# **Technical Scientific Report: Cold Plasma for Cancer Treatment**

#### Abstract

This report analyzes patents related to cold plasma for cancer treatment. The inventions aim to improve cancer therapy by utilizing cold atmospheric plasma (CAP) to selectively kill cancer cells, overcome drug resistance, stimulate the immune system, and enhance the efficacy of existing treatments like chemotherapy and radiotherapy. The approaches include direct plasma application, CAP-stimulated media, and plasma-induced cancer cell vaccination.

# **Background**

Conventional cancer treatments, such as surgery, chemotherapy, and radiation therapy, often face challenges including incomplete tumor ablation, drug resistance, and damage to healthy tissues. Cold plasma technology has emerged as a promising alternative and adjunctive therapy due to its ability to selectively induce cancer cell death through various mechanisms, including apoptosis and immunogenic cell death, while minimizing harm to surrounding healthy tissues. The patents discussed herein address these challenges by developing novel methods, devices, and systems for cold plasma-based cancer treatment.

### **Technical Fields of Invention**

The inventions discussed in this report span several technological areas:

- **Plasma Generation Devices:** Development of devices for generating cold atmospheric plasma (CAP) (WO2016035339A1, US11771770B2).
- **Plasma Delivery Systems:** Design of systems for targeted delivery of plasma to tumors, including plasma guns and helmets (US11523856B2, US10039927B2, WO2019177211A1).
- **Plasma-Treated Media:** Methods for producing and stabilizing CAP-stimulated media with enhanced anti-cancer properties (US10479979B2, US20220168565A1).
- **Combination Therapies:** Integration of CAP with existing cancer treatments like chemotherapy and radiotherapy (US20200069958A1, US20170319256A1).
- **Immunotherapy:** Utilizing plasma-treated cancer cells for vaccination to stimulate the immune system (US20220256682A1).

 Adaptive Plasma Treatment: Systems for adjusting plasma parameters based on real-time feedback of cell viability (US11517366B2).

## **Inventions Related to Cold Plasma for Cancer Treatment**

**Selective Cancer Cell Ablation:** Several inventions focus on selectively killing cancer cells while sparing healthy tissue. US10023858B2 describes a method for elevating TRAIL-R1 expression in cancer cells using cold plasma to induce apoptosis. US20170319256A1 details a method combining kinase inhibitors, circadian rhythm synchronization, and low-temperature plasma to selectively target cancer cells. (Relevant)

- Novelty and Objectives: These inventions aim to overcome the non-selective nature of traditional cancer therapies by targeting specific pathways or vulnerabilities in cancer cells.
- Technical Problems Solved: The inventions address the problem of off-target effects and toxicity associated with conventional treatments.
- Improvement: By selectively ablating cancer cells, these methods reduce damage to healthy tissues and potentially minimize side effects.
- Cold Atmospheric Plasma (CAP)-Containing Solutions: US11771770B2 introduces a system for producing CAP-containing solutions for cancer treatment. The system comprises a gas source, a plasma generating device, and a container for housing a fluid, where the plasma is discharged directly into the fluid. (Relevant)
  - Novelty and Objectives: The invention aims to provide an alternative cancer treatment by selectively eradicating cancer cells with minimal harm to surrounding healthy tissue.
  - Technical Problems Solved: The invention addresses the problem that direct CAP jetting only results in cell death in the upper 3-5 cell layers of the tissues in contact with the CAP, whether used externally or internally on a patient.

- Improvement: The CAP-containing solutions can be used for sterilization of infected tissues, inactivation of microorganisms, promotion of wound healing, skin regeneration, blood coagulation, teeth bleaching/whitening, and treatment of cancer cells.
- Targeted Plasma Delivery Systems: US11523856B2 presents a plasma gun designed for in vivo tumor treatment, enabling plasma to reach and contact tumors internally. WO2019177211A1 describes a probe-shaped device for treating cervical cancer by delivering plasma directly to the cervix. US10039927B2 details a cold plasma helmet for treating large surface areas of the head, including brain cancer. (Relevant)
  - Novelty and Objectives: These inventions aim to improve the accessibility and precision of plasma treatment for various cancer types.
  - Technical Problems Solved: The inventions address the challenge of delivering plasma to deep-seated tumors or large surface areas.
  - Improvement: By providing targeted delivery, these devices enhance the efficacy of plasma treatment and minimize exposure of healthy tissues.
- **CAP-Stimulated Media:** US10479979B2 and US20220168565A1 focus on the preparation and stabilization of CAP-stimulated cell culture media with enhanced anti-cancer properties. (Relevant)
  - Novelty and Objectives: These inventions aim to provide a more effective anti-cancer therapy by optimizing the preparation and storage of CAP-stimulated media.
  - Technical Problems Solved: The inventions address the need for more effective anti-cancer therapies and the degradation of CAP-stimulated media during storage.
  - Improvement: By controlling factors such as well size, gap between plasma source and liquid, and media volume, the anticancer properties of the media are enhanced and stabilized for extended periods.
- Adaptive Cold Atmospheric Plasma Treatment: US11517366B2 describes a system for adaptive cold atmospheric plasma treatment of

diseased tissues, particularly cancerous cells, by adjusting plasma jet parameters based on real-time feedback of cell viability. (Relevant)

- Novelty and Objectives: The invention aims to provide a system that can selectively eradicate cancerous cells while minimizing damage to normal cells by adjusting plasma parameters based on real-time feedback of cell viability.
- Technical Problems Solved: The invention addresses the challenge of optimizing plasma treatment parameters for individual patients and cancer types.
- Improvement: By providing real-time feedback and control, the system enhances the efficacy and safety of plasma treatment.
- **Combination Therapies:** US20200069958A1 discloses a method for treating breast cancer by combining cold atmospheric plasma with Trastuzumab to overcome Trastuzumab resistance. (Relevant)
  - Novelty and Objectives: The invention aims to enhance the outcome of breast cancer therapy in both HER2-positive and negative cancer cells.
  - Technical Problems Solved: The invention addresses the technical problem of Trastuzumab resistance or invalidity in breast cancer therapy.
  - Improvement: By combining cold atmospheric plasma with Trastuzumab, the treatment outcomes for breast cancer are improved.
- **Plasma-Induced Immunotherapy:** US20220256682A1 presents a method of vaccinating a subject against cancer by treating cells with plasma to induce immunogenic cell death (ICD), thereby stimulating the subject's adaptive immune response. (Relevant)
  - Novelty and Objectives: The invention aims to address the limitations of existing cancer treatment strategies by using plasma-treated cancer cells to stimulate the patient's adaptive immune system for improved cancer therapy outcomes.
  - Technical Problems Solved: The invention addresses the problem of cancer recurrence and resistance to therapy.
  - Improvement: By stimulating the immune system, the method enhances the body's ability to fight cancer.

# Applicability and Uses

The inventions described have broad applicability in cancer treatment:

- **Direct Tumor Ablation:** Plasma guns (US11523856B2) and cervical cancer treatment devices (WO2019177211A1) can be used for direct ablation of tumors in various locations. The plasma helmet (US10039927B2) is suitable for treating cancers of the head and neck. (Relevant)
- Adjuvant Therapy: Cold plasma can be used in combination with chemotherapy (US20200069958A1) or radiation therapy (US9682254B2) to enhance their efficacy and overcome drug resistance. (Relevant)
- **Treatment of Cancer Stem Cells:** Cold plasma can be used to target and eradicate cancer stem cells (US10329535B2), which are often resistant to conventional therapies. (Relevant)
- **Treatment of Skin Cancer:** Cold atmospheric plasma (CAP) can be used for treating therapy-refractory actinic keratosis and non-melanoma skin cancer (EP3525706B1). (Relevant)
- **Immunotherapy:** Plasma-treated cancer cells can be used as a vaccine to stimulate the immune system to fight cancer (US20220256682A1). (Relevant)
- **Liquid Plasma application:** Liquid plasma can be applied to treat cancers such as thyroid cancer, oral cavity cancer, pharynx cancer, liver cancer, lung cancer, melanoma, and head and neck cancer (US9750951B2). (Relevant)

### **Conclusion**

The patents analyzed demonstrate the diverse and innovative applications of cold plasma technology in cancer treatment. These inventions address critical challenges in cancer therapy, including selective tumor ablation, drug resistance, and the need for more effective treatment modalities. By developing novel devices, methods, and systems, these patents contribute to the advancement of cold plasma as a promising approach for combating cancer.

### **Citations**

WO2019039496A1 (Relevant)

US20190231411A1 (Relevant)

US20170319256A1 (Relevant)

US10329535B2 (Relevant)

US10023858B2 (Relevant)

US9750951B2 (Relevant)

US10479979B2 (Relevant)

US11523856B2 (Relevant)

EP3525706B1 (Relevant)

US8894644B2 (Relevant)

US20200069958A1(Relevant)

US11771770B2 (Relevant)

US20220256682A1 (Relevant)

US10039927B2 (Relevant)

WO2016035339A1 (Relevant)

WO2019177211A1 (Relevant)

US11517366B2 (Relevant)

US20220168565A1 (Relevant)

Contexts: US9682254B2 :: Cancer surface searing apparatus and method of use thereof\n WO2019039496A1 :: METHOD FOR PRODUCING CELL DEATH INDUCER FOR CANCER CELLS, AND METHOD FOR INDUCING CELL DEATH OF CANCER CELLS\n US20190231411A1 :: METHOD FOR PREDICTING CYTOTOXICITY OF COLD ATMOSPHERIC PLASMA TREATMENT ON CANCER CELLS\n US20170319256A1 :: METHOD OF SELECTIVELY KILLING CANCER CELLS USING LOW-TEMPERATURE PLASMA JET DEVICE AND METHOD OF TREATING TUMORS USING THE

US10329535B2 :: System and method for cold atmospheric plasma treatment on cancer stem cells\n

US10023858B2 :: System and method for selective ablation of cancer cells with cold atmospheric plasma\n

US9750951B2 :: Liquid type plasma for preventing or treating cancer\n US10479979B2 :: Method for making and using cold atmospheric plasma stimulated media for cancer treatment\n

US11523856B2 :: Plasma gun for treating tumors in vivo and use method thereof\n EP3525706B1 :: COLD ATMOSPHERIC PLASMA TREATMENT OF ACTINIC KERATOSIS AND NON-MELANOMA SKIN CANCER\n

US8894644B2 :: Plasma device for selective treatment of electropored cells\n US20200069958A1 :: System and Method for Cold Plasma Therapy with HER-Family Receptors\n

US11771770B2:: Compositions for treatment of cancer, methods and systems for forming the same\n

US20220256682A1 :: METHOD OF VACCINATION AGAINST CANCER USING PLASMA TREATED CANCER CELLS\n

US10039927B2 :: Cold plasma treatment devices and associated methods\n WO2016035339A1 :: PLASMA GENERATION DEVICE AND METHOD FOR PRODUCING ANTI-TUMOR AQUEOUS SOLUTION\n

WO2019177211A1 :: PLASMA THERAPY DEVICE FOR TREATMENT OF CERVICAL CANCER\n

US11517366B2 :: Adaptive and self-adaptive plasma cancer therapeutic platform\n US20220168565A1:: STABILIZED ANTI-CANCER COLD ATMOSPHERIC PLASMA (CAP)-STIMULATED MEDIA AND METHODS FOR PREPARING AND USING SAME\n , WO2019039496A1 :: METHOD FOR PRODUCING CELL DEATH INDUCER FOR CANCER CELLS, AND METHOD FOR INDUCING CELL DEATH OF CANCER CELLS\n US20190231411A1 :: METHOD FOR PREDICTING CYTOTOXICITY OF COLD **ATMOSPHERIC** PLASMA **TREATMENT** ON CELLS\n CANCER US20170319256A1:: METHOD OF SELECTIVELY KILLING CANCER CELLS USING LOW-TEMPERATURE PLASMA JET DEVICE AND METHOD OF TREATING TUMORS USING THE SAME\n

US10329535B2 :: System and method for cold atmospheric plasma treatment on cancer stem cells\n

US10023858B2 :: System and method for selective ablation of cancer cells with cold atmospheric plasma\n

US9750951B2 :: Liquid type plasma for preventing or treating cancer\n US10479979B2 :: Method for making and using cold atmospheric plasma stimulated media for cancer

treatment\n

US11523856B2 :: Plasma gun for treating tumors in vivo and use method thereof\n EP3525706B1 :: COLD ATMOSPHERIC PLASMA TREATMENT OF ACTINIC KERATOSIS AND NON-MELANOMA SKIN CANCER\n

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WO2019177211A1 :: PLASMA THERAPY DEVICE FOR TREATMENT OF CERVICAL CANCER\n

US11517366B2 :: Adaptive and self-adaptive plasma cancer therapeutic platform\n US20220168565A1 :: STABILIZED ANTI-CANCER COLD ATMOSPHERIC PLASMA (CAP)-STIMULATED MEDIA AND METHODS FOR PREPARING AND USING SAME\n