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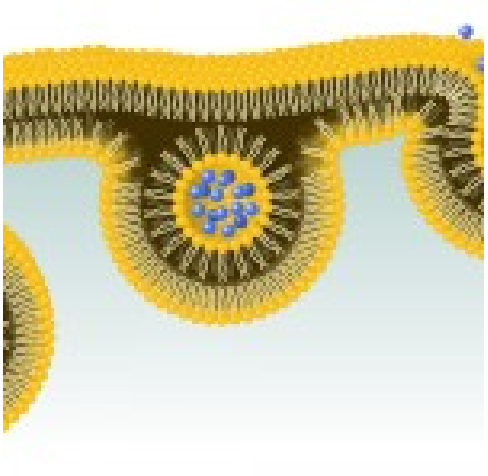
Fighting Cancer, Tiny Particles Pack a Powerful Punch

By Lila Abassi — January 21, 2016



exocytosis via shutterstock [1]

It is no secret that cancer is very tough to treat. Cancers [2] that have metastasized and/or developed resistance to chemotherapy are generally considered to be incurable. An additional, and very difficult problem, is drug delivery getting the most drug to the cancer while sparing healthy cells.

This is because the surviving cancer, cancer stem cells (CSCs), tend to be both aggressive most likely to metastasize, or spread to distal organs and also be substantially resistant to the chemotherapy and radiation treatment that left them behind in the first place.

A huge advance the treatment would be addressing these issues, and such research [3], is being done at the University of North Carolina at Chapel Hill. Scientists there have discovered a method for using the body s own immune system to deliver chemotherapeutic agents, at much lower doses, selectively to cancer cells. The cancer drug is packaged into tiny vesicles, which are derived from a type of white blood cell, called a macrophage. This makes it unlikely that the vesicles will be recognized and destroyed by the immune system, thus enabling much more drug to be delivered to its intended site.

This work [4] was led by Elena Batrakova, Ph.D., an associate professor in the UNC Eshelman School of Pharmacy and her colleagues. Batrakova stated, That means we can use 50 times less of the drug and still get the same results. That matters because we may eventually be able to treat patients with smaller and more accurate doses of powerful chemotherapy drugs resulting in more effective treatment with fewer and milder side effects.

The drug delivery particles are called exosomes [5]. They are part of the body s innate immune system but they can be derived from a wide variety of cells. These macrophages release exosomes

[6] loaded with Paclitaxel [7] (PTX), a chemotherapeutic agent that is used in the treatment of breast, ovarian, lung, bladder, prostate, melanoma, esophageal, as well as other types of solid tumors. Cancer cells tend to have molecular tags that allow for targeted recognition by exosomes.

The researchers used a mouse model of lung cancer in their study, and discovered a high loading efficiency (capacity to get the drug into the exosomes) and sustained drug release and most important of all, when exosomes were loaded with PTX, it increased cytotoxicity (the ability to kill cells) by more than 50 times in drug resistant cells in comparison to standard therapy. The authors believe that this form of drug delivery holds significant promise in overcoming a fundamental difficulty in chemotherapy killing drug resistant cancer cells.

Exosomes have attracted considerable attention, as vehicles for drug delivery in other systems. Since they are part of the immune system, can specifically bind to targeted cancer cells, and locally increase the concentration effect of the drug where it is needed, would significantly decrease the systemic side effects of chemotherapy (i.e. nausea, fatigue, pain, hair loss).

Exosomes are engineered by nature to be the perfect delivery vehicles, said Batrakova, who has also used this technique as a potential therapy for Parkinson s disease. By using exosomes from white blood cells, we wrap the medicine in an invisibility cloak that hides it from the immune system. We don t know exactly how they do it, but the exosomes swarm the cancer cells, completely bypassing any drug resistance they may have and delivering their payload.

The technology is not quite ready to be tested in humans. However, this drug delivery method is a potential game changer and not just against cancer, but many other disease processes as well (i.e. Parkinson's disease, rheumatoid arthritis, heart disease).
