Posting Date: March 8, 2021

Closing Date: March 18, 2020 11:30 a.m. ET

Reference Number: 21-022432

To: NCI Bid Board

From: Tanika Crossen
NCI P-ARC Program Analyst
crossent@nih.gov

Subject: NCI Bid Board Posting – to perform staining on nine FFPE tissue slides for the Kahn lab's Imaging Mass Cytometry (IMC) project.

Among the defining concepts of the Genetics Branch is one that underlies its basic research focus and others that form the foundation of its clinical and translational research activities. The concept that underlies basic research is that cancer is a genetic disease caused by genetic instability. That instability is a function of all the inherited and acquired effects that mediate plasticity and alterability at the level of DNA. The success of molecular genetics over the past two decades has been the identification of genes involved in pathways of growth and development, and the identification of the mechanisms by which the normal regulation and/or products of these genes are altered in cancer. The elucidation of the necessary and sufficient factors that govern genetic instability, the description of the common and disparate themes among different types of instability, and the cataloging of distinct patterns of gene expression in tumors compared to the normal tissues from which they arise are within the purview and distinct perspective of this branch. There is, in addition, a clinical/translational mantle that this branch is called upon to shoulder.

The Genetics Branch hypothesize that the immune microenvironment in pediatric solid tumors changes under therapeutic pressures, has a significant impact on a patient's response to cellular immunotherapy, and is associated with clinical outcomes. Using imaging CyTOF (IMC) of patient tissue microarrays (TMAs) of pediatric solid tumors, we will determine not only which immune cells are present, but specifically which cells are interacting with tumor cells and thus allow for an informed approach for designing novel immunotherapeutic strategies.
The objective of this project is for Fluidigm Therapeutic Insights Services to perform staining on nine FFPE tissue slides for the Kahn lab's Imaging Mass Cytometry (IMC) project. The data generated from these slides will be used to address the following specific aims:
Specific Aim 1*:* To uncover the spatial immune landscape in multiple subtypes of pediatric solid tumors
Specific Aim 2: To understand the effects of chemotherapy, radiation therapy, metastasis on the tumor immune microenvironment (TME) in multiple subtypes of pediatric solid tumors
Specific Aim 3: To understand the effects of the pediatric solid TME on clinical outcome, including overall and event free survival
Specific Aim 4: To assess the

Sole Source Justification: It appears Fluidigm is the only company that has the imaging mass cytometry technology.

Attached Documents:
SF18
Statement of Work
FAR Clause 52.204-24 Representation Regarding Certain Telecommunications and Video Surveillance Services or Equipment.

FAR Clause 52.213-4 Simplified Acquisitions Terms and Conditions (AUG 2019) is applicable and available in full text upon request.

REQUEST FOR QUOTATION
(THIS IS NOT AN ORDER)

THIS RFQ ☐ IS ☒ IS NOT A SMALL BUSINESS SET-ASIDE

PAGE 1 OF PAGES 1

1. REQUEST NO.	2. DATE ISSUED	3. REQUISITION/PURCHASE REQUEST NO.	4. CERT. FOR NAT. DEF. UNDER BDSA REG. 2 AND/OR DMS REG. 1	RATING
21-022432	3/82021			

5a. ISSUED BY
NCI CCR Purchasing Administrative Resource Center

6. DELIVER BY *(Date)*

5b. FOR INFORMATION CALL *(NO COLLECT CALLS)*

NAME	TELEPHONE NUMBER	
	AREA CODE	NUMBER
Tanika Crossen, Program Analyst	301	480-0602

7. DELIVERY ☒ FOB DESTINATION ☐ OTHER *(See Schedule)*

9. DESTINATION

a. NAME OF CONSIGNEE
NIH, NCI

8. TO:

a. NAME	b. COMPANY	b. STREET ADDRESS
	Fluidigm Corp	

c. STREET ADDRESS	c. CITY
	Bethesda

d.. CITY	e.. STATE	f.. ZIP CODE	d.. STATE	e. ZIP CODE
			MD	20892

10. PLEASE FURNISH QUOTATIONS TO THE ISSUING OFFICE IN BLOCK 5a ON OR BEFORE CLOSE OF BUSINESS *(Date)*
3/18/2021 12:00 EST

IMPORTANT: This is a request for information, and quotations furnished are not offers. If you are unable to quote, please indicate on this form and return it to the address in Block 5a. This request does not commit the Government to pay any costs incurred in the preparation of the submission of this quotation or to contract for supplies or services. Supplies are of domestic origin unless otherwise indicated by quoter. Any representations and/or certifications attached to this Request for Quotations must be completed by the quoter.

11. SCHEDULE *(Include applicable Federal, State and local taxes)*

ITEM NO. (a)	SUPPLIES/SERVICES (b)	QUANTITY (c)	UNIT (d)	UNIT PRICE (e)	AMOUNT (f)
	Service perform staining on FFPE tissue slides for the Kahn lab's Imaging Mass Cytometry (IMC) project Notice of Intent: If submitting a capability statement, please e-mail only 1 copy of the technical capability statement to Tanika Crossen @ crossent.mail.nih.gov See attached statement of work This will be awarded as a Firm-Fixed Price Contract.				

12. DISCOUNT FOR PROMPT PAYMENT	a. 10 CALENDAR DAYS (%)	b. 20 CALENDAR DAYS (%)	c. 30 CALENDAR DAYS (%)	d.. CALENDAR DAYS NUMBER	d.. CALENDAR DAYS PERCENTAGE

NOTE: Additional provisions and representations ☐ are ☐ are not attached.

13. NAME AND ADDRESS OF QUOTER	14. SIGNATURE OF PERSON AUTHORIZED TO SIGN QUOTATION	15. DATE OF QUOTATION
a. NAME OF QUOTER		
b. STREET ADDRESS	16. SIGNER	
	a. NAME *(Type or print)*	b. TELEPHONE AREA CODE
c. COUNTY		
d. CITY / **e. STATE** / **f. ZIP CODE**	c. TITLE *(Type or print)*	NUMBER

STATEMENT OF WORK (SOW)

1.0 TITLE

Understanding Tumor-Immune Cell Interactions Across Subtypes of Pediatric Solid Tumors

2.0 BACKGROUND

Pediatric malignancies are a leading cause of morbidity and mortality in children. Significant improvements in the understanding of cancer biology, advancements in therapeutic strategies, and implementation of risk stratification have driven the 5 year survival rate from less than 10% in the mid-twentieth century to approaching 80% today. Despite these successes, survival remains dismal for patients who relapse and those with certain tumor types, such as metastatic disease and central nervous system malignancies. Additionally, the standard-of-care therapeutics, such as surgical resection, radiotherapy, and traditional chemotherapy, carry a high burden of morbidities including neurocognitive loss, developmental delays, psychosocial challenges, motor deficiencies, endocrine abnormalities, and mortality from secondary malignancies, which have a lifelong impact. These side effects critical the desperate need for novel, targeted therapeutic strategies for pediatric patients.

One obvious hurdle to finding effective targets in pediatric malignancies remains in the relatively low mutational burden of these tumors, which we and others have shown is correlated with a decrease of immune-cell infiltrate, particularly lymphocytes, and a “hostile” tumor microenvironment. This decrease of tumor immune infiltrates along with a low tumor mutational burden has been associated with poor response rates to checkpoint inhibitors. Despite this association of increased responses to checkpoint inhibitors in tumors with high levels of tumor-infiltrating lymphocytes secondary to a high tumor mutational burden, there are a few exceptions in the pediatric population. These include alveolar soft part sarcoma (ASPS) and atypical rhabdoid teratoid tumors (ATRT), which are tumors with low somatic mutational burden tumors and yet have been proven to show infiltration of lymphocytes and dramatic responses to checkpoint blockade. In recent years, immunotherapy has revolutionized the treatment approach for an increasing number of adult cancer types. These clinical breakthroughs have led to a heightened interest in understanding the molecular basis for immunotherapy response.

We have previously shown that the MYCN non amplified (*MYCN*-NA) subtype of neuroblastoma, not only has an increase infiltrate of immune cells, but there is clonal T cell expansion, suggesting the presence of tumor specific targets that can be exploited for cellular-based immunotherapeutic approaches. While this is strong evidence, current data does not indicate whether these immune responsive cells are penetrating the tumors themselves, excluded on the periphery, or entering the tumors and having their response dampened by an immunosuppressive microenvironment. Detailed classification of the tumor’s immune microenvironment into either “hot”, meaning infiltrated by a patient’s own immune cells, or “cold”, when the tumor remains hidden and excludes the immune system, can help identify the best treatment strategy for the tumor type. Further classification of these tumors into “immune deserts”, “immune-excluded”, “inflamed”, or “immunosuppressive” microenvironments will allow for the development of novel therapeutic strategies. Possibilities include the co-administration of epigenetic drugs to modulate expression of MHC class I, development of cellular immunotherapies from other compartments of the immune system, or immune checkpoints inhibitors alongside target specific cellular immunotherapies therapies directed at cancer specific differentially expressed developmental genes, cancer testes antigens, mutations, or fusions.

STATEMENT OF WORK (SOW)

2.1 OBJECTIVE

We hypothesize that the immune microenvironment in pediatric solid tumors changes under therapeutic pressures, has a significant impact on a patient's response to cellular immunotherapy, and is associated with clinical outcomes. Using imaging CyTOF (IMC) of patient tissue microarrays (TMAs) of pediatric solid tumors, we will determine not only which immune cells are present, but specifically which cells are interacting with tumor cells and thus allow for an informed approach for designing novel immunotherapeutic strategies.

The objective of this project is for Fluidigm Therapeutic Insights Services to perform staining on nine FFPE tissue slides for the Kahn lab's Imaging Mass Cytometry (IMC) project. The data generated from these slides will be used to address the following specific aims:

Specific Aim 1: To uncover the spatial immune landscape in multiple subtypes of pediatric solid tumors
Specific Aim 2: To understand the effects of chemotherapy, radiation therapy, metastasis on the tumor immune microenvironment (TME) in multiple subtypes of pediatric solid tumors
Specific Aim 3: To understand the effects of the pediatric solid TME on clinical outcome, including overall and event free survival
Specific Aim 4: To assess the clinical utility of immune focused imaging mass cytometry for pediatric patients with solid tumors.

3.0 SCOPE

- 3.1 Biological Sample
  - 3.1.1 Customer will provide 9 FFPE tissue slides
    - 3.1.1.1 5x rhabdomyosarcoma;
    - 3.1.1.2 1x Ewing sarcoma;
    - 3.1.1.3 1x Osteosarcoma/chondrosarcoma;
    - 3.1.1.4 1x soft tissue sarcoma;
    - 3.1.1.5 1x neuroblastoma
- 3.2 Panel Design
  - 3.2.1 31 marker panel
    - 3.2.1.1 23 catalog antibodies
    - 3.2.1.2 1 retag antibody
    - 3.2.1.3 7 custom antibodies; custom clones selected by Customer
  - 3.2.2 Cell-ID Intercalator for nucleic acid
  - 3.2.3 IMC Cell Segmentation kit for 9 slides
  - 3.2.4 Custom Conjugation
    - 3.2.4.1 Custom clones will be sourced as described in Table 1. Note: Purified antibodies provided must be unconjugated, IgG, at least 100ug each, BSA-free/carrier-free
    - 3.2.4.2 In the event where Biological Verification is needed, procedure(s) will be performed on positive control slides provided by the customer. Positive staining of custom antibodies will be confirmed based on preexisting immunohistochemistry data. Fluidigm will consult with the customer should unexpected costs due to reagents or labor be required to complete the project (e.g. SOW amendment for sourcing and testing additional clones).

3.2.4.3 Positive control tissues for verification tests are recommened in Table 2. Customer and Fluidigm will coordinate on final verification tissue selection.

Table 1) Tentative panel design

Target	Clone	Tag	Notes
aSMA	1A4	141Pr	
CD19	6OMP31	142Nd	
CD14	EPR3653	144Nd	
CD33	polyclonal	145Nd	
CD16	EPR16784	146Nd	
CD278 [ICOS]	D1K2T	148Nd	
CD11b/Mac-1	EPR1344	149Sm	
CD274 [PDL1]	SP142	150Nd	
CD134 [OX40]	polyclonal	151Eu	
CD45	D9M8I	152Sm	
CD223 [LAG3]	D2G40	153Eu	
CD11c	polyclonal	154Sm	
FOXP3	PCH101	155Gd	
CD4	EPR6855	156Gd	
CD68	KP1	159Tb	
CD20	H1	161Dy	
CD8	D8A8Y	162Dy	
CD279 [PD-1]	EPR4877	165Ho	
Granzyme B	EPR20129-217	167Er	
CD3	polyclonal	170Er	
CASP3	5A1E	172Yb	
CD276	Polyclonal	173Yb	
HLA-DR	LN3	174Yb	
CD45RO	UCHL1		Retag, sourced by Fluidigm
FGFR4	D3B12		Custom, sourced by Fluidigm
GPC2	CT3		Custom, sourced by Customer
PRAME	E7I1B		Custom, sourced by Fluidigm
IGF2BP3	Polyclonal		Custom, sourced by Customer
PAX3-FOXO1	M2		Custom, sourced by Customer
HLA-ABC	5C5B7		Custom, sourced by Fluidigm
TGFB1	Polyclonal		Custom, sourced by Customer
Cell ID Intercalator		191Ir, 193Ir	
IMC Cell Segmentation Kit		195Pt, 196Pt, 198Pt	

Table 2) Recommended positive control tissues for verification tests

Antibody Target	Positive Tissues
FGFR4	**liver**, lung, colon, lung cancer, breast cancer
GPC2	**neuroblastoma**,
PRAME	testis, **melanoma**, lung carcinoma, ovarian carcinoma
IGF2BP	pancreas, **osteosarcoma**
PAX3/7-FOXO1	**rhabdomyosarcoma**
HLA-ABC	**tonsil**
TGFB1	neurons, spleen, **lung**
CD45RO retag	tonsil

3.3 Staining

3.3.1 9 slides, provided by Customer to be stained by Fluidigm with panel (Table 1)

3.4 Data Acquisition

3.4.1 IMC ablation to be performed by Customer; not included in scope.

3.5 Data Anlaysis

3.5.1 Data analysis to be performed by Customer; not included in scope.

3.6 Sample Transfer:

3.6.1 Customer will ship samples and antibodies to the following address.

Attn: Dongxia Lin
Fluidigm Corporation
2 Tower Place
Suite 2000
South San Francisco, CA 94080

3.6.2 Fluidigm will ship deliverables to the following address.

Attn: Young Song, 37 Convent Drive, Rm 2016, Bethesda, MD, 20892

3.7 Shipping Guidelines:

- Ensure samples are shipped under appropriate conditions (temperature, padding, tracking). We recommend the following:
  - FFPE slides should be stored in separate slots within a slide box. For the outermost slots, make sure tissue sections are facing the interior of the slide holder. Pre-stained or unstained FFPE slides can be shipped at room temperature.
  - Frozen tissue slides should be shipped in an appropriate container/slide box. Pre-stained frozen tissue slides can be shipped at room temperature. Unstained frozen tissues slides must remain frozen until they are ready to be stained and should be shipped on dry ice.
  - For long-term storage of pre-stained FFPE or frozen tissue samples, slides can be stored in a zip-top or vacuum-sealed bag with desiccant (e.g. silica gel) as high humidity can damage tissue integrity and decrease shelf life of stained sample slides.

- Mark the package as fragile

- Label your samples with project identifier (provided above) and sample/slide identifier
- Provide a sample manifest (sample identifiers, slide orientation, ROI selection, etc.) via email and with the shipment
- Label any customer-provided purified antibodies with target name, clone name (if available), isotype (IgG), host, reactivity, concentration, amount in the vial, and tag. And, indicate the antibody's carrier buffer
- Please share your tracking number once the package has been shipped

3.8 Deliverables:

3.8.1 Ship 9 slides stained with IMC panel described above to Customer

4.0 CONTRACT REQUIREMENTS/ AND PERSONNEL QUALIFICATIONS

The contractor shall perform the following tasks:

4.1 Staining: 9 slides, provided by Customer to be stained by Fluidigm with panel of antibodies described in Table 1 in section 3.2.4

4.2 Shipping: 9 stained slides to be shipped to the address specified in section 3.6.2

5.0 TYPE OF ORDER

This is a firm fixed price purchase order.

6.0 PERIOD OF PERFORMANCE

The period of performance shall be for 4 weeks from receipt of antibodies, biological samples, and PO; pending results of verification testing. Deliverables will be sent early if work is completed in less than 4 weeks.

7.0 PLACE OF PERFORMANCE

Services shall be performed at 2 Tower Place Suite 2000 South San Francisco, CA 94080

8.0 REPORT(S)/DELIVERABLES AND DELIVERY SCHEDULE

Physical deliverables (e.g. stained slides) will be shipped to the address specified per the deliverable schedule.

DELIVERABLE	DELIVERABLE DESCRIPTION / FORMAT REQUIREMENTS	DUE DATE

Deliverable 3.8.1	9 stained slides	4 weeks after receipt of antibodies, samples and PO; pending results of verification testing

9.0 PAYMENT

9.2 Payment schedule

Invoices shall be generated and payments shall be made per the following payment schedule.

Description	Amount	Expected Invoice Date
1. Upfront costs • Catalog Antibody (TIS-102-0093) • Misc. Reagents (TIS-102-0100) • Shipping		Agreement

2. Remainder due	Project Completion Date
• Custom Conjugation (TIS-102-0094) • IMC Cell Segmentation Kit (TIS-102-096) • Staining Service (TIS-102-0097)	

Payment authorization requires submission and approval of invoices to the COR and NIH OFM, in accordance with the attached payment provisions listed below:

The following clause is applicable to all Purchase Orders, Task or Delivery Orders, and Blanket Purchase Agreement (BPA) Calls: PROMPT PAYMENT (JUL 2013) FAR 52.232-25. Highlights of this clause and NIH implementation requirements follow:

I INVOICE REQUIREMENTS

A. An invoice is the Contractor's bill or written request for payment under the contract for supplies delivered or services performed. A proper invoice is an "Original" which must include the items listed in subdivisions 1 through 12, below, in addition to the requirements of FAR 32.9. If the invoice does not comply with these requirements, the Contractor will be notified of the defect within 7 days after the date the designated billing office received the invoice (3 days for meat, meat food products, or fish, and 5 days for perishable agricultural commodities, dairy products, edible fats or oils) with a statement of the reasons why it is not a proper invoice. (See exceptions under II., below.) Untimely notification will be taken into account in the computation of any interest penalty owed the Contractor.

1. Vendor/Contractor: Name, Address, Point of Contact for the invoice (Name, title, telephone number, e-mail and mailing address of point of contact).
2. Remit-to address (Name and complete mailing address to send payment).
3. Remittance name must match exactly with name on original order/contract. If the Remittance name differs from the Legal Business Name, then both names must appear on the invoice.
4. Invoice date.
5. Unique invoice #s for all invoices per vendor regardless of site.
6. NBS document number formats must be included for awards created in the NBS: Contract Number; Purchase Order Number; Task or Delivery Order Number and Source Award Number (e.g., Indefinite Delivery Contract number; General Services Administration number); or, BPA Call Number and BPA Parent Award Number.
7. Data Universal Numbering System (DUNS) or DUNS + 4 as registered in the Central Contractor Registration (CCR).
8. Federal Taxpayer Identification Number (TIN). In those exceptional cases where a contractor does not have a DUNS number or TIN, a Vendor Identification Number (VIN) must be referenced on the invoice. The VIN is the number that appears after the contractor’s name on the face page of the award document.
9. Identify that payment is to be made using a three-way match.
10. Description of supplies/services that match the description on the award, by line billed.*

11. Freight or delivery charge must be billed as shown on the award. If it is included in the item price do not bill it separately. If identified in the award as a separate line item, it must be billed separately.
12. Quantity, Unit of Measure, Unit Price, Extended Price of supplies delivered or services performed, as applicable, and that match the line items specified in the award.*

* NOTE: If your invoice must differ from the line items on the award, please contact the Contracting Officer before submitting the invoice. A modification to the order or contract may be needed before the invoice can be submitted and paid.

B. Shipping costs will be reimbursed only if authorized by the Contract/Purchase Order. If authorized, shipping costs must be itemized. Where shipping costs exceed $100, the invoice must be supported by a bill of lading or a paid carrier's receipt.

C. Mail an original and 1 copy of the itemized invoice to:

National Institutes of Health
Office of Financial Management, Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

For inquiries regarding payment call: (301) 496-6088

In order to facilitate the prompt payment of invoices, it is recommended that the vendor submit a photocopy of the invoice to the "Consignee" designated for the acquisition in blocks 6A – 6E of the face page of the Order/Award document.

II. INVOICE PAYMENT

A. Except as indicated in paragraph B., below, the due date for making invoice payments by the designated payment office shall be the later of the following two events:

1. The 30th day after the designated billing office has received a proper invoice.
2. The 30th day after Government acceptance of supplies delivered or services performed.

B. The due date for making invoice payments for meat and meat food products, perishable agricultural commodities, dairy products, and edible fats or oils, shall be in accordance with the Prompt Payment Act, as amended.

III. INTEREST PENALTIES

A. An interest penalty shall be paid automatically, if payment is not made by the due date and the conditions listed below are met, if applicable.
1. A proper invoice was received by the designated billing office.
2. A receiving report or other Government documentation authorizing payment was processed and there was no disagreement over quantity, quality, or contractor compliance with a term or condition.

3. In the case of a final invoice for any balance of funds due the contractor for supplies delivered or services performed, the amount was not subject to further settlement actions between the Government and the Contractor.

B. Determination of interest and penalties due will be made in accordance with the provisions of the Prompt Payment Act, as amended, the Contract Disputes Act, and regulations issued by the Office of Management and Budget.

IV. PROVIDING ACCELERATED PAYMENT TO SMALL BUSINESS SUBCONTRACTORS, FAR 52.232-40 (DEC 2013)

a) Upon receipt of accelerated payments from the Government, the Contractor shall make accelerated payments to its small business subcontractors under this contract, to the maximum extent practicable and prior to when such payment is otherwise required under the applicable contract or subcontract, after receipt of a proper invoice and all other required documentation from the small business subcontractor.
b) The acceleration of payments under this clause does not provide any new rights under the prompt Payment Act.

Include the substance of this clause, include this paragraph c, in all subcontracts with small business concerns, including subcontracts with small business concerns for the acquisition of commercial items.