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Contact: Cha-Mei Tang, Ph.D. President and CEO, Creatv MicroTech, Inc. 240-441-3311 cmtang@creatvmicrotech.com

Discovery of Giant Macrophages in the Blood of Cancer Patients



Four exemplary giant macrophages are shown along with some white blood cells denoted by "w". All are multinucleated (blue color) and have varying diffuse expression of epithelial marker (green) and epithelial cell adhesion molecule (red). Not all express the white blood cell marker CD45 (violet). ROCKVILLE, Md., March 11, 2014-Creatv MicroTech, Inc. collaborates with cancer researchers from a number of universities to study circulating tumor cells (CTCs) in the blood of cancer patients. When cancers become advanced, tumor cells from the primary tumor can enter the bloodstream and cause metastasis at another organ—such as liver, lung, bone, or the brain—with deadly effect. While researching the biological implications of CTC spread, Creatv's research team found a group of previously unreported cells associated with primary cancer spread. These unusual cells were named "circulating cancer-associated macrophage-like cells" (CAMLs). Their very large size-25 to 300 micronsstands out, and they have five different morphologies. Their biological implications were recently reported in Proceedings of the

National Academy of Sciences (<u>http://www.pnas.org/content/early/2014/02/14/1320198111</u>).

The initial research was for breast cancer, undertaken in collaboration with the University of Maryland School of Medicine, and was expanded to prostate and pancreatic cancers in collaboration with Thomas Jefferson University, Northwestern University, Fox Chase Cancer Center, and the Medical College of Wisconsin.

Although CTCs have many clinical utilities, they are not consistently found in some patients, even in later-stage disease. In contrast, according to lead author Daniel Adams, "This study showed that CAMLs are a cancer-associated biomarker found in all stages of breast, prostate, and pancreatic cancers and in greater abundance than CTCs."



Massimo Cristofanilli, MD, of Thomas Jefferson, stated, "Detecting cancer-associated immune cells indicates that the blood of cancer patients holds significant information that can lead to a more advanced understanding of how tumor cells affect other patient factors, including immunity, before and during treatment. The data suggest that if we are able to detect circulating cancer cells along with these circulating macrophages, we will have the unique ability to predict both prognosis and what happens when the disease becomes resistant to treatment and spreads. This novel finding advances the concept of 'liquid biopsy' from mere detection of cancer cells in the blood to detecting and monitoring both cancer cells and immune cells. This new approach can change the way we evaluate, monitor and treat patients, particularly immunotherapies."

Creatv's novel platform technology, based on CellSieve[™] precision microfilters, enables the isolation of CTCs and CAMLs. CellSieve[™] is the only commercially available microfilter that is strong and optically suited for high-resolution fluorescent microscope imaging, with uniform pore size and distribution for maximum capture of both CAMLs and CTCs. CellSieve's ability to simultaneously capture both CAMLs and CTCs makes it especially suited for use in research and clinical applications. This technology is now also used in additional cancers in which other methods have been less effective.

CellSieve[™] was made possible by the lithographic microfabrication expertise of Creatv scientists. In addition, the company developed a filtration system that is:

- fast, taking only three minutes to filter 7.5 ml of blood
- easy and clean, with the whole assay performed inside a filter holder
- gentle, not damaging the fragile cells

CTCs and CAMLs maintained their three-dimensional shape after isolation, providing researchers and clinicians the high-quality cells that enabled the discovery and characterization of CAMLs.

Unlike other methods, cells captured by CellSieve[™] are not blocked by ferrofluids or magnetic beads, thereby allowing high definition visualization of their morphology.

"The ideal optical properties of the microfilters, transparency, and non-fluorescence allow cytologists to observe fine cellular details of CTCs and CAMLs with high contrast, providing well-defined microscope images," said Cha-Mei Tang, Sc.D., Creatv's President and CEO.

About Creatv MicroTech

Creatv MicroTech (<u>www.creatvmicrotech.com</u>) is a privately held company founded in 2000. Creatv has amassed expertise in both biodetection and microfabrication, which were applied to the development of the CellSieve[™] microfiltration platform and the analysis of CTCs and CAMLs. Creatv has been recognized by an R&D 100 Award, inclusion on the Micro/Nano 25-Technologies of Tomorrow List, and Montgomery County Maryland's Bioscience Company of the Year Award. The CellSieve[™] platform and assays are available commercially for research use only and are currently in use in hospitals and clinics with nine different cancers. The research was partially funded by an award from Maryland TEDCO (<u>http://tedco.md</u>).