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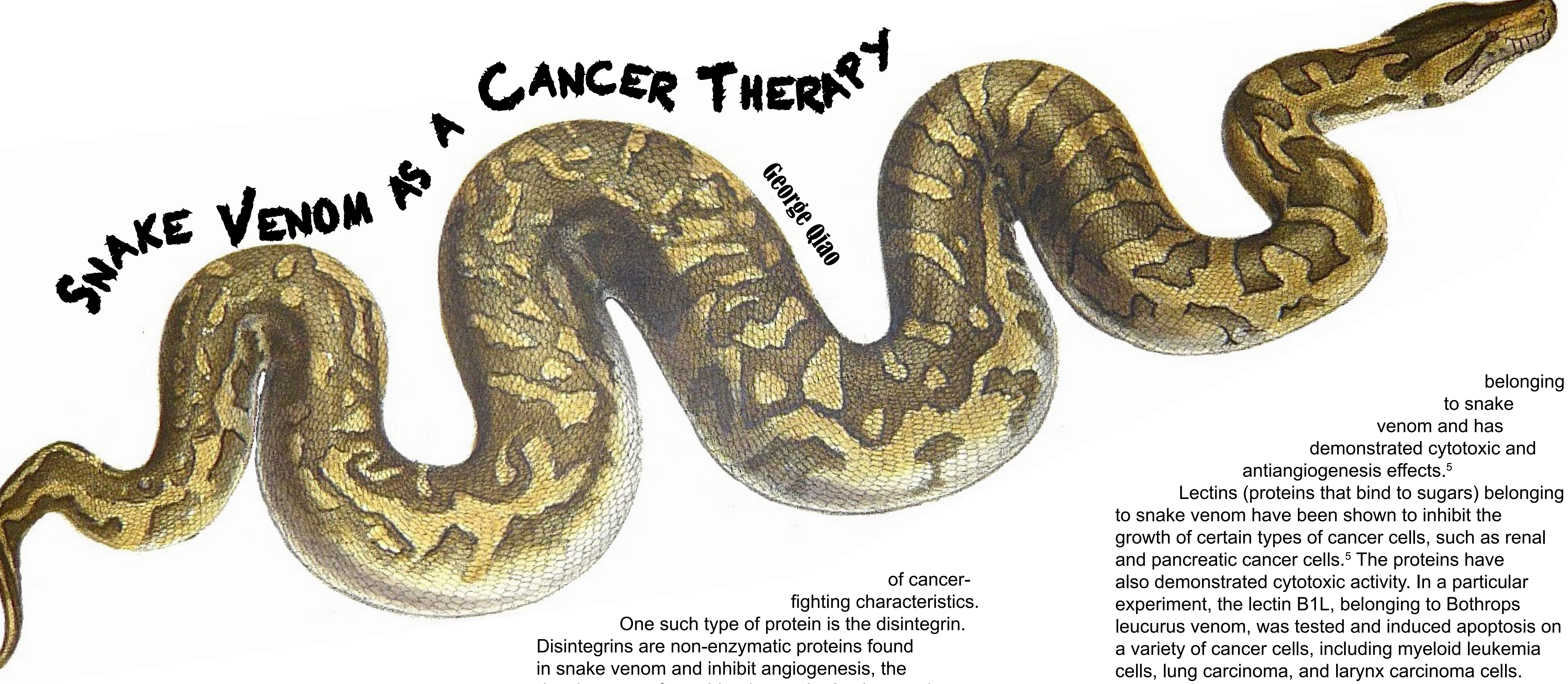

George Qiao

Cancer is a deadly disease affecting and killing many people every year. For 2019, the estimated number of new cancer cases exceeds 1.5 million, and the estimated number of deaths caused by cancer exceeds six-hundred thousand.[1] Treatments for cancer certainly exist; although current treatments are often costly and are not always effective in the long-run. The treatments also come with side effects often associated with the destruction of healthy, noncancerous cells. The expansion of alternatives for treating cancer is a constant objective for the medical community, and researchers are experimenting with many new solutions in order to provide new opportunities to treat cancer. One potential treatment in development is snake venom, a substance that is normally poisonous to humans in its unmodified form.

Although snake venom as a whole can be harmful to humans, it is composed of many different proteins, enzymes, and carbohydrates. If the different molecules constituting the venom are extracted and isolated, the individual molecules can provide benefits for humans without the harmful effects of the entire venom. For example, the drug captopril is derived from snake venom and treats high blood pressure and heart failure. As long as the entire venom is not used, the separate components can elicit healthy effects in humans. In the 1940s, researchers began isolating enzymes and non-enzyme proteins from snake venom and experimented with the proteins for effects on tumor cells. Clinical testing with the venom became more prevalent from the 1960s onward.[2, 3]

The proteins in snake venom harbor a variety of cancer-fighting characteristics. One such type of protein is the disintegrin. Disintegrins are non-enzymatic proteins found in snake venom and inhibit angiogenesis, the development of new blood vessels. Angiogenesis allows tumor cells to invade nearby healthy tissue and metastasize. Treatment with disintegrins has been shown to suppress the spread of tumors due to the antiangiogensis activity of disintegrins.[3]

L-amino acid oxidases (LAAOs) are enzymatic proteins found in snake venom and demonstrate anti-tumor effects. LAAO converts L-amino acid to alpha-keto acid and releases the byproducts ammonia and hydrogen peroxide. Hydrogen peroxide is a major proposed mechanism of LAAO-induced toxicity, as it can act as reactive oxygen species (ROS) that can diffuse into cancer cells and cause cell death. Studies have shown that the effects of ROS are more likely to harm cancer cells than normal cells, possibly due to the higher metabolic activity present in cancer cells. The higher metabolic activity leads to higher levels of ROS in cancer cells; hence, the cancer cells are more susceptible to further increases in ROS levels than normal cells. The evidence of selectivity of LAAO activity towards cancer cells is beneficial for cancer therapy, as the enzyme does not seem to have a high potential to harm healthy cells.[4]

Metalloproteases (MPs) are another group of enzymes derived from the venom and can also exhibit anti-tumor activity.[5] One type of MP, known as jarahagin (produced by the species Bothrops jararaca), has demonstrated cytotoxic effects on melanoma cells, as well as inhibition of cancer cell adhesion.[6] Cell adhesion contributes to tumor spread; thus, by inhibiting adhesion, jarahagin can prevent metastasis, which is the spread of cancer to a secondary site.

Phospholipase A2 (PLA2) is another enzyme belonging to snake venom and has demonstrated cytotoxic and antiangiogenesis effects.[5]

Lectins (proteins that bind to sugars) belonging to snake venom have been shown to inhibit the growth of certain types of cancer cells, such as renal and pancreatic cancer cells.[5] The proteins have also demonstrated cytotoxic activity. In a particular experiment, the lectin B1L, belonging to Bothrops leucurus venom, was tested and induced apoptosis on a variety of cancer cells, including myeloid leukemia cells, lung carcinoma, and larynx carcinoma cells. Furthermore, healthy cells were not harmed by the protein.[7] Thus, snake venom lectins can be especially helpful in treating certain types of cancer.

The process of collecting the venom and determining its effects on cancer takes multiple steps. The species of snake from which the venom is collected depends on the proteins of interest, as the type of venom varies among species. It may be easier to collect venom in the summer as opposed to the winter, as the venom is more liquefied in the summer.[8] Once the species is identified and captured, the snake must be kept in conditions suitable for living. A snake can die when kept in conditions unlike its natural habitat, and high occurrences of snake deaths could shift a vulnerable species closer to becoming endangered.[2] Once the venom is collected, the proteins must be isolated using various purification techniques, such as size-exclusion, ion exchange, and affinity chromatography. Edman sequencing can be used to determine the sequences of small proteins, if necessary.[9] Once the individual proteins of the venom are identified and isolated, researchers can test the effects of the proteins on cancer cell activity.

The isolation and utilization of snake venom components is a valuable cancer-fighting technique but is not without its flaws. The immune system can possibly react to foreign proteins injected into the bloodstream. Immunosuppression may help prevent rejection of the proteins by the immune system, but would also render the body vulnerable to infectious agents. Encapsulation of the proteins in nanocarriers for slow, controlled release of the proteins may help prevent adverse reactions by the immune system. The technique of encapsulation, however, has not fully been mastered and is currently in development.[3, 10] Furthermore, the mechanisms of action of many cancer-fighting proteins have not yet been confirmed, which is why many of these proteins are not yet available for purchase from pharmacies.[11] Until the exact behavior of the snake venom components are made certain, there is no guarantee that these proteins cannot destroy healthy, noncancerous cells. Although many of the proteins have demonstrated selectivity towards tumor cells in experiments, further research should be done to confirm the abilities of these molecules to discriminate between cancerous and healthy cells and to determine potential methods to circumvent any possibility of the proteins harming healthy cells.

Snake venom as a treatment for cancer is promising and could be an effective alternative to current treatments. Whether or not the use of snake venoms would be more cost effective or less painful than current treatments has not yet been confirmed, as the treatment is not a common practice. Further research on the behavior of these proteins and on potential costs of treating cancer patients with the venom should provide more insight about the value of the treatment. In the future, when more information is made available, snake venom could potentially serve as an incredibly valuable alternative to current cancer treatments.

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