Research Portfolio Online Reporting Tools (RePORT)

Project Information

1R01CA190121-01

DESCRIPTION | DETAILS | RESULTS | HISTORY | SUBPROJECTS

Project Number: 1R01CA190121-01
Title: (PQ #4) SINGLE CELL BARCODING FOR STUDIES OF STUDY CLONAL EVOLUTION IN GLIOBLASTO

Contact PI / Project Leader: VERHAAK, ROELAND
Awardee Organization: UNIVERSITY OF TX MD ANDERSON CAN CTR

Abstract Text:

DESCRIPTION (provided by applicant): Glioblastomas (GBM) are the most common and aggressive type of adult brain tumors. Despite the standard of care, concomitant radiation and temozolomide based chemotherapy treatment, disease relapse typically occurs within a year for most patients. The complexity of the disease is underlined by recent discoveries of regional differences within the tumor that may contribute to therapy resistance. Through high throughput sequencing and tagging of individual GBM cells using shRNA barcodes, the heterogeneity of the tumor cell mix can be investigated under variable circumstances. The first goal of this grant is to apply this methodology when growing GBMs in mice, to evaluate the degree of complexity after proliferation in absence of therapeutic challenges. To study whether the heterogeneity of the tumor cell mix contributes to the sensitivity to chemo- and radio-therapy, we will apply standard treatment protocols to mouse xenografts and analyze the cellular diversity of the resulting tumors. The second aim of this grant is to evaluate whether tumor complexity can be modulated using therapeutics and whether this property plays a role in developing treatment resistance. Through computational and mathematical approaches, the genomic abnormality profile can be analyzed to infer clonal and subclonal cell populations. When applied to multiple related genomic profiles, such as from diagnostic tumors and matching post-treatment tumor biopsies, patterns of clonal evolution can be uncovered. These can be related to patient features such as outcome, but also to tumor biology characteristics such as the presence of specific genomic alterations. The final aim of this grant is to construct the evolutionary path tha GBM take to escape treatment and result in recurrence. In summary, by evaluating the patterns of clonal evolution of single cells under normal growth properties, under the stress of treatment and in patient tumors, this proposal aims to improve our understanding of why GBM are so resistant to the toxic effects of therapy.

Public Health Relevance Statement:

PUBLIC HEALTH RELEVANCE: This proposal investigates the evolution of individual glioblastoma (GBM) cells during progression under stress conditions in model systems and patient tumors. The goal of this study is to trace clonal evolution in GBM, to evaluate the genomic properties of dominant, therapy resistant clones relative to therapy sensitive cells and to compare findings in model systems with observations from clinical tumors. We propose to study how GBM cells progress under variable circumstances to improve our understanding of how tumor cell heterogeneity relates to treatment sensitivity.

NIH Spending Category:

Biotechnology; Brain Cancer; Brain Disorders; Cancer; Genetics; Human Genome; Neurosciences; Rare Diseases

Project Terms:

Address; Adult; Aftercare; base; Behavior; Biological Markers; Biological Models; Biopsy; Blood - brain barrier anatomy; BRAF gene; Brain Neoplasms; Case Study; Cells; Characteristics; chemotherapy; Clinical; Clinical Trials; Clonal Evolution; Data; Development; Diagnostic; Disease; Disease Resistance; Engraftment; Epidermal Growth Factor Receptor; Equilibrium; Erlotinib; Evaluation; Event; Evolution; Excision; fluidity; Gene Mutation; Genetic; Genome; Genomics; Glioblastoma; Glioma; Goals; Grant; Growth; Heterogeneity; High-Throughput Nucleotide Sequencing; improved; Individual; Knowledge; Malignant neoplasm of lung; Malignant Neoplasms; mathematical methods; Measures; melanoma; Methodology; Methods; Microscopic; Mus; mutant; Mutate; Nature; neoplastic cell; Newly Diagnosed; novel; novel diagnostics; novel therapeutics; oncology; Operative Surgical Procedures; Outcome; Pathway interactions; Patients; Pattern; Phylogenetic Analysis; Play; Population; Process; Property; public health relevance; Radiation; Radiation therapy; Radio; Recurrence; Recurrent disease; regional difference; Relapse; Relative (related person); Residual state; Resistance; Role; Sampling; small hairpin RNA; Solid Neoplasm; standard care; standard of care; Stress; Structure; System; Techniques; temozolomide; The Cancer Genome Atlas; Therapeutic; Therapeutic Uses; therapy resistant; Toxic effect; Transplantation; Treatment Protocols; treatment response; Trees; tumor; Tumor Biology; Tumor Debulking; tumor progression; Tumor-Derived; United States; Xenograft Model; Xenograft procedure

Contact PI Information:	Program Official Information:	Other PI Information:
Name: VERHAAK, ROELAND **Email**: Click to view contact PI email address	**Name**: MIETZ, JUDY **Email**: Click to view PO email address	SULMAN, ERIK

Title: ASSISTANT PROFESSOR

Organization:	Department / Educational Institution Type:	Congressional District:
Name: UNIVERSITY OF TX MD ANDERSON CAN CTR **City**: HOUSTON Country: UNITED STATES (US)	INTERNAL MEDICINE/MEDICINE HOSPITALS	State Code: TX District: 09

Other Information:

FOA: RFA-CA-13-018
Study Section: Special Emphasis Panel (ZCA1-RPRB-M (A1))
Fiscal Year: 2014 **Award Notice Date**: 17-SEP-2014

DUNS Number: 800772139
Project Start Date: 17-SEP-2014
Budget Start Date: 17-SEP-2014

CFDA Code: 393
Project End Date: 31-AUG-2018
Budget End Date: 31-AUG-2015

Administering Institutes or Centers:

NATIONAL CANCER INSTITUTE

Project Funding Information for 2014:

Total Funding: $332,000 **Direct Costs:** $207,500 **Indirect Costs:** $124,500

Year	Funding IC	FY Total Cost by IC
2014	NATIONAL CANCER INSTITUTE	$332,000

Categorical Spending by IC:

Click here for more information on NIH Categorical Spending

History:

Project Number	Sub #	Project Title	Contact Principal Investigator	Organization	FY	Admin IC	Funding IC	FY Total Cost by IC
1R01CA190121-01		(PQ #4) SINGLE CELL BARCODING FOR STUDIES OF STUDY CLONAL EVOLUTION IN GLIOBLASTO	VERHAAK, ROELAND **et al.**	UNIVERSITY OF TX MD ANDERSON CAN CTR	2014	NCI	NCI	$332,000

Subprojects:

Project Number	Sub #	Project Title	Contact Principal Investigator	Organization	FY	Admin IC	FY Total Cost by IC
No Subprojects information available for 1R01CA190121-01							

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