Cold Plasma-based Redox Therapy for Breast-to-Bone Metastasis Tumor Growth Control

L. Bouret[1], JB. Billeau[1], M. Weber[2], D. Rosenzweig[2], S. Reuter[1]
[1]*Polytechnique Montreal, Montreal, QC, Canada*
[2]*McGill University, Montreal, QC, Canada*

Abstract: Bone metastases often require invasive treatments that damage healthy tissue. This project explores cold plasma therapy as a non-invasive alternative, using reactive species to target cancer cells. A bioprinted bone model coculturing cancer and healthy cells showed selective plasma effects on tumors. Results highlight plasma's potential to treat metastases while preserving healthy tissue. The platform enables precise studies of plasma-based therapies

1. Introduction

Bone, especially the spine, is a common site of metastasis for breast, lung and prostate cancers. These tumors pose a significant challenge, demanding aggressive treatments like chemotherapy and invasive surgery. To fully remove metastatic lesions, surgical procedures need to extend onto healthy tissue which reduces the probability of remaining malignant cells. Such surgery often involves the removal of healthy tissue, necessitating reconstruction and carrying a risk of infection. Cold plasma therapy, operating at temperatures below 40°C, offers a non-invasive solution by delivering reactive oxygen and nitrogen species (RONS) locally. While research shows promising results, the reaction mechanism between plasma and tissues, and proper treatment dosage and reactive species composition to reach the right effects are still topic of current research. The purpose of this project is to develop and characterize a cold plasma source and investigate its potential in mitigating bone cancer metastasis, hypothesizing its anti-tumor properties. The overall objective is to create a tissue-plasma platform for cold plasma therapy, aiming to control the metastatic spread of breast cancer cells to bone tissue.

2. Methods

We have developed a platform combining tailored plasma reactivity through a kHz coaxial dielectric barrier discharge source and a highly reproducible bioprinted circular bone tissue model. The bone tissue model was bioprinted (Cellink BioX) using cell-laden hydrogel. A multi-well plate was generated with identical “breast-to-bone” metastasis as a coculture model of MDA- MB-231 and human bone marrow mesenchymal stem cells (hbmMSCs). Liquid RONS are measured by UV-VIS colorimetry. For each set of plasma treatment at different parameters, metabolic activity through Alamar blue assays at day 1, 2 and 3 and live/dead measurements are used to detail the biological response of the tumor cells.

3. Results and Discussion

Results have shown that A1G7 cell-laden hydrogel was bioprinted with reproducible results in a model of cocultured MDA-MB-231 breast cancer cells and hbmMSCs. Dose responses of plasma on cancer cells and healthy cells were assessed in 2D and 3D cultures. Furthermore, plasma showed a selective antitumoral effect on MDA-MB-231 cancer cells over hbmMSCs healthy cells in 2D and 3D cultures. Colorimetric assays have also confirmed that long-lived species (H2O2 and NO2-) can be tailored through the energy, the distance, the duration of treatment and the composition of the atmosphere around the plasma.

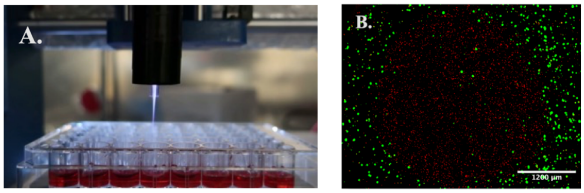

Fig. 1. **Plasma Treatment Platform.** A. The plasma jet has been automatized with the help of a computer numerical control (CNC). B. Control of the temperature of the plasma jet. E. Live (green) / Dead (red) image of the bioprinted model after 45 seconds of plasma treatment with MDA-MB-231 cancer cells the central ring and hbmMSCs in the outer ring.

4. Conclusion

In essence, our platform allows us to create unique biological chemistry, observing its impact on cancerous tissue for a plasma redox-based treatment. Using a bioprinted model ensures reproducibility and precise control, enabling detailed studies of tumor migration. With a tailored plasma jet, our platform is crucial for exploring novel therapeutic approaches using exogenous reactive species.

Acknowledgement

Fonds de Recherche du Québec – Nature et Technologie (FRQNT), New Frontiers in Research Fund (NFRF), Apogee Canada First Research Excellence Fund, OPSIDIAN ("Optimizing Power Skills in Interdisciplinary, Diverse & Innovative Academic Networks") studentship funded by the Natural Sciences and Engineering Research Council of Canada (NSERC).