TITLE (***Arial 11***):

Inhibition of polyamine biosynthesis by DFMO reverts partially Ca^{2+} remodeling in colon cancer cells

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

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ABSTRACT (maximum 300 words; Arial 11)

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 µM, 12 h) decreased significantly SOCE and store-operated currents in colon cancer cells. DFMO had no effect on Icrac 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.

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

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

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This is to certify that

Ms. Lucía González Gutiérrez

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