STATEMENT OF WORK (SOW)

<u>Instructions:</u> This document should be used for the acquisition of SERVICES. Instructions (and sample language) for completion are in red, and should be excluded from the completed document.

1.0 TITLE

Effects of CD47 expression on the global metabolomic profile of natural killer (NK) cells.

2.0 BACKGROUND

CD47 is an immunoglobulin superfamily transmembrane glycoprotein, ubiquitously expressed in different organs and tissues. CD47 is a known regulator of mitochondrial homeostasis and metabolism. Prevous studies in our lab has shown that the natural killer cell recruitment and activation are regulated by CD47 expression in the tumor microenvironment. B6H12 is a function-blocking antibody that inhibits CD47 interactions with TSP1, SIRPα, some integrins, and EGF receptor. Treating human NK cells with B6H12 that blocks thrombospondin-1 binding abrogated its inhibitory effect on NK cell proliferation. Relevant to the role of CD47 in tumor immunology, B6H12 directly induces killing of tumor cells by NK cells, B cell migration, and regulatory T cell differentiation. CD47 limits mitochondrial metabolism and ROS production in NK cells. Gene-expression and functional studies in NK cells identified impaired mitochondrial function and an enhanced proapoptotic signature in Cd47-/- NK cells when subjected to stress. Wild type and Cd47-/- NK cells differ in glucose metabolism and respond differently to inhibition or uncoupling of mitochondrial respiratory pathways. Thus, CD47 regulates NK cell transcriptional responses to activating stimuli, and its absence results in a defect in mitochondrial metabolism. Here, we aim to study the effects of the CD47 expression in the global metabolomic status of the human NK cell (NK92). Metabolomics is an analytical technique for studying metabolic pathways by examining the overall changes of small metabolites in biological systems using mass spectrometry (MS).

2.1 OBJECTIVE

The main objective of this project is to understand the metabolic alterations regulated by CD47 in human NK cells.

3.0 SCOPE

A comparative global metabolomics analysis will be done in the naïve and cytokine (interleukin-15) activated NK92 cells, in the presence and absence of B6H12. NK92 is an interleukin-2 (IL-2) dependent natural killer cell line derived from peripheral blood mononuclear cells from a 50 year old caucasian male with rapidly progressive non-Hodgkin's lymphoma. The effects of TSP1 on the metabolomic profile of the NK92 cells in different treatments will also be analyzed at two time points (6 hrs and 24 hrs). The data obtained under this analysis will help us to understand the metabolic alterations governed by the expression of CD47 in human NK cell and will contribute to the knowledge and research of cancer therapy.

4.0 CONTRACT REQUIREMENTS/ AND PERSONNEL QUALIFICATIONS (IF APPLICABLE)

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Metabolon's Precision Metabolomics™ LC-MS global metabolomics platform provides a high-fidelity, reproducible analysis of the current-state of a biological system to help identify pharmacodynamic, efficacy and response biomarkers and reveal changes in key biological pathways. Metabolon's unmatched chemical library and expertise identifies, tracks, and maps the different classes of metabolites and pathways that inform this study and reveal meaningful actionable insights. The company qualifications, the quality of data generation and assembly along with the tasks and plan of work for this analysis package is further described in the supporting file with this order as 'Metabolon Quote for National Cancer Institute'.

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 12 months from date of award.

7.0 PLACE OF PERFORMANCE

NCI address where services shall be performed: Center for Cancer Research, National Cancer Institute, Building 10, Room 2N252, Bethesda, MD 20892-1500

Contractor's address where the analysis will be performed: Metabolon, Inc. 617 Davis Drive, Suite 100 Morrisville, NC 27560 US

8.0 REPORT(S)/DELIVERABLES AND DELIVERY SCHEDULE

Product Description (Deliverables)

1. A relative concentration profile of all structurally named small-molecule entities, which can include both endogenous compounds, xenobiotics, and their metabolites, extracted from the samples and detected by our Global Metabolomics platform. Provided in the Client Data Table format (Excel file).

2. A statistical analysis of the resulting data, which typically consists of univariate significance tests (t-tests, ANOVA, repeated measures analysis, etc.) and, if appropriate, classification analyses.

3. Summary biochemical interpretation of selected, statistically significant metabolites provided in a Word report. An outline of the analytical methods is provided in the report Appendix.

4. Access to the MyMetablon Client Portal for downloading the study deliverables. The MyMetablon Client Portal also provides data analysis and visualization tools that allow for further data exploration. Turnaround Time from receipt of samples and required information: 9-13 weeks for Standard Preferred or Supported tubes. 10-14 weeks for NonStandard tubes.

9.0 PAYMENT

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Payment shall be made ONE TIME. 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.*

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* 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.