Porous bioaffinity membranes for the isolation of circulating tumor cells

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Background & objectives

In cancer diagnosis, a liquid biopsy to determine the presence of circulating tumor cells (CTCs) in a patient's blood can allow for early detection of cancer. This can be made possible through the isolation and counting of CTCs, which may number in the single digits for a 7.5 ml sample of blood. This small number of cells requires a highly accurate method of isolation, as well as the ability to remove contamination from other cells in blood such as white and red blood cells. One method to achieve this is through a bioaffinity membrane, which combines dead-end filtration and selective capture surface comprised of immobilized antibodies which interact with proteins on the surface of the CTCs.

Methods

A copolymer of poly (dimethyl acrylamide) (PDMAA) and methacryloyloxy benzophenone (MABP), a crosslinking group, is coated onto membranes with pore sizes of 6-8 μm. UV-light is then used to activate the benzophenone groups to simultaneously crosslink and attach the copolymer to the surface through the CH-insertion crosslinking (CHic) reaction.

Results

This has been demonstrated both on track-etched polycarbonate membranes, as well as nickel membranes with defined pore locations with the inclusion of a priming step. Following attachment of the hydrogel, streptavidin molecules are attached to the surface using the same CHic-reaction. Using the biotin-streptavidin interaction, antibodies specific to the CTCs of interest may then be immobilized on the surface. This allows for a highly specific surface, tailored to the CTCs of interest, and a high sensitivity, as a result of the immobilization of the CTCs through their interaction with the antibodies. After filtration of a patient blood sample spiked with varying amounts of MCF-7 cells, nearly all CTCs were able to be recovered using these coated and functionalized nickel membranes.

Conclusion

This bioaffinity filtration technique has been shown give high recovery rates of MCF-7 and SHP-77 spiked in blood, as well as identify CTCs in patient samples with a volume of 7.5 ml with results comparable to the industry benchmark, CellSearch.