**Prospective cancer treatment found in the Cowpea Mosaic Virus.**

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**The Cowpea Mosaic Virus (CPMV) shows encouraging results as an immunotherapy against multiple forms of cancerous cells and tumors. The nanoparticles in the Cowpea Mosaic Virus have been administered to cancer-infected mice by *in situ* vaccination. Not only do the results show improved conditions of the cancerous tumors, it completely eliminated the metastases in some cases. Furthermore, the Cowpea Mosaic Virus nanoparticles do not impose any viable risk factors or dangerous side effects. Possible future treatment of various malignant tumors may be reliant on direct injection of the Cowpea Mosaic Virus nanoparticles.**

**Introduction**

According to the World Health Organization, cancer is among the leading causes of death worldwide. In 2012, there were 14 million new cases and 8.2 million cancer-related deaths worldwide (Stewart, 2016). The National Cancer Institute stated, “that 1,685,210 new cases of cancer will be diagnosed in the United States and 595,690 people will die from the disease in 2016.” Some researchers and scientist believe they may have a prospective therapeutic treatment for those cancer patients and it lies within the Cowpea Mosaic Virus (also known as CPMV). The Cowpea Mosiac Virus is a comovirus which is defined by the National Library of Medicine as, “a genus of plant viruses of the family COMOVIRIDAE in which the bipartite genome is encapsidated in separate icosahedral particles. Mosaic and mottle symptoms are characteristic, and transmission is exclusively by leaf-feeding beetles.” CMVP can infect either humans, animals and the cowpea leaves. The virus causes a mosaic pattern, showing the evidence of infection. The Cowpea Mosaic Virus was first discovered in 1959 in Africa, where it was determined to be pathogenic (Joseph, 2012). CPMV was of interested due to its pathogenicity. As research was conducted on the virus, it was found that the virus contained many antioxidants, like flavonol (Joseph, 2012). The antioxidant in CPMV lead to cancer treatment studies, including tests using inhalation or direct injection of the virus. More recently, the Cowpea Mosaic Virus is used as a virus like particle (or VLP for short) because it does not have any nucleic acids. The lack of nucleic acids makes the virus nanoparticles non-toxic to its receiver and is referred to as empty CPMV (eCPMV). The Cowpea Mosaic Virus nanoparticles also present themselves as antigens in the antiviral vaccine. When extracted, the eCPMV can be used as an immunostimulatory agent and/or immunotherapy towards metastases treatment (Lizotte, 2015). Model mice have been used to explore the options of cancer therapy by ingestion and in situ vaccination with nanoparticles from the Cowpea Mosaic Virus. The results showed that diseased mice with lung tumors had substantial delay of tumor growth. Some of these mice completely defeated the carcinoma and, when reintroduced to the same type of cancer cells, the mice’s immune response did not allow the cancerous cells to grow or survive.

**Recent Progress**

Inhalation or direct injection of eCPMV provokes specific antitumor immunities. When dealing with injections of the CMPV, the virus like particles are directly injected to the area of which the cancer is contained, typically the cancerous tissue or an organ. This method is defined as *in situ* vaccination. The VLPs induce bone marrow derived dendritic cells, macrophages and, most importantly, it activates a large pool of neutrophils, which then employ adaptive immune responses. An increased supply of neutrophils results in production of cytokines and chemokines, recruitment of T lymphocytes and Natural Killer cells, and explicit destruction of the malignant cells. These reactions break the immunity tolerance of carcinogenic cells by creating a new immune response and/or promoting a memory immune response. These responses make the Cowpea Mosaic Virus particles immunogenic. These results were found when eCPMV was both inhaled and injected by model mice with various types of cancers. When the particles were inhaled, the result was a slow growth process for lung tumors. When the empty virus fragments were injected, it resulted in a massive delay of tumor growth and in half of the treated mice, the malignant tumors were destroyed only after two treatments (Lizotte, 2015). Furthermore, 3 out of 4 mice who were cured of their lung tumors were then re-introduced the same cancerous cells back into their lungs to study the effects. It was found that their bodies rejected the carcinomas due to the effect of eCPMV producing a memory immune response against that specific type of tumor (Lizotte, 2015). It is key to note that none of the model mice showed any signs of harmful side effects. Because CPMV nanoparticles do not contain immunogenic contaminants they can be considered highly therapeutic. Scientists verified their results by using monoclonal antibodies to reduce the number of neutrophils produced by eCPMV. They concluded that the production of neutrophils from introducing eCPMV to the tumor by inhalation or injection is the most important effect of this treatment. Without the increased neutrophil population, the carcinomas were more resistant to treatment. To confirm their results, scientist used model mice with other forms of cancer, specifically colon tumors, ovarian carcinomas and dermal melanomas. Researchers introduced to eCPMV to those cancer-infected mice by either inhalation or injection (Lizotte, 2016). It was found that those three cancerous tissues resulted in the same conclusions as the mice with malignant lung tumors. Model mice with ovarian cancer had the most positive outcomes through faster destruction time and stronger survival signs (Lizotte, 2016). These findings show that usage of the Cowpea Mosaic Virus is interchangeable.

**Discussion**

The positive effects of inhalation or injection of Cowpea Mosaic Virus nanoparticles give an enthusiastic outlook for cancer treatments. To aid the case even more, CPMV can be manufactured in molecular farms which makes it highly scalable. Scientists believe that direct injections aided with checkpoint inhibitors could be the most favorable treatment for tumors and metastases. However, research on *in vivo* methods have not been conducted. That method could either conclude the same findings that the *in situ* tests found or the results could vary between the two types of studies (Lizotte, 2016). With further research conducted, scientist hope to unveil the therapeutic efficacy for a much needed and concrete treatment plan.

**References**

"Cancer Statistics." *National Cancer Institute*. N.p., n.d. Web. 04 Feb. 2016. <http://www.cancer.gov/about-cancer/what-is-cancer/statistics>

“Comovirus” University Of Massachusetts Medical School. (n.d.). Retrieved February 23, 2016, from <http://profiles.umassmed.edu/Profiles/display/123761.>

Joseph, A., Susanne, T., & Singh, B. (n.d.). Increasing Utilization of Cowpeas to Promote Health and Food Security in Africa. Texas A&M University Research. Retrieved February 24, 2016 <http://legumelab.msu.edu/uploads/files/TAMU-1 Tech Prog Rpt FY11 Final.pdf>.

Lizotte, P. H., A. M. Wen, M. R. Sheen, J. Fields, P. Rojanasopondist, N. F. Steinmetz, and S. Fiering. "In Situ Vaccination with Cowpea Mosaic Virus Nanoparticles Suppresses Metastatic Cancer." *Nature Nanotech Nature Nanotechnology* (2015).

Stewart, Bernard W., and Christopher P. Wild. "Cancer." *World Health Organization*. IARC, 2014. Web. <http://www.who.int/mediacentre/factsheets/fs297/en/>.