Molecules on branched-polymer surfaces can capture rare tumor cells in blood

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The removal of rare tumor cells circulating in the blood might be possible with the use of biomolecules bound to dendrimers, highly branched synthetic polymers, which could efficiently sift and capture the diseased cells, according to new research at the University of Illinois at Chicago.

Dendrimers have been used to encapsulate drug molecules and serve as a delivery vehicle, but in the new study they were employed to capture circulating tumor cells by biomimicry -- using nanotechnology to create artificial surfaces much like those in real cells.

"We want to take advantage of what nature gives us," says Seungpyo Hong, lead researcher of the study, published in the journal *Angewandte Chemie.* "We want to create new biomimetic surfaces that will allow us to remove damaged cells from the blood."

Hong, assistant professor of biopharmaceutical sciences at UIC, and his coworkers created a highly sensitive surface that enables multivalent binding -- the simultaneous binding of many molecules to multiple receptors in a biological system. The biomimetic surface was created using dendrimers of seventh-generation polyamidoamine, or PAMAM, and the anti-epithelial cell adhesion molecule, or aEpCAM.

In the body, cancer cells can detach from a primary tumor and flow throughout the bloodstream, enabling them to seed distant new tumors. Rare and difficult to capture, only a few circulating tumor cells can be

found in a milliliter of blood in a cancer patient. By comparison, the same volume of blood contains several million white blood cells and a billion red blood cells, Hong said.

Three breast cancer cell lines were used as circulating tumor cell models, with each used to compare the cell adhesion of the dendrimer surfaces to a linear polymer of polyethylene glycol. PEG is commonly used to bind molecules to improve the safety and efficiency of therapeutics.

The nano-scale PAMAM dendrimers were chosen because their size and surface dimension could accommodate multiple anti-epithelial cell adhesion molecules, Hong said. This enabled the multivalent binding, along with the physiological process of "cell rolling" induced by E-selectin, which mimics the process by which circulating tumor cells are recruited to the endothelia and enhances the surface sensitivity toward tumor cells.

The surface developed by the UIC research team demonstrated up to a million-fold increase in binding strength, and up to 7-fold increase in detection efficiency, as compared to the aEpCAM-coated PEG surface that is the current gold standard for circulating tumor cell detection.

Hong says this is the first study to capture the tumor cells on the surface exploiting the multivalent effect, which is most likely due to the spherical architecture of dendrimers. The research was selected as a "Hot Paper" by *Angewandte Chemie* and highlighted in Faculty of 1000 by Donald Tomalia, the inventor of PAMAM dendrimers.

The results demonstrate that the combination of nanotechnology and biomimicry has a "great potential to be applied for highly sensitive detection of rare tumor cells from blood," Hong said.

Provided by University of Illinois at Chicago