Netrin G1 as a Biomarker for Enhancing Tumor Treatment Efficacy
(Ref. No. 439-EC)

Background

Pancreatic ductal adenocarcinoma (PDAC) is becoming the second most lethal cancer in the United States. Specific characteristics of this cancer include desmoplasia, which is a unique fibrous microenvironmental reaction with an expansion of activated cancer associated fibroblasts (CAFs) and the active remodeling of their extracellular matrix. Desmoplastic stroma plays a role in epithelial tumor development and progression whereas homeostatic normal or innate mesenchymal stroma supports a natural tumor suppressive microenvironment. Reprograming desmoplastic stroma back to its restrictive innate state bears the strong therapeutic potential and reinstitution of anti-tumor immune activity. Thus, there remains a need to manipulate desmoplastic stroma to improve the treatment efficacy.

Summary of the Invention

Researchers at Fox Chase Cancer Center observed that Netrin G1 (a neural pre-synaptic protein) is unexpectedly expressed in the pancreatic stroma and its levels and localization together with its ligand NGL1 and focal adhesion kinase activity (phosphor FAK) may serve as a biomarker indicative of active desmoplasia. High levels of Netrin G1 and active FAK indicate active stroma that prevents immune cells from accessing the tumor which is detrimental. Accordingly, the detection of these markers in patient samples (tumor surgical or bodily fluids) may provide information regarding the stroma, its condition, and stage of desmoplasia. This biomarker combinatorial approach may be used to detect the development of early stage cancers associated with fibrosis predisposition and fibrosis per se, or to alter a treatment course and to predict the efficacy of therapy. Additionally, the immune priming by gamma interferon treatment can be used to induce stromal changes sufficient to weaken the stromal barrier to immune system-mediated tumor obliteration. Thus, therapeutic regimens of inducing desmoplastic stroma to express a normal phenotype and to limit the stroma's ability to metabolically support tumor cells, as well as harness the immune system to attack cancer cells can be used for enhancing tumor treatment efficacy.

Patent Status: A patent application has been filed.

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