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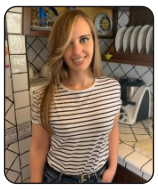
Abstract



Hydroxytyrosol decreases phosphatidylserine exposure and inhibits suicidal death induced by lysophosphatidic acid in human erythrocytes.

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Abstract:

Background/Aims: Lysophosphatidic acid (LPA) is a phospholipid signal molecule that regulates many cellular processes both physiological and pathological. Moreover, its high plasma concentrations are toxic for several cellular types, including erythrocytes (RBC), as it acts as a pro-thrombotic and pro-atherogenic agent. It is therefore essential to explore the potential protective role of nutrition in protecting cells from the possible toxic effects of high plasma concentrations of LPA by testing bioactive nutrients. In particular, our focus was on hydroxytyrosol (HT), a phenolic antioxidant occurring naturally in virgin olive oil, investigating its possible protective effect in preventing LPA-induced programmed cell death (eryptosis) in human RBC.

Methods: Intact RBC were incubated in the presence of 2.5 µM LPA and increasing concentrations of HT. Phosphatidylserine (PS) exposure with cell shrinkage, influx of extracellular calcium (Ca2+), ATP and glutathione levels were measured by FACS analysis. In addition, confocal laser scanning microscopy was used to determine RBC morphological alterations, as well as microvesicle formation.

Results: Our study confirms that LPA- induced eryptosis is characterized by PS exposure at the cell surface, with cell shrinkage and ATP and glutathione depletion; (Ca2+) influx is also a key event that triggers eryptosis. Here we report for the first time that cell co-incubation with LPA and in quantities as low as 0.1 µM HT causes a significant decrease in PS-exposing RBC, along with significant protection from the decrease in cell volume. Moreover, treatment of RBC with HT countered the influx of extracellular Ca2+ and has completely restored ATP and glutathione content at 1 µM. Finally, under the same experimental conditions, HT exerts a protective effect on RBC morphological changes and microvescicle release, completely restoring the typical biconcave shape at 1 µM. Conclusions. Taken together, the findings reported in this paper point to a novel biological effect of HT in preventing programmed suicidal death in anucleated cells and indicate that prevention from LPA toxic effects may represent an additional mechanism responsible for the claimed health-promoting effect of this dietary phenol, particularly related to cardiovascular diseases.

Biography:

Fabiana Tortora is a PhD student at the University of Campania "Luigi Vanvitelli" of Naples, who will be awarded the PhD title in "Biochemical and Biotechnological Sciences" this December 2019. During the 3 years of her PhD she repeatedly exposed in individual way with seminars addressed to the College and to other teachers the results on the progress of the thesis work. Furthermore, these three years of doctoral studies have been enriched, also by research activities abroad, by publications and participations in conferences. In particular, during the second year for a period of 3 months, part of the research activity was carried out in Germany at the "Medizinische Fakultät, Physiologisches Institut I, Wilhelmstrasse 56 D-72076 Tübingen", under the guidance of Prof. Dr. med. Dr. h.c. Florian Lang. The work focused on a greater understanding of eriptosis, a programmed death process that red blood cells encounter, with the aim of improving the side effects of anemia caused by chemotherapy drugs in cancer patients. Moreover, Fabiana holds a Second Level Degree in Biology specializing in Nutrition with 110 cum laude and a First Level Degree in Biological Science specializing in Pathophysiology at the Federico II University of Naples.

Publication of speakers:

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2. Chung S-M, Bae O-N, Lim K-M, Noh J-Y, Lee M-Y, Jung Y-S, et al. Lysophosphatidic acid induces thrombogenic activity through phosphatidylserine exposure and procoagulant microvesicle generation in human erythrocytes. Arterioscler Thromb Vasc Biol. 2007 Feb;27(2):414–21.

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