New device for identifying aggressive breast cancers

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A new disposable device based on advances in microfluidics may help identify advanced breast cancer patients who are candidates for therapy with the drug trastuzumab (Herceptin). The device is described in the American Institute of Physics' journal *Biomicrofluidics*.

Aggressive breast cancers with poor prognosis typically have abnormal levels of the protein HER2 (the tyrosine kinase human epidermal growth factor receptor 2). The new elastomeric, rubber-like device is designed to efficiently capture cancer cells overexpressing HER2 in circulating blood.

Finding a way to identify these cells is medically relevant because HER2 positive patients with early breast cancer have been found to significantly benefit from treatment with Herceptin or trastuzumab, the humanized monoclonal antibody against HER2, which can lower recurrence risk by about half. Given the cost ($50,000 - $65,000 per year in the United States) and possible side effects of Herceptin therapy, establishing HER2 status is crucial.

Current methodologies for determining HER2 status include immunohistochemistry and fluorescence in situ hybridization (FISH), both of which require biopsies. But biopsy-based testing may lead to ineffective treatment choices because in about 20% of breast cancers, the HER2 status of the primary tumor may differ from that of a metastatic tumor. This fact has made the non-invasive alternative of profiling circulating tumor cells a long-sought but elusive goal. Isolating

circulating tumor cells, which are present at ratios as low as 1 to 10 per billion blood cells, is extremely challenging.

Recently, interest in microfluidic devices for capturing circulating tumor cells (CTCs) has intensified because of their greatly improved capabilities. A microfabricated device developed by researchers at the Massachusetts General Hospital and designed to bind to cells of epithelial origins (most cancers originate from epithelial tissues) circulating in the blood demonstrated near-perfect ability to isolate circulating tumor cells across a range of cancers.

In a study supported by the National Health and Medical Research Council Australia, Benjamin Thierry and colleagues at the Ian Wark Research Institute at the University of South Australia developed a plastic-based disposable microfluidic device offering several improvements for capturing circulating tumor cells. The device is designed to take advantage of the features of an organic silicone found in contact lenses and shampoos called polydimethylsiloxane (PDMS), which is compatible with soft molding techniques, transparent, and permeable to gasses.

The device is significantly easier and cheaper to make than the prior microfabricated one. The major challenge associated with PDMS use in biodiagnostic applications is its lack of chemical reactivity. The team used a novel plasma-based polymerization process to overcome that problem. The process creates a durable polymeric layer on the device's surface containing a high number of reactive molecules, which can readily be used to attach proteins able to capture cancer cells but not normal blood cells.

With a commonly used breast cancer cell line (SK-BR-3) as a model for cells overexpressing HER2, Dr. Thierry's device demonstrated an ~80% immuno-capture efficacy of HER positive cells from full blood in model

and validation studies.

Thierry concluded, "Microfluidic-based devices offer a unique opportunity to efficiently isolate CTCs from patient's blood, thereby opening a window on the pathophysiology of cancer and its progression. We hope that our device will provide a fast, reliable and affordable methodology to establish HER2 status for breast cancer patients presenting metastases, thereby enabling the selection of more potent therapy based on trastuzumab. We are aiming to achieve clinical validation in the coming months and, with the support of a fellowship from the Prostate Cancer Foundation of Australia, to extend the study to the detection of aggressive forms of prostate cancer."

More information: The article, "Herceptin-Functionalized Microfluidic PDMS Devices for the Capture of HER2 Positive Circulating Breast Cancer Cells Benjamin Thierry, Mahaveer Kurkuri, Jun Yan Shi, Lwin Ei Mon Phyo Lwin and Dennis Palms (University of South Australia) appears in the journal *Biomicrofluidics*. bmf.aip.org/

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