Venom gets good buzz as potential cancer-fighter

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Bee, snake or scorpion venom could form the basis of a new generation of cancer-fighting drugs, scientists will report here today. They have devised a method for targeting venom proteins specifically to malignant cells while sparing healthy ones, which reduces or eliminates side effects that the toxins would otherwise cause.

The report was part of the 248th National Meeting of the American Chemical Society (ACS), the world's largest scientific society. The meeting, attended by thousands of scientists, features nearly 12,000 reports on new advances in science and other topics.

"We have safely used venom toxins in tiny nanometer-sized particles to treat breast cancer and melanoma cells in the laboratory," says Dipanjan Pan, Ph.D., who led the study. "These particles, which are camouflaged from the immune system, take the toxin directly to the cancer cells, sparing normal tissue."

Venom from snakes, bees and scorpions contains proteins and peptides which, when separated from the other components and tested individually, can attach to cancer cell membranes. That activity could potentially block the growth and spread of the disease, other researchers have reported. Pan and his team say that some of substances found in any of these venoms could be effective anti-tumor agents. But just injecting venoms into a patient would have side effects. Among these could be damage to heart muscle or nerve cells, unwanted clotting or, alternately, bleeding under the skin. So Pan and his team at University of

Illinois at Urbana-Champaign set out to solve this problem.

He says that in the honeybee study, his team identified a substance in the venom called melittin that keeps the cancer cells from multiplying. Bees make so little venom that it's not feasible to extract it and separate out the substance time after time for lab testing or for later clinical use. That's why they synthesized melittin in the lab.

To figure out how melittin would work inside a nanoparticle, they conducted computational studies. Next, they did the test and injected their synthetic toxin into nanoparticles. "The peptide toxins we made are so tightly packed within the nanoparticle that they don't leach out when exposed to the bloodstream and cause side effects," he explains.

What they do is go directly to the tumor, where they bind to cancer stem cells, blocking their growth and spread. He says that synthetic peptides mimicking components from other venoms, such as those from snakes or scorpions, also work well in the nanoparticles as a possible cancer therapy.

Pan says the next step is to examine the new treatment approach in rats and pigs. Eventually, they hope to begin a study involving patients. He estimates that this should be in the next three to five years.

More information: Title: Controlled and safer therapeutic delivery of venom toxins using well-defined polymeric nanoparticles for cancer inhibition

Abstract
Myriad of advancement has been made to identify naturally abundant substances for use as therapeutic agents. Host defence peptides (eukaryotic cells) from animal venoms have been identified to possess substantial anticancer properties. However, their therapeutic potential

cannot be fully realized without acontrolled delivery mechanism because of off-target toxicity, non-specificity, complement activation issues and unfavorable pharmacokinetics, all contributed to negatively to translate these agents to clinic. Towards a safer, translatable approach, we have developed a viable chemical methodology based on well-defined, self-assembled polymeric nano-architecture for controlled delivery of venom peptides. Although our methodology is applicable for peptides of 5-30 aa, as a specific example, a well-studied cytolytic peptide, Melittin (26 aa), was selected for preliminary studies. The melitin-incorporated polymeric nanoparticles (hydrodynamic diameter: 50 ± 5nm) were prepared by applying a post-incubation methodology. The parent nanoparticles were self-assembled as aqueous suspension of amphiphilic diblock-co-polymer PS-b-PAA and Polyoxyethylene (20) cetyl ether. These particles showed significant stability over time and the release of melittin remained well controlled in time and concentration dependent manner. The cytotoxicity of these nanoparticles was studied in MCF-7 and MDA-MB231 breast cancer cells using MTT assay and showed IC50 value of 50nM. This construct promises to address the serious off-target toxicity of the membrane-bound venom peptides when systemically delivered and simultaneously protects the integrity of the peptide itself that may complicate systemic application. The presentation will discuss characterization and application of these particles using dynamic light scattering, atomic force microscopy, transmission electron microscopy, electrophoretic potential, and cytotoxicity analysis. We anticipate this unique anticancer agent found in nature coupled with the delivery approach has the potential for the development of a novel anticancer treatment. Many active secretions produced by animals have been employed in the development of new drugs to treat diseases such as hypertension and cancer. Snake venom toxins contributed significantly to the treatment of many medical conditions. There are many published studies describing and elucidating the anti-cancer potential of snake venom. Cancer therapy is one of the main areas for the use of protein peptides and enzymes originating from animals of different species.

Some of these proteins or peptides and enzymes from snake venom when isolated and evaluated may bind specifically to cancer cell membranes, affecting the migration and proliferation of these cells. Some of substances found in the snake venom present a great potential as anti-tumor agent. In this review, we presented the main results of recent years of research involving the active compounds of snake venom that have anticancer activity.

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