Areas of Interest

October 2022

NICO is offering **research grants** for a variety of qualified topics using NICO technologies leading to significant changes or improvements in **pre-clinical, clinical, economic, or operational outcomes**. Below are several **Areas of Interest (AOI),** in no specific order, for the Investigator Initiated Study (IIS) program, or independent research. These concepts are provided to help guide project development and do not encompass the many topics which may be represented through an IIS submission or independent study.

All studies ranging from laboratory science, animal study, and clinical features have equal opportunity for acceptance. Those in "black" are of the highest priority currently and not addressed by current research. However, topics in "grey" may still be included as part of study designs being submitted.

Pre-Clinical: Tissue (Tumor/Vascular)

1. Maintain **biological integrity** of tissue – avoiding exposures which damage proteins, RNA, or other important cellular information
2. Define **standards** of tissue preservation which increase consistency and quality of tissue samples obtained for research (compared to traditional methods) for novel use (including therapeutics)
    a. Methods should be reproducible
    b. Highlight consistency of samples
    c. Identify areas of improved tissue quality
3. Increase **understanding of progression** of tumoral disease
4. Understanding of tumoral:
    a. Metabolic profiles and stability of individual metabolites
    b. Global metabolic function
    c. Cell yields (of all types of cells – tumor, macrophages, T-cells, stem and non-stem cells dynamics) using the intraoperative APS versus previous means of tissue acquired data
    d. Chemokines/cytokines
    e. Drug levels of intact tumor
5. Identify timeline from initial treatment to recurrence points of **mutation or therapeutic response** (also discoverable through murine model investigation)
6. Use of BrainPath and Myriad for guided biopsy to regionalized tumor areas for sample collection and annotation confirmed by measured molecular and genetic schematics matched to tumor regionality
7. Effects of post-surgical cryogenic freezing versus use of fresh tissue acquired with the Myriad/APS
        i. Opinion (recalibration) paper on biobanking and historical challenges – related to molecular information
            1. What would be requirements in biobanking of tissue in today's molecular world
            2. What has changed with greater knowledge of genetics, what's possible to come

Pre-Clinical: Murine (or Other Animal)

1. Standardize a variety of high quality PDX models for neurologic disease to afford widespread research advancing disease management or treatment
2. Extend the survival of lab developed models from patient derived tissues
    a. Research progression over time, Improves Reproducibility and Consistency, Extends Survival of the Murine Model (implied economic benefit)
    b. Economic impact of long-lasting tissue models
3. Identify along timeline from initial treatment to recurrence points of **mutation or therapeutic response** through **longitudinal analysis without animal sacrifice**
4. Develop stable avatar models for *various neurological diseases or abnormalities* to increase understanding of **molecular biomarkers** and tissue **microenvironment**
5. Maintain **biological integrity** of tissue – avoiding exposures which damage proteins, RNA, and other important cellular information
    a. Understand biological information at greater depth
    b. Analyze and study various therapeutics for impact to disease, driving into pharma needs
6. IIS projects that are intended to lead to grants or Clinical Trials with Pharma are ideal due to *Novel Nature*
7. Projects that include study of delivering or testing of novel therapeutics (this topic should include Car-T cell in addition to any possibilities related to neo-adjuvant and adjuvant therapies)
8. Projects related to brain computer interface science

Clinical: Surgical

1. Understand **injury and preservation** beyond white matter
    a. L**ymphatic** and **vasculature** impact among surgical techniques including MIPS
2. Development of Surgical Education Models and Practice
3. Identify areas of new appropriate surgical intervention over standard management (non-surgical)
    a. Compared outcomes
    b. Economic Impact
4. Develop protocols and standards for **efficient surgical intervention**
    a. ICH-ENRICH
    b. Tumor- Evaluate patient selection, OR set-up, operative time from access to resection, and post-operative care for improved recovery
    c. ERAS: Enhanced Recovery after Surgery
5. Investigate **novel applications** of minimally disruptive access through transsulcal MIPS
    a. Advanced practices
    b. Underrepresented disease states in current published evidence
    c. Brain Computer Interface study available through safe access
6. Clinical observations matched to scientific data on the impact of instrumentation on tissue:
    a. Heat generation through bipolar or ultrasonic aspiration, other
    b. Dissociation of tissue (as in automated mechanical dissociation with Myriad)
    c. Impact of extended exposure of tissue to blood product vs. flushing/infusion with medium
    d. Volume of tissue obtained usable for research purposes (not just extent of resection)
7. Enhanced visualization and tissue differentiation
    a. Impact of light delivery as a function of distance to target
    b. Improvements in 5ALA or Fluorescein supported resection

Clinical: Tissue

1. Improvements in **volume** obtained and **micro-cellular** quality of tissue for oncology development and advancement
2. Identify ideal **location intratumorally** to harvest tissue for **specific research** needs including subsequent science and cell lines, and/or creation of viable therapy for specific delivery (immuno, neo-adjuvant, adjuvant, targeted chemo, etc)
3. Identification of potential **pathophysiological targets in tissue** (obtained via APS) for attenuating secondary injury
4. Publish defined standards **limiting variability** of biospecimen procurement in the OR increases **efficiency of intraoperative collection**, **consistency** of samples and safeguards quality for scientific evaluation
    a. Methods supporting tissue banking improvements
    b. Evidence generated for APS to improve current process in **CAP** certified tissue banks
5. Novel applications and future potential resulting from tissue quality improvement:
    a. Greater understanding of **microenvironments**
    b. Learnings on **disease impact** to healthy tissue
    c. Possibilities in **therapeutic delivery**
6. Study of **longitudinal genomic profiling** to understand impact of initial treatment at molecular level to provide information on mutation of primary disease to properly select treatment adjustments
7. Report biospecimens/tissue collected with an ultrasonic aspirator or other technique, against Myriad & APS methods
    a. Consistency of tissue collected for research – reproducible results
    b. Volume of tissue viable for research
    c. Impact of operating room methods on tissue quality
        i. Time related to mechanical dissociation and enzymatic dissociation
            1. Time to cell death – genetic information and proteomics
            2. Time in OR, lab management, etc
        ii. Key protein and genetic information impacted by
            1. Exposure to blood product
            2. Heat/Temperature
                a. Cooled tissue with/without EDTA for protein analysis
                b. Cooled tissue for RNA analyses (use of specific RNAse inhibitors)