Microdevices for Advancing Preclinical and Clinical Research

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The biological activity of proteins is the driving force underlying oncogenic cell behavior, including promotion of entry into the cell cycle, escape from apoptotic signals, survival under hypoxic conditions, and enhanced migration leading to metastasis. It is now believed that pharmacologic targeting of normal as well as abnormal proteins may well lead to improved therapeutic responses, particularly if upregulated activity of normal proteins can be identified in the individual patient. Microelectrophoretic methods can make direct measurements of the activity of normal and oncogenic kinases in tumor cells. Issues of heterogeneity within cell populations, both in terms of cell type and biochemical behavior, are attainable by performing single-cell measurements using these tools. Single-cell assays for the measurement of lipid and protein kinases including phosphoinositide 3-kinase, PTEN, sphingosine kinase, Bcr-Abl, Akt, src, epidermal growth factor receptor and others is under way using combinatorial peptide synthesis and other strategies. Automated capillary-based and microfluidic devices for the continuous separation of the contents of single cells possess a current throughput of ~30 cells/min. To date these devices can operate in a stable manner over a 2 h-time span for the analysis of >600 cells. The ability to manipulate and analyze single cells is crucial to understanding the molecular processes controlling cell behavior and these microengineered platforms and assays provide the experimentalist with unprecedented opportunities for cell manipulation and analysis on a single-cell basis.