Posting Date: June 1, 2021

Closing Date: June 11, 2021 11:30 a.m. ET

Reference Number: 21-035690

To: NCI Bid Board

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

Subject: NCI Bid Board Posting – Epimutation of DRD1 as a biomarker of lung cancer risk

The Laboratory of Human Carcinogenesis (LHC) has a multifaceted research program integrating basic, translational, clinical, and population research, with a major focus on common and lethal human cancers that include tumors of the breast, colon, esophagus, liver, lung, pancreas and prostate. LHC studies utilize a Precision Medicine Strategy. It's main objectives are to conduct investigations that assess: (1) Mechanisms of carcinogenesis including the cellular functions of cancer driving genes; (2) experimental approaches in biological systems for the extrapolation of carcinogenesis data and mechanisms from in vitro models and experimental animals to humans; (3) molecular integrative epidemiology of human cancer risk; and (4) cancer biomarkers of diagnosis, prognosis, and therapeutic outcome.

Epigenetic modifications, such as DNA methylation and histone modifications, play a critical role in controlling gene expression. An epimutation occurs when alterations in DNA methylation change gene expression. In cancer, epimutations frequently occur in genes involved in DNA repair and the cell cycle, promoting malignant transformation. The lab has previously shown that the dopamine receptor D1 (DRD1) is a tumor suppressor in lung cancer and that its expression is down-regulated by promoter methylation. Additionally, in DNA from peripheral blood mononuclear cells (PBMCs), a SHS-induced epimutation has been observed in *DRD1* in adults persisting 30 years after the SHS exposure.
Current research in the field of epigenetic biomarkers is limited due to the primary focus on current and former smokers and the lack of exposure data from patient samples. Therefore, a key unanswered question is whether or not these epimutations in individuals exposed to SHS are associated with risk of lung cancer and if so, whether they can serve as biomarkers.

This project has two research goals. The first is to characterize childhood SHS-induced epimutations in the *DRD1* gene. The second is to determine if an epimutation in *DRD1* is associated with relative risk of lung cancer, thereby potentially discovering the first ever biomarker for lung cancer risk in never smokers. The proposed research will utilize PBMC samples from the NCI-Maryland lung cancer case-control study. I will characterize childhood SHS-induced epimutations using targeted NextGen bisulfite sequencing of the *DRD1* promoter – **a custom assay designed in collaboration with Roche Sequencing.** This will enable us to study the *DRD1* promoter in unprecedented detail with roughly 250x more of the *DRD1* gene analyzed compared to the Illumina EPIC probe-based platform. This work will be completed in NCI/CCR/Laboratory of Human Carcinogenesis.

Sole Source Justification:

KAPA NGS library preparation kits will be used for the highest-quality sequencing libraries, for use on Illumina sequencing platforms. This kit leverages high-quality enzymes selected through the directed evolution technology, and is formulated in convenient, easy-to-use master mixes. The genomic region chr5: 174550325 – 175465587 will be assay which corresponds to the DRD1 gene region. This will enable us to detect methylation at the base level of the DRD1 genomic region. This product is exclusively available through Roche, therefore full and open competition are not feasible. Included in purchase is an interface with the Roche design team so that product (primers) can be custom made for experiment. No other company has the expertise or offers the service of designing KAPA probes.

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 2020) 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
21-035690	6/1/2021			

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
	Roche Diagnostics	

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)*
6/11/2021 11:30 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)
	Epimutation of DRD1 as a biomarker of lung cancer risk 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 NEED (SON)

1.0 TITLE

Epimutation of DRD1 as a biomarker of lung cancer risk

2.0 BACKGROUND

Epigenetic modifications, such as DNA methylation and histone modifications, play a critical role in controlling gene expression. An epimutation occurs when alterations in DNA methylation change gene expression. In cancer, epimutations frequently occur in genes involved in DNA repair and the cell cycle, promoting malignant transformation. Our lab has previously shown that the dopamine receptor D1 (DRD1) is a tumor suppressor in lung cancer and that its expression is down-regulated by promoter methylation. Additionally, in DNA from peripheral blood mononuclear cells (PBMCs), a SHS-induced epimutation has been observed in *DRD1* in adults persisting 30 years after the SHS exposure.
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This project has two research goals. The first is to characterize childhood SHS-induced epimutations in the *DRD1* gene. The second is to determine if an epimutation in *DRD1* is associated with relative risk of lung cancer, thereby potentially discovering the first ever biomarker for lung cancer risk in never smokers. The proposed research will utilize PBMC samples from the NCI-Maryland lung cancer case-control study. I will characterize childhood SHS-induced epimutations using targeted NextGen bisulfite sequencing of the *DRD1* promoter – **a custom assay designed in collaboration with Roche Sequencing.** This will enable us to study the *DRD1* promoter in unprecedented detail with roughly 250x more of the *DRD1* gene analyzed compared to the Illumina EPIC probe-based platform. This work will be completed in NCI/CCR/Laboratory of Human Carcinogenesis.

3.0 TYPE OF ORDER

This is a Firm Fixed-Price Purchase Order.

4.0 SPECIAL ORDER REQUIREMENTS

4.1 PRODUCT FEATURES/SALIENT CHARACTERISTICS

We have discussed the project with the staff in the Genomics Core at Frederick (Xiolin Wu, Monika Mehta, et al.). This assay was selected in particular due to a history of success with Roche products. The sequencing core will prep the libraries and run them on the hiSeq. Data files will be analyzed in R.

STATEMENT OF NEED (SON)

The following product features/characteristics are required for this requirement:

- **Staff/expertise in the genomics core**
- **hiSeq sequencer**
- **R (freely available computer program)**

4.2 DELIVERY / INSTALLATION

Deliver to Adriana Zingone, items shall be delivered within 60 days of purchase
Adriana Zingone MD, PhD
Research Biologist
Laboratory of Human Carcinogenesis
Centre for Cancer Research, NCI
Building 37, Room 3060
Bethesda, MD, 20892
Tel: *240 760 6862*
Email: *adriana.zingone@nih.gov*

4.3 TRAINING

N/A

5.0 PAYMENT

1x payment

Payment shall be made (*once, at purchase*)____. Payment authorization requires submission and approval of invoices to the COR and NIH OFM, in accordance with the 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.