

TITLE (Arial 11):

Inhibition of polyamine biosynthesis by DFMO reverts partially Ca²⁺ remodeling in colon cancer cells

AUTHORS (Name and surname. Underline the name of the presenting author. Arial 10)

Lucía G. Gutiérrez¹, Miriam Hernández-Morales^{1,*}, Diego Sobradillo¹, Lucía Núñez^{1,2} and Carlos Villalobos¹.

AFFILIATION (Arial 9) if the authors have more than one affiliation indicates them with a number.

1. *Institute of Molecular Biology and Genetics (IBGM).*
2. *Dept. of Biochemistry and Molecular Biology and Physiology, University of Valladolid and Spanish National Research Council (CSIC).*

ABSTRACT (maximum 300 words; Arial 11)

Recently we have shown that colon cancer cells undergo remodeling of intracellular Ca²⁺ homeostasis including changes in store-operated Ca²⁺ entry (SOCE), store-operated currents and Ca²⁺ store content associated to changes in molecular players involved in SOCE (Sobradillo et al., 2014). Reversing this remodeling could contribute to protection against cancer and cancer chemoprevention. Difluoromethylornithine (DFMO) or Eflornithine is a suicide inhibitor of ornithine decarboxylase (ODC), the limiting step in the synthesis of polyamines that is considered one of the best chemopreventive compounds against colon cancer. Here we tested the effects of DFMO treatment on SOCE, SOCs, Ca²⁺ store content, the molecular players involved and resistance to cell death, a critical cancer hallmark. We found that ODC was largely overexpressed in colon cancer cells suggesting increased synthesis of polyamines in colon cancer cells. Short-term treatment with DFMO (500 μM, 12 h) decreased significantly SOCE and store-operated currents in colon cancer cells. DFMO had no effect on I_{crac} but prevented selectively the appearance of the outward component of store-operated current likely mediated by TRPC1. DFMO also increased Ca²⁺ store content and the fraction of cells undergoing early apoptosis induced by H₂O₂. At the molecular level, we found DFMO tend to decrease all molecular players involved in SOCE except Stim2 but the effects were statistically significant only for TRPC1 mRNA. In summary, inhibition of polyamine synthesis decreases SOCE and SOCs in human colon cancer cells acting probably on expression of TRPC1 and tends to increase Ca²⁺ store content and susceptibility to apoptosis in human colon cancer cells. Thus, reverting partially Ca²⁺ remodeling in colon cancer cells and likely contributing to colon cancer chemoprevention. This work was supported by grants BFU2012-37146 and BFU2015-70131R from MINECO and BIO/VA46/14 JCyL, Spain. LGG and DS were supported by University of Valladolid and CSIC.

IMPORTANT: YOU MUST SEND THE ABSTRACT IN WORD LIKE IN THE EXAMPLE (NEXT PAGE)

TOPIC

- Molecular basis of pathology and genomics
- New therapeutic approaches
- Pharmacology
- Neuroscience
- Developmental biology and reproduction
- Gene engineering and regulation
- Microbiology, parasitology and metagenomics

Marca una de las siguientes opciones: Comunicación oral Póster Asistencia

INHIBITION OF POLYAMINE BIOSYNTHESIS BY DFMO REVERTS PARTIALLY Ca^{2+} REMODELING IN COLON CANCER CELLS

Lucía G. Gutiérrez¹, Miriam Hernández-Morales^{1,*}, Diego Sobradillo¹, Lucía Núñez^{1,2} and Carlos Villalobos¹.

1. Institute of Molecular Biology and Genetics (IBGM).
2. Dept. of Biochemistry and Molecular Biology and Physiology, University of Valladolid and Spanish National Research Council (CSIC).

Recently we have shown that colon cancer cells undergo remodeling of intracellular Ca^{2+} homeostasis including changes in store-operated Ca^{2+} entry (SOCE), store-operated currents and Ca^{2+} store content associated to changes in molecular players involved in SOCE (Sobradillo et al., 2014). Reversing this remodeling could contribute to protection against cancer and cancer chemoprevention. Difluoromethylornithine (DFMO) or Eflornithine is a suicide inhibitor of ornithine decarboxylase (ODC), the limiting step in the synthesis of polyamines that is considered one of the best chemopreventive compounds against colon cancer. Here we tested the effects of DFMO treatment on SOCE, SOCs, Ca^{2+} store content, the molecular players involved and resistance to cell death, a critical cancer hallmark. We found that ODC was largely overexpressed in colon cancer cells suggesting increased synthesis of polyamines in colon cancer cells. Short-term treatment with DFMO (500 μ M, 12 h) decreased significantly SOCE and store-operated currents in colon cancer cells. DFMO had no effect on I_{crac} but prevented selectively the appearance of the outward component of store-operated current likely mediated by TRPC1. DFMO also increased Ca^{2+} store content and the fraction of cells undergoing early apoptosis induced by H_2O_2 . At the molecular level, we found DFMO tend to decrease all molecular players involved in SOCE except Stim2 but the effects were statistically significant only for TRPC1 mRNA. In summary, inhibition of polyamine synthesis decreases SOCE and SOCs in human colon cancer cells acting probably on expression of TRPC1 and tends to increase Ca^{2+} store content and susceptibility to apoptosis in human colon cancer cells. Thus, reverting partially Ca^{2+} remodeling in colon cancer cells and likely contributing to colon cancer chemoprevention. This work was supported by grants BFU2012-37146 and BFU2015-70131R from MINECO and BIO/VA46/14 JCyL, Spain. LGG and DS were supported by University of Valladolid and CSIC.

I CONGRESO NACIONAL DE JÓVENES INVESTIGADORES EN BIOMEDICINA

III CONGRESO BIOMEDICINA PREDOCS VALENCIA

28-29 DE NOVIEMBRE DE 2016

ENCUENTRO NACIONAL DE INVESTIGADORES EN SUS PRIMERAS
FASES DE FORMACIÓN PARA EL FOMENTO DE LA COMUNICACIÓN
Y LA COLABORACIÓN EN BIOMEDICINA



INSCRIPCIÓN:

1er PLAZO	1 DE JULIO	50€
2do PLAZO	31 DE OCTUBRE	70€

ORGANIZAN:

Comisión Predoctorales Biomedicina de Valencia
Eduardo Primo Yúfera 3, Valencia 46012, España

 +34 963 289 680  FAX +34 963 289 701

 conbiopreval@gmail.es  @conbiopreval

 Congreso Biomedicina Predocs Valencia



This is to certify that

Ms. Lucía González Gutiérrez

attended the

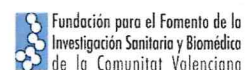
**I CONGRESO NACIONAL
DE JÓVENES INVESTIGADORES EN
BIOMEDICINA**

III Congreso Biomedicina Predocs Valencia

held in CIPF, Valencia (Spain) on the 28th to 29th November
2016 with a poster communication.



Organizing Committee
Valencia, 2016



I NATIONAL CONGRESS OF YOUNG RESEARCHERS IN BIOMEDICINE

III CONGRESS OF BIOMEDICINE OF PHD STUDENTS IN VALENCIA

I CONGRESO NACIONAL DE JÓVENES INVESTIGADORES EN BIOMEDICINA

III CONGRESO DE BIOMEDICINA PREDOCS VALENCIA



POSTER COMMUNICATION ACCÉSIT PRIZE

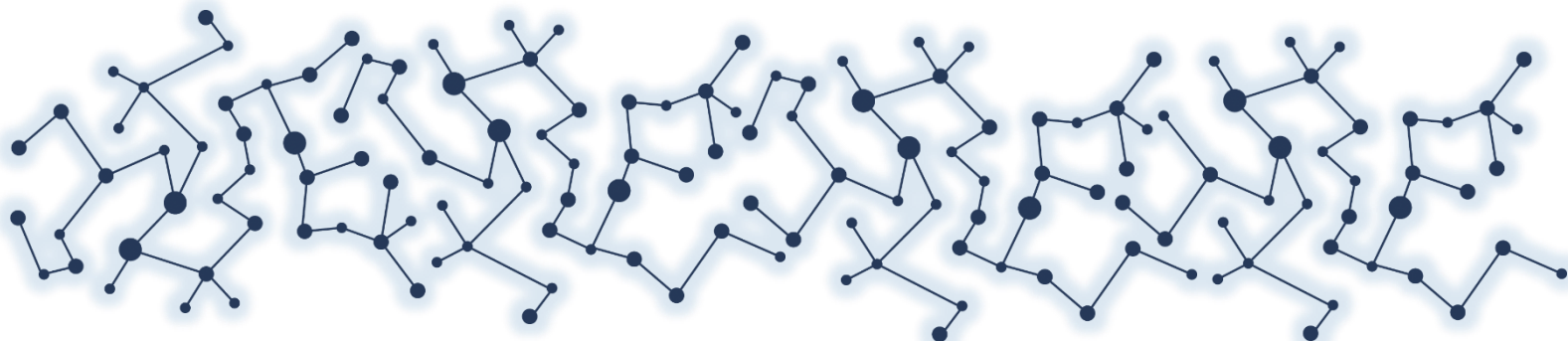
awarded to

Ms. Lucía González Gutiérrez

for the work presented in CIPF, Valencia (Spain) on the 28th to 29th November 2016 with the title *“Inhibition of polyamine biosynthesis by DFMO reverts partially Ca²⁺ remodeling in colon cancer cells”*.

Organizing Committee
Valencia, 2016

Centro de investigación Príncipe Felipe (CIPF). C/ Eduardo primo Yúfera, 3, Valencia 46012, Spain



Congress organized by members of:

