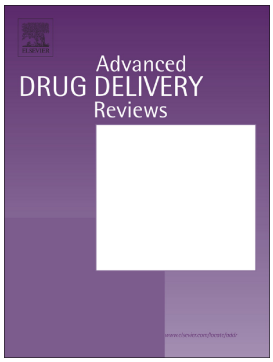

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NanoVelcro Rare-Cell Assays for Detection and Characterization of Circulating Tumor Cells

Yu Jen Jan[1,2†], Jie-Fu Chen[1†], Yazhen Zhu[2†], Yi-Tsung Lu[3†], Szu Hao Chen[2], Howard Chung[2], Matthew Smalley[2,4], Yen-Wen Huang[2,4], Jiantong Dong[2], Hsiao-Hua Yu[5], James S. Tomlinson[6,8,9], Shuang Hou[6], Vatche G. Agopian[6,7*], Edwin M. Posadas[1*], Hsian-Rong Tseng[2*]*

1 Urologic Oncology Program and Uro-Oncology Research Laboratories, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA
2 Department of Molecular and Medical Pharmacology, California NanoSystems Institute, Crump Institute for Molecular Imaging, University of California, Los Angeles, Los Angeles, California, USA
3 Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, California, USA
4 CytoLumina Technologies Corp., Los Angeles, California, USA
5 Institute of Chemistry, Academia Sinica, Taipei, Taiwan
6 Department of Surgery, University of California, Los Angeles, Los Angeles, California, USA
7 Liver Transplantation and Hepatobiliary Surgery, University of California, Los Angeles, Los Angeles, California, USA
8 Center for Pancreatic Disease, University of California, Los Angeles, Los Angeles, California, USA
9 Department of Surgery, Greater Los Angeles Veteran's Affairs Administration, Los Angeles, California, USA

† These authors contribute equally to this work.

Abstract

Circulating tumor cells (CTCs) are cancer cells shredded from either a primary tumor or a metastatic site and circulate in the blood as the potential cellular origin of metastasis. By detecting and analyzing CTCs, we will be able to noninvasively monitor disease progression in individual cancer patients and obtain insightful information for assessing disease status, thus realizing the concept of "tumor liquid biopsy". However, it is technically challenging to identify CTCs in patient blood samples because of the extremely low abundance of CTCs among a large number of hematologic cells. In order to address this challenge, our research team at UCLA pioneered a unique concept of "NanoVelcro" cell-affinity substrates, in which CTC capture agent-coated nanostructured substrates were utilized to immobilize CTCs with remarkable efficiency. Four generations of NanoVelcro CTC assays have been developed over the past decade for a variety of clinical utilities. The 1st-gen NanoVelcro chips, composed of a silicon nanowire substrate (SiNS) and an overlaid microfluidic chaotic mixer, were created for CTC enumeration. The 2nd-gen NanoVelcro chips (i.e., NanoVelcro-LMD), based on polymer nanosubstrates, were developed for single-CTC isolation in conjunction with the use of the laser microdissection (LMD) technique. By grafting thermoresponsive polymer brushes onto SiNS, the 3rd-gen Thermoresponsive NanoVelcro chips have demonstrated the capture and release of CTCs at 37 and 4 °C respectively, thereby allowing for rapid CTC purification while maintaining cell viability and molecular integrity. Fabricated with boronic acid-grafted conducting polymer-based nanomaterial on chip surface, the 4th-gen NanoVelcro Chips (Sweet chip) were able to purify CTCs with well-preserved RNA transcripts, which could be used for downstream analysis of several cancer specific RNA biomarkers. In this review article, we will summarize the development of the four generations of NanoVelcro CTC Assays, and the clinical applications of each generation of devices.