Increasing vitamin D_3 metabolite levels enhances prostate cancer cell death following cryoablation

In vitro study details how the gradual dose escalation of calcitriol, a hormonally active metabolite of vitamin D_3, increases prostate cancer cell sensitivity to freezing injury and may provide an alternate combinatorial approach in the treatment of prostate cancer

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OWEGO, NY - CPSI Biotech announced today the publication of a peer-reviewed article detailing the potential benefit of the combination of calcitriol pre-treatment and freezing (cryoablation) for targeting prostate cancer. The study, titled *Dose Escalation of Vitamin D_3 Yields Similar Cryosurgical Outcome to Single Dose Exposure in a Prostate Cancer Model*, published in the open access journal *Cancer Control* was a multi-institutional collaboration between researchers from CPSI and Binghamton University.

The article details the impact of exposing prostate cancer cells to a gradually increasing dose of calcitriol over a one month period and then exposing cells to mild sub-freezing temperatures associated with a cryoablative procedure. The study investigated the impact of the application of a gradual calcitriol dose escalation regime in comparison to a single (1 day) high dose exposure regime as well as freezing alone in an *in vitro* prostate cancer cell model. The data show that exposing cancer cells to calcitriol in combination with mild freezing resulted in increased cell death compared to either treatment alone. Further, the data demonstrated that gradual dose escalation of calcitriol yielded a similar outcome as acute high dose exposure. Commenting on the study, Dr. John M. Baust (President and Lead Scientist, CPSI Biotech) stated "cryoablation is a very effective treatment modality used widely to treat various cancers. One limitation of Cryo is that different cancer cells (stages and types) have been shown to have differing tolerances to mild freezing temperatures associated with the outer edge of the frozen mass. In addition to developing advanced cryoablative devices, one of our foci at CPSI is to identify new combinatorial strategies to increase cancer destruction at these mild sub-freezing temperatures. This study demonstrates that the combination of calcitriol and freezing can yield prostate cancer destruction at temperatures as warm as -15°C, whereas typically temperatures of -40°C or colder are necessary for complete destruction."

This study was conducted as part of CPSI's ongoing research and technology development program which involves the development of next generation cryoablation devices and approaches for the treatment of various cancers. Speaking to the study findings, Dr. Kimberly Santucci (CPSI Research Scientist and the study's first author) stated "the anticancer properties of VD3 metabolites, including calcitriol, have been extensively studied and we previously reported on the benefits of the combination of calcitriol and freezing. While beneficial, previous studies focused on the acute administration and short term exposure of high dose calcitriol. Clinical translation of that approach would require multiple surgical procedures over several days. The objective of this study was to model the gradual increase of calcitriol concentration such as might be obtained via a one month oral dosing regimen. Our findings suggest that the application of gradual dose escalation results in similar sensitization of cancer cells to freezing as an acute high dose regime." Dr. Kristi Snyder (CPSI Director of Operations and Principal Scientist) continued "another interesting observation was this combinatorial approach resulted in enhanced cancer

destruction in a late stage, highly metabolically active, actively dividing aggressive prostate cancer model. This is noteworthy as most previous studies have utilized early stage or less active cancer models. These studies coupled with the current study suggest that the combinatorial approach of calcitriol pre-treatment followed by cryoablation may provide universal benefit for the future treatment of prostate cancer regardless of stage."

Ongoing efforts at CPSI continue to build upon this success and are focusing on further development, optimization and testing of new minimally invasive surgical devices designed to treat cancers including prostate, pancreatic, bladder, kidney, esophageal and breast cancer among others. Speaking to the broader device development program at CPSI, Dr Baust noted "an ongoing Phase II SBIR award from NCI has provided CPSI the opportunity to ramp up our R&D studies around our advanced cryoablation device platform in combination with vitamin D_3 metabolite pre-treatment for the treatment of liver and pancreatic cancers. This project incorporates several of CPSI's patented technologies, including our cryoengines, thermal ablation probes and catheters and adjunctive anticancer agents (*SensitICER*s). With success, these efforts will provide an advanced minimally invasive approach for treating various cancers." With development underway, CPSI is poised to embark down the commercialization path. To this end, Baust commented "We are actively seeking investors and partners through a variety of mechanisms to join our team to bring this potentially lifesaving technology platform to the market."

The open access article appeared in January-March edition of Cancer Control (25:1) and is timely in view of the increased use of cryoablation for the treatment of cancer. The article can be accessed free of charge via the Cancer Control website at: http://journals.sagepub.com/doi/full/10.1177/1073274818757418

More information on the CPSI's cryoablation and *SensitICER* technologies can be found on CPSI's website at www.CPSIBiotech.com.

About CPSI Biotech - CPSI Biotech, a private, integrative bio/medtech greenhouse company, develops and designs life science research products and cryo-medical devices for applications in cancer, cardiovascular disease treatments and cell therapy bioprocessing. Ongoing R&D and business development activities continue to produce innovative technologies, devices and intellectual property for commercialization, licensing or sales in support of diverse clinical and research applications. By leveraging the innovation, flexibility and R&D strengths of CPSI in combination with the development, commercialization, manufacturing and clinical expertise of partnering organizations, rapid and efficient product development is attainable.

Disclosure Notice: The information contained in this release is as of March 7, 2018 CPSI assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments. CPSI's technologies do not have regulatory clearance for commercial sale and are currently intended for "Research Use Only".

With the exception of the historical information contained in this release, this release contains materials and statements related to future business, financial performance, future events and/or developments involving CPSI which constitute forward-looking statements. The matters described herein contain forward-looking statements that involve risk and uncertainties that may individually or mutually impact the matters herein described, including but not limited to, CPSI's ability to develop and market new products, to retain and attract key employees, to obtain regulatory clearances and approvals for its products, to effectively react to other risks and uncertainties, such as fluctuation of quarterly financial results, contract and grants acquisition, reliance on third party manufacturers and suppliers, litigation or other proceedings, economic, competitive, governmental impacts, whether pending patents will be granted or defendable, validity of intellectual property and patents, the ability to license patents, the ability to commercialize developmental products, competition from existing and new products and procedures and CPSI's ability to raise the capital that is required to accomplish the foregoing.

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