Assessment of Diverse Cancer Types: mAb Detection of Cell Surface Biomarker in Circulating Tumor Cells or Biopsy Tissue

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BACKGROUND

Although many cancer types respond to treatment with tyrosine kinase Inhibitors (e.g., imatinib and erlotinib), tumors often become resistant. Acquired drug resistance is a complicated process that involves alternate routes of kinase pathway activation. Hence the processes of identifying the mechanisms underpinning acquired drug resistance and targeting appropriately is challenging due to the complexity and diversity of these cell-type specific processes and downstream growth factor signaling. However, studies of diverse drug-resistant carcinomas identified a unified approach for patient-specific assessment of tumor status, prognosis and treatment options.

TECHNOLOGY DESCRIPTION

UC researchers have identified a biomarker (beta3 integrin of alpha-v/beta3) that is detectable in circulating tumor cells (CTCs) and that correlates with poor patient prognosis, metastatic potential, tumor “stemness” and drug resistance. Presence on CTCs may also provide an early indication of cancer progression, as CTCs may be the more stem-like tumor cells that seed secondary metastatic tumors. In this context, assessing CTCs may proscribe improved treatment options as treating a patient with a growth factor inhibitor may actually drive cells toward a beta3-positive phenotype and growth factor inhibitor resistance.

APPLICATIONS

The invention provides methods for determining the course of cancer therapy at the level of personalized medicine. Applications include early detection of cancer as well as an ability to predict tumor progression, metastasis and growth factor resistance. In this latter application, results demonstrate that screening for β3 expression in biopsies (blood or tissue) could identify patients who would benefit from alternative/combinatorial approaches (e.g., growth factor inhibitors and NfKb inhibitors.

ADVANTAGES

The ability to assess circulating tumor cells in a blood sample:

- is less invasive than a tumor biopsy and may complement information derived from a primary tumor biopsy
- avoids issues of tumor non-homogeneity
- is compatible with testing pathology slides, fluorescence-activated cell sorting (FACS) or flow cytometry analysis

In addition, the commercial availability of an $\alpha_V\beta_3$-specific mAb (LM609) enhances the translation to clinical practice.

STATE OF DEVELOPMENT

UC researchers found that up-regulated expression of integrin β3 on primary tumor cells as well as circulating tumor cells was:

- common to all tumor types tested (breast, colon, lung, and pancreas)
- linked to tumor progression and resistance to tyrosine kinase inhibitors
- an indicator of tumor cells “stemness”, which predicted metastatic capacity.

RELATED MATERIALS

- Desgrosellier et al, Integrin avß3 Drives Slug Activation and Stemness in the Pregnant and Neoplastic Mammary Gland, Developmental Cell, 11 August 2014 - 08/11/2014

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OTHER INFORMATION

KEYWORDS

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CATEGORIZED AS

- Medical
- Disease: Cancer

RELATED CASES

2013-211-0, 2012-245-0, 2012-245-4

▶ Seguin et al. An integrin ß3–KRAS–RalB complex drives tumour stemness and resistance to EGFR inhibition, Nature Cell Biology, 20 April 2014 - 04/20/2014

PATENT STATUS

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INTELLECTUAL PROPERTY INFO

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