy

Abstract

In this work we exploit the widely used, well known in vitro Cell Transformation Assay (CTA), which allows following healthy cells transformation into a malignant phenotype, to understand the early metabolic deregulation and events in cadmium-induced carcinogenesis.

Introduction

Cadmium is a widespread carcinogen.¹ We previously showed that the administration of low CdCl₂ doses for 24 hours to healthy C3H10T1/2Cl8 mouse embryonic fibroblast cell line at the beginning of Cell Transformation Assay (CTA), up regulates genes involved in metal scavenging and antioxidant defense, like metallothioneines, Glutathione S-transferases and heat shock proteins.² Still, although most cells thrive normally in the following weeks, malignancy is triggered by CdCl₂ and leads to the appearance of foci of transformed cells at the end of the CTA.^{3,4}

Materials and Methods

Respiratory metabolism was investigated through Seahorse Agilent assays, while oxidative stress level was assessed through fluorescent probes; DNA damage was evaluated by Comet assay, and mitochondrial morphology was analyzed in confocal microscopy.

Results

Results show that the initial response to CdCl₂ involves mitochondria rearrangement into a perinuclear network. However, SOD1 and SOD2 activities are inhibited, leading to increased superoxide anion level, which in turn causes DNA strand breaks. From the metabolic point of view, cells increase their glycolytic flux, while all extra NADH produced is still efficiently reoxidized by mitochondria.

Discussion and Conclusions

Our results confirm previously shown response against cadmium toxicity; new data about glycolytic increase and mitochondrial rearrangements suggest pathways leading to cell transformation.

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Correspondence: Monica Oldani, Dipartimento di Biotecnologie e Bioscienze, Università degli Studi di Milano-Bicocca, Piazza della Scienza 2, 20126, Milano. Tel.: 02 64483409 E-mail: m.oldani12@campus.unimib.it

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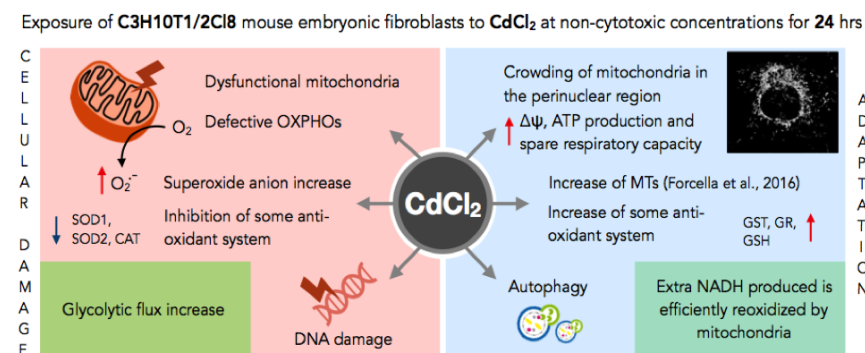


Figure 1. Summary of the results.