



On the use of Plasma Activated Liquids for the treatment of cancer cells

Alina Bisag^{1,2}, **Cristiana Bucci**^{1,2,3,4}, **Sara Coluccelli**^{1,2,3,5,6}, **Giulia Girolimetti**^{2,3,6},
Romolo Laurita^{1,2,7}, **Pierandrea De Iaco**^{2,3,5}, **Anna Myriam Perrone**^{2,5}, **Matteo Gherardi**^{1,2,7},
Lorena Marchio^{2,3,6}, **Anna Maria Porcelli**^{2,4,8}, **Eleonora Turrini**⁹, **Carmela Fimognari**⁹,
Vittorio Colombo^{1,2,7}, **Giuseppe Gasparre**^{2,3,6}

Alma Mater Studiorum-University of Bologna,

¹ Department of Industrial Engineering, ² Centro di Studio e Ricerca sulle Neoplasie Ginecologiche,

³ Department of Medical and Surgical Sciences, ⁴ Department of Pharmacy and Biotechnology,

⁵ Unit of Gynecologic Oncology, S. Orsola-Malpighi Hospital, ⁶ Centre for Applied Biomedical Research,

⁷ Interdepartmental Center for Industrial Research Advanced Mechanical Engineering Applications and Materials Technology, ⁸ Interdepartmental Center for Industrial Research Life Sciences and Technologies for Health, ⁹ Department for Life Quality Studies.

E-mail: romolo.laurita@unibo.it

Abstract

Several studies focus on the treatment of liquids via cold atmospheric pressure plasma (CAP) to enable the production of plasma-activated liquids (PALs) containing reactive oxygen and nitrogen species (RONS) having selective anticancer activity [1,2]. In this work, a microsecond pulsed dielectric-barrier-discharge jet was used to produce PAL for the treatment of T-leukemia cells, spleen lymphoblast cell line and normal lymphocytes; while a multiwire plasma source was used for the production of PAL for the treatment of Epithelial Ovarian Cancer (EOC) and non-cancer epithelial cell lines of ovarian origin (HOSE).

On T-lymphoblastic cell line, PAL induced apoptosis through the activation of the intrinsic pathway and inhibited cell-cycle progression. The use of the scavengers NAC or O-phenantroline significantly decreased PAL pro-apoptotic activity. For the first time, results of PAL on leukemia cells cultivated in hypoxia, which plays a critical role in promoting chemoresistance, are presented [1,3].

The PAL treatment showed a selective cytotoxic effect on EOC with respect to HOSE. Moreover, further investigation showed the ability of non cancer cells to adapt to the oxidative burst, induced by PAL, by increasing antioxidant proteins (*i.e.* superoxide dismutase) levels [2].

Taken together, our results provide a deeper understanding on the cellular and molecular impact of PAL on cancers cells, highlighting its partial selectivity towards malignant cells and its cytotoxic activity in model of chemoresistance, such as cell cultured in hypoxia.

This work was supported by AlmaIDEA Senior Grant by Alma Mater Studiorum-Università di Bologna: “Chemo-physical and biological mechanisms behind the anticancer activity of plasma activated liquids for the treatment of peritoneal carcinosis from primitive epithelial ovarian/fallopian tube tumor” and by by National SIR Grant [RBSI14DBMB] of the Italian Ministry of Education, Universities and Research, MIUR.

References

- [1] E. Turrini, *et alii*, *Oxidative Medicine and Cellular Longevity* 1–13 (2017)
- [2] A. Bisag, *et alii* *Cancers* 12-2,476 (2020)
- [3] E. Turrini, *et alii*, *Plasma Processes and Polymers* Submitted (2020)