Microfilters with Nanotopography for Isolation of Circulating Tumor Cell from Blood

Olga V Makarova
Creatv MicroTech Inc., 2242 West Harrison St., Chicago IL 60612

Ralu Divan and Daniel Rosenmann
Argonne National Laboratory, 9700 South Cass Av., Argonne IL 60439

Daniel Adams, Peixuan Zhu, Shuhong Li, Platte Amstutz and Cha-Mei Tang
Creatv MicroTech Inc., 11609 Lake Potomac Dr., Potomac MD 20854 and 9900 Belward Campus Drive, Suite 330, Rockville, MD 20850

Circulating tumor cells (CTCs) are cells shed from a primary tumor into the blood of patients with metastatic cancer. Analysis of CTCs has great clinical significance for treatment of solid tumor cancers, because they can be used to determine personalized therapy, monitor treatment response, and for early detection of recurrence. Detection of CTCs is technically challenging, because of their extremely low numbers (1-3 per milliliter of blood). CTCs are larger than blood cells and can be isolated by size-exclusion using microfilters with precision pores. The efficiency of the CTC capture can be increased by introducing nanoscale topography to the filter surface. Capture of CTCs using a nanoroughened glass surface has been shown [1], demonstrating that cancer cells exhibit different adhesion preference to nanoscale topography compared to normal blood cells. Size, morphology, organization, and separation of nanofeatures affect cell response.

In this work, microfilters are fabricated by UV lithography using resist that is strong, biocompatible, and optically transparent. Low fluorescence for wavelengths over 400 nm make it suitable for fluorescent microscope imaging. We use an anodized aluminum oxide (AAO) layer as a template to achieve nanotopography on the filter surface. AAO has a highly ordered porous structure, and the pore spacing and diameter can be easily controlled by experimental conditions, such as electrolyte solution, anodization voltage, time, and working temperature. AAO is fabricated directly on the filter membrane and serves as an etching template to create various surface reliefs using reactive ion etching. The utility of the microfilters with various topographies is evaluated using cancer cell lines spiked into normal human blood.

1. W. Chen et al., ACS Nano, DOI: 10.1021/nn304719q, Web publication: Nov.29, 2012

Use of the Center for Nanoscale Materials, Argonne National Laboratory was supported by the U. S. Department of Energy, Office of Science, Office of Basic Energy Sciences, under Contract No. DE-AC02-06CH11357.