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September 28th, 2011

Dear Dr. Andy Wyrobek,

I am sending you this letter for inclusion with the final report as part of the subcontract to U.C. Davis on Task 9. of the "RAPID" BARDA project.

Over the one year period of the project, Task 9 generated and completed Human Institutional Review Board certification across 3 individual institutes to include LBNL, UCD and UCSF. In addition we collected whole blood for processing and biomarker analysis from 9 radiotherapy patients. The information included complete dosimetry and chemo exposure information for each of the 4 patients that were total body irradiated and 5 patients that were partial body irradiated. Two consented patients did not stay in the study. The Task 9 team also generated 5 SOPs and helped in biomarker target selection as well as provided scientific insight in to data analysis. During the project we also provided you with approximately 20 project updates, as power point presentations, that were separate from the required input for the BARDA Quarterly Reports and In Process Review.

Below is the general summary for Task 9:

1. IRB wrap up for terminating the recruitment at UC Davis, UCSF, and MDA Cancer Center - Task 9 collected a total of 9 samples from patients receiving whole body or partial body radiation therapy. Two additional patients were consented but unable to give samples on the day of treatment. Samples were obtained from 4 whole body patients and 5 partial body exposures.

2. Generation of radiotherapy patient data and information - Final compilation of radiotherapy patients who provided blood samples in the base year, including complete dosimetry and chemo exposure information for each of the ~10 patients TBI and PBI that were collected under BARDA funding in the base year. We conducted a physical inventory of all the samples related to Task 9 at both LBNL and UCD. This information was collated in "The TASK9_Radiotherapy_Data_Sheet". This includes the following: 1) Task 9 de-identified patient information and exposure data; 2) Task 9 sample inventory and location; and 3) Task 9 Calculations of dosimetry for irradiated blood volumes in partial body exposures.

3. Dosimetry calculations of irradiated body volumes in PBI patients and tissue doses - During Feb and Mar. Dr. Coleman worked with Dr. Julian Perks to convert radiotherapy image data and dosimetry to absolute volumes as part of the file "The TASK9_Radiotherapy_Data_Sheet" for completing BARDA project requirements. Data was calculated based on the planning system contour taking in to account the entire skin volume based on the patient's CT scan. This was done for 6 patients. Data was generated for the entire volume and then used to obtain the dose volume histogram. The cumulative dose volume histogram is read as the volume of tissue that receives at least that amount of dose (5cGy, 10cGy and 180 cGy). Finer dose points of 0.5-1 Gy were limited to the treatment volume (no scatter). What we found was that the volume of tissue receiving at least 1cGy was almost the same as the total scanned volume, showing that it is a reasonable

assumption that the whole body gets 1cGy per treatment. Dose volumes were than calculated for cubic centimeters over several dose levels for 25-50% of the patients body volume, which can be used for estimting the total blood volume. Blood volumes representing 1-20% are estimated for doses greater than 1 Gy, which is essentially equilivent to the treatment area for the irradiated tumor.

4. Plasma sample handling using pilot radiotherapy samples - UC Davis initiated pilot studies using UC Davis reagents to look at protein yield, sample load normalization and alternative antibodies for use in Task 6 because of problems related to running human plasma samples and obtaining negative data using ELISA-based techniques. To address these issues we started generating data late December before the IPR results were known. Data was used to support Task 6 for inclusion in the final report. This work resulted in a table that compared three methods for analyzing protein concentration in 22 total samples from Task 7 and Task 9. A comparison was made between NanoDrop (A_{280} absorbance), BCA measurement and Life technologies Qubit fluorescent protein analysis. The data indicated a better correlation between BCA and Qubit for determining the yield of protein concentration. SDS-PAGE was used to confirm these findings for 6 samples form Task 9 and 3 samples from Task 7.

5. Plasma-based Bax biomarker studies - Summation of his BAX biomarker results for ex vivo human plasma was conducted in support of Task 7 LBNL manuscript. The first round of blotting looked at 2 baseline samples and two additional donors sampled 24 hrs after exposure to 0, 2, and 6 Gy. The pilot methods came directly from a Invitrogen/Life Technologies protocol in a PDF format, which is available for inclusion in the final report as a pilot SOP. These blots were replicated a second time to validate the findings. The experiment indicated that there was an ~1.5-2 fold increase for the 2 Gy sample when compared to the 0 Gy samples obtained from two healthy donors. Data analysis was based on total protein loaded. This data was presented in the Feb. BARDA report.

All referenced material (IRB, SOPs, Patient information) are included as part of the final report as attachments (listed below). Additional copies of the detailed documents this information was derived from were hand-delivered to LBNL on a flash drive prior to April 27th, 2011.

Attachment 1. T9_BARDA_Letter.
Attachment 2. UCD BARDA IRB.
Attachment 3. Patient Information.
Attachment 4. Sample Information.
Attachment 5. T9_BARDA SOPs.

Sincerely,

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March 31st, 2011

Dear Dr. Andy Wyrobek,

Here are the key activities for Task 9. during the final three months of the "RAPID" BARDA project. Items 1-4 cover specific requirements for wrapping up sample collection, data entry and data analysis. Items 5 and 6 cover work on sample processing and limited analysis by Western blotting to support manuscripts. The final item covers a potential paper related to Task 9. that would require additional effort and analysis. All referenced files are part of the final report and will be hand-delivered on a flash drive as part of the final report.

1. Generation of radiotherapy patient data and information - Final compilation of radiotherapy patients who provided blood samples in the base year, including complete dosimetry and chemo exposure information for each of the ~10 patients TBI and PBI that were collected under BARDA funding in the base year. Two meetings were held during Jan and Feb at LBNL for rectifying the sample inventory. At the meeting task were delineated for conducting the inventories at both LBNL and UCD to ensure proper sample control, labeling and storage at the end of the project. During the month of Feb. we conducted a physical inventory of all the samples related to Task 9 at both LBNL and UCD. During the month of March all of this information was collated in "The TASK9_Radiotherapy_Data_Sheet" for inclusion in the BARDA final report. This includes the following: 1) Task 9 de-identified patient information and exposure data; 2) Task 9 sample inventory and location; and 3) Task 9 Calculations of dosimetry for irradiated blood volumes in partial body exposures.

2. IRB wrap up for terminating the recruitment at UC Davis, UCSF, and MDA Cancer Center - Task 9 collected a total of 11 samples from patients receiving whole body or partial body radiation therapy. Two additional patients were consented but unable to give samples on the day of treatment. Samples were obtained from 4 whole body patients and 6 partial body exposures. Although 5 patients were available for treatment during Jan (2 at UCSF and 3 UCD), after reviewing the cases Dr. Coleman consented for one additional patient in the middle of Jan at UCD. This sample was collected and analyzed by Mr. Wei He at UCD. In addition, during the final three months Dr. Coleman spent time organizing and conducting multiple meetings with LBNL, UCSF, Texas Children/MD Anderson and UCD clinical staff to finalize information needed for closing down the BARDA project. This included gathering additional input information for IRBs at UCD, clarifying treatment data (chemotherapy and Radiotherapy at UCSF) and reviewing physical dosimetry at UCD. Interactions between the different IRB centers only involved Dr. Colemans' effort, as the clinical staff at UCD was not paid on the BARDA project after the month of Dec. Travel cost associated with Dr. Coleman's trips to UCSF for meetings as well as patient sampling throughout the entire year were included in the final three months invoices.

3.Dosimetry calculations of irradiated body volumes in PBI patients and tissue doses - During Feb and Mar. Dr. Coleman worked with Dr. Julian Perks to convert radiotherapy image data and dosimetry to absolute volumes as part of the file "The TASK9_Radiotherapy_Data_Sheet" for completing BARDA project requirements. Data was calculated based on the planning system contour taking in to account the entire skin volume based on the patient's CT scan. This was done for 6 patients. Data was generated for the entire volume and then used to obtain the dose volume histogram. The cumulative dose volume histogram is read as the volume of tissue that receives at least that amount of dose (5cGy, 10cGy and 180 cGy). Finer dose points of 0.5-1 Gy were limited to the treatment volume (no scatter). What we found was that the volume of tissue receiving at least 1cGy was almost the same as the total scanned volume, showing that it is a reasonable assumption that the whole body gets 1cGy per treatment. Dose volumes were than calculated for cubic centimeters over several dose levels for 25-50% of the patients body volume, which can be used for estimting the total blood volume. Blood volumes representing 1-20% are estimated for doses greater than 1 Gy, which is essentially equilivent to the treatment area for the irradiated tumor. This data is presented as a signal table on sheet three in the TASK 9 Data sheet titled PBI patients irradiated volumes" for inclusion in the final report.

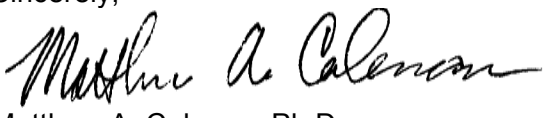
4. Generation of final report figures - Final consolidation of experimental data and patient samples was compiled during the month of March and is available for supporting future papers. Western data is in a folder titled "IR_Westerns Task 7_9". The folder contains separate files related to the number of rounds we ran Western blots in support Task 7 and Task 9 samples. This includes power-point summaries with all experimental data, TIFF images used for data analyses, data analysis files and a single summary file. The summary file contains two tables for inclusion in the final report. Table 1. "Antibodies tested table", which list of antibodies tested by Western blots and coloration to indicate if a strong signal was generated. For radiation patient data this was all compiled in the "The TASK9_Radiotherapy_Data_Sheet" for inclusion in the BARDA final report. This includes the following: 1) Task 9 de-identified patient information and exposure data; 2) Task 9 sample inventory and location; and 3) Task 9 Calculations of dosimetry for irradiated blood volumes in partial body patients.

5. Plasma sample handling using pilot radiotherapy samples - UC Davis initiated pilot studies using UC Davis reagents to look at protein yield, sample load normalization and alternative antibodies for use in Task 6 because of problems related to running human plasma samples and obtaining negative data using ELISA-based techniques. To address these issues we started generating data late December before the IPR results were known. Data was used to support Task 6 for inclusion in the final report. This work resulted in a table that compared three methods for analyzing protein concentration in 22 total samples from Task 7 and Task 9. A comparison was made between NanoDrop (A_{280} absorbance), BCA measurement and Life technologies Qubit fluorescent protein analysis. The data indicated a better correlation between BCA and Qubit for determining the yield of protein concentration. SDS-PAGE was used to confirm these findings for 6 samples form Task 9 and 3 samples from Task 7. A summary table has been generated for inclusion in the final report titled "Task 9 - Protein yield comparisons using three independent Assays". We also generated a proprietary list of 20 different antibodies at UCD for sharing with COREB members for comparison to the antibodies used for ELISA. During Feb and Mar we used the above procedures for validating delected responses in two TBI as well as 5 PBI patients. This data is included in the final report as a table titled "Task 9. Tested antibodies".

6. Plasma-based Bax biomarker studies - Summation of his BAX biomarker results for ex vivo human plasma was conducted in support of Task 7 LBNL manuscript. The first round of blotting looked at 2 baseline samples and two additional donors sampled 24 hrs after exposure to 0, 2, and 6 Gy. The pilot methods came directly from a Invitrogen/Life Technologies protocol in a PDF format, which is available for inclusion in the final report as a pilot SOP. These blots were replicated a second time to validate the findings. The experiment indicated that there was an ~1.5-2 fold increase for the 2 Gy sample when compared to the 0 Gy samples obtained from two healthy donors. Data analysis was based on total protein loaded. This data was presented in the Feb. BARDA report. During March we conducted a third round of Westerns to include 5 additional healthy donor samples 24 hours after exposure to 0 and 2 Gy. This data was summarized as a figure, but will need further data analysis for comparison to actin, which we used as normalization control. This data will potentially be included in the Task 7-related manuscript.

7. Preparation and outline of future manuscript based on Task 9 results - In Jan and Feb. we attended meetings to go over the timeline for wrapping up the BARDA project and completing experiments in support of manuscripts. Dr. Coleman presented the following title and paper scope "**Protein biodosimeters of radiation exposure using human radiotherapy patients". Scope:** To determine the efficacy and applicability of sensitive antibody-based assays ELISAs and Westerns to identify exposures to ionizing radiation. Comparisons would look at whole body and partial body exposures as part of a study to determine the use of such a model system for validating irradiation exposures. In support of the final report we prepared an outline of data, samples and future experiments that would be required to complete this endeavor.

Sincerely,



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INSTITUTIONAL REVIEW BOARD
University of California, Davis

Attachment 2

PROTECTION OF HUMAN SUBJECTS – DECLARATION / ASSURANCE OF IRB APPROVAL

Principal Investigator Matthew Coleman MD	**Protocol No.** 201018353-1	**Approval Date** 09/01/10	**Expiration Date** 08/31/11	**Risk Level** Minimal Risk - Level 1
PI Department MED: RADIATION ONCOLOGY	**Sponsor Name** Biomedical Advanced Research and Development Authority	**Level of Review** Expedited	**Expedited Category** 2b	**Status** New
The following research study has been reviewed by the IRB in accordance with the Common Rule and any other governing regulations: Human-Based Biodosimetry Using Protein Biomarkers Found in Blood				

The above referenced activity has been determined to meet the definition of human subjects research as defined by Federal Regulations and UC Davis IRB Policy. As principal investigator for a study involving human subjects, you assume certain responsibilities, specifically:

1. You will conduct the study according to the protocol approved by the IRB. As the PI you will be accountable for your own research and the protection of human subjects. You will ensure, at all times, that you have the appropriate resources and facilities to conduct this study. You will ensure that all research personnel involved in the conduct of the study have been appropriately trained on the protection of human subjects, in addition to the study procedures.
2. Any unanticipated problems involving risks to participants or others will be reported to the IRB in accordance with IRB policy. Changes in approved research initiated without IRB approval to eliminate apparent immediate hazards to the participant, are to be reported to the IRB in accordance with the policy "Reporting of Unanticipated Problems Involving Risks to Participants or Others."
3. Any changes in your research plan must be submitted to the IRB for review and approval prior to implementation of the change. Proposed changes in approved research cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants.
4. Your protocol must be renewed prior to expiration of the study. Although a courtesy renewal notice will be issued to you three months prior to expiration, should you fail to receive this notice it is your responsibility to contact the IRB Administration for a duplicate copy. Failure to submit renewal documents to the IRB Administration by the Administrative Due Date may result in termination of the study by the IRB.
5. Advertisements for the recruitment of subjects must be approved by the IRB prior to implementation.
6. If you plan to collect protected health information, you are required to comply with HIPAA requirements.
7. Studies conducted at the CCRC must be reviewed and approved by the VA Research & Development Committee prior to initiation of the study. Contact the VA R&D Committee for submission requirements.
8. Should your study involve the use of investigational drugs, you are required to provide a complete copy of the approved protocol to the Investigational Drug Service Pharmacy.

If this is a Clinical Study, the Hospital Health System requires that:

- A complete copy of the IRB approved Description of Study and signed Consent Form be placed in the patient's medical record. Ensure that you have swiped the patient's name plate card or printed the patient's name at the top of page 1 of the consent document. Medical procedures should be documented in the patient's medical record.
- All investigational drugs be distributed through the UCDMC Pharmacy. A copy of the signed consent form must be submitted to the Pharmacy if investigational drugs are dispensed through the Outpatient Pharmacy.
- If the study involves radiation use, a copy of the IRB approved consent form be sent to: RUC, Health Physics, 2500 FSSB.

Name and Address of Institution: University of California, Davis IRB Administration 2921 Stockton Blvd., Suite 1400, Rm. 1429 Sacramento, CA 95817	**Signature : The IRB Chair/Designee signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.**
Institutional Administrator: Eric C. Mah, MHS Director, Institutional Review Board Administration ecmah@ucdavis.edu	**Name:** John Anderson MD
Phone No.(916) 703-9151	**Title:** Chair
Fax No. (916) 703-9160	**Date:** 09/01/2010
This Assurance, on file with the Department of Health and Human Services, covers this activity: FWA No: 00004557 Expiration Date: August 17, 2013 IORG: 0000251	

If your study includes the use of a consent form(s), your study will require the use of the HIPAA *Research Authorization Form.* Please see the website address below for the form, instructions and requirements. Note: the IRB does not require submission of the *Research Authorization Form* with your IRB protocol application form.

- **http://compliance.ucdmc.ucdavis.edu/guidance/privacy/resauth.html**

DESCRIPTION OF STUDY

Principal Investigator: Matthew Coleman

Title of the Study: Human-based Biodosimetry Using Protein Biomarkers Found In Blood

PURPOSE AND PROCEDURES:

1. Describe the study format and whether it is single or multi-center; industry-sponsored or investigator initiated; and the funding source.

   This is a multi-center, federally funded pilot study.

2. Briefly describe the specific aims of the study, research methods and procedures.

   Summary/Abstract
   In the aftermath of a terrorist incident that makes use of "dirty bombs" or detonates a nuclear device, thousands of people may require medical attention to mitigate the effects of ionizing radiation (IR). In these situations, the first need is to rapidly separate the exposed from the unexposed individuals by measuring the appearance of radiation-specific changes in easily sampled tissues. We propose to develop novel signatures of ionizing radiation exposure for use in a magneto-nano chip device capable of multiplex biomarker identification. Our role will be the following: 1) Selection of affinity reagents for ionizing radiation and tissue damage biomarkers (in collaboration with LBL and Stanford University). 2) Application of peripheral blood model system irradiated ex vivo for verifying proteins that are useful for biodosimetry (in collaboration with PPD and Stanford University). 3) Testing of affinity reagents for multiplex detection using Western blot and ELISAs in the peripheral blood model system irradiated ex vivo as well as radiotherapy patients. 4) Translation of affinity reagents for multiplex detection on a magneto-nano chip platform. 5) Validation of affinity reagents for multiplex detection on a magneto-nano chip platform using samples peripheral blood and radiotherapy patient samples. These studies will form the foundation for establishing rapid, precise, high-throughput assay systems that are practical in a variety of radiation exposure scenarios.

   Relevance
   The human peripheral blood model system applied in this proposal will identify proteins that are important for understanding the radiation response, the outcome and predicting risk associated with radiation exposure. This model may also prove important for identifying susceptibility factors involved in individual responses to irradiation that will help mitigation and follow-on consequence management of exposed individuals. It is expected that this integrated approach will produce a multiplex capable devices that is robust and reliable for medical assessment to distinguish between the truly injured and expected very large numbers of worried well.

   The study aims to validate and measure radiation biomarkers in patients that are being treated for either total body irradiation e.g. pre bone marrow transplant or partial body irradiation e.g. female pelvis treatment for cervical cancer, treatment of the mediastinum related to lung cancer. The presence of biomarkers has been demonstrated ex vivo in peripheral blood mononuclear cells and in mice. This model will be tested in humans. The aim of this pilot study is to determine the levels of detectable biomarkers in a controlled population with accurately known radiation dosimetry. Patient's treatment plans will not be altered from the regular prescribed standard of care.

3. Address if therapeutically removed tissue will be collected, what types, and for what purposes.

   Blood samples will be taken from the subjects both prior and following a session of radiation. A total of three samples will be drawn if patients are treated twice a day – the first before the treatment, the second after the first radiation session and the third 24 hours after the first.

4. Specify the nature, frequency and duration of tests, if any.

   The first blood sample will be taken immediately prior to the first radiation session and the second will be taken 24 hours later for patients that are treated once per day. Total body irradiation patients are typically treated twice per day and in this case the first sample will be drawn before treatment, the second after the first radiation session and the third 24 hours after the first.

5. If blood samples will be collected, identify in what manner and the maximum amount that will be collected over any 6 week period (if subjects are co-enrolled in other research studies, the volume of blood from the other study should also be included)

   __X_venipuncture _X__venous catheter ___arterial puncture ___arterial catheter ___cutaneous

   5cc will be drawn prior to the first radiation session and another 5cc will be drawn 24 hours later, immediately prior to the second radiation session

6. Any additional procedures (noninvasive) involved in this study activity must be described.

   No other procedures will be performed

7. If the study involves incomplete disclosure, provide the rationale.

   The study only involves complete disclosure to the patient

8. If this activity will be utilizing existing data, specify the source and how the data will be retrieved, reviewed, coded and stored.

   Health information will only be obtained from subjects in order to identify which type of treatment they are prescribed (total or partial body irradiation). This information is held within a secure computer database – the record and verify system (IMPAC) within radiation oncology. The information will not be transferred from this database.

9. Address the location and duration of the study including follow-up period

   Subjects will be recruited from the patients routinely treated at UC Davis Cancer Center. The location of the study will be the Department of Radiation Oncology. Patients will be on the study for 24 hours to obtain the two blood draws. There is not expected to be a follow up period with the patient unless the have side effects from the blood draw.

10. Clarify how you plan to monitor data to ensure subject safety.

    The patient data is currently held in a secure database and no identifying information will be recorded when the blood samples are taken.

11. Address whether you have the appropriate resources (study personnel and facilities) to conduct this study.

    The study is fully funded by BARDA (The Biomedical Advanced Research and Development Authority, within the Office of the Assistant Secretary for Preparedness and Response in the U.S. Department of Health and Human Services), in terms of funding for personnel – laboratory resources – data analysis costs

12. Describe the role of each key member of your study personnel.

Matthew Coleman – Overall project management, data analysis
Julian Perks – Patient selection and dosimetry
Physician and resident staff – Patient selection and consent
Nursing staff – Blood sample collection

SUBJECT SELECTION:

1. Identify the subject population.

   Radiation oncology patients treated at UC Davis that are routinely prescribed either total body irradiation or partial body irradiation e.g. whole pelvis, mediastinum, prostate, lung etc. as part of their regular care.

2. Address how subjects will be recruited: __X_direct person to person solicitation, ___by telephone, ___letter, ___advertisement, ___press release, ___notices, ___other. Provide the text.

3. State from where subjects will be recruited, when and how many.

   Subjects will be recruited at their new patient consultation in the department of radiation oncology, following identification by their attending physician.

4. Specify the age of the research subjects.

   Total body irradiation patients are typically teenagers or young adults, so the age range here is expected to be 14 – 29. partial body irradiation patients are both men and women generally in middle to old age so the age range expected here is 35 – 89.

5. List all criteria for including and excluding subjects.

   Inclusion criteria:
   Patient receiving total or partial body irradiation

   Exclusion criteria:
   Pregnant patients.

6. If women and minorities are excluded, provide rationale for such exclusion.

   Women and minorities will not be excluded

7. Attach the translated documents for subjects whose primary language is not English.

   N/A

   SPECIAL/VULNERABLE POPULATION (if applicable):

   Surrogate consent for participation in a research study should be employed only to the extent that it is consistent with the intent of the Common Rule (45 CFR 46, Subpart A) and all other federal and state laws and regulations pertaining to protecting human subjects participating in research. Carefully review the IRB Policy on *Surrogate Consent For Research* for compliance with all applicable laws, regulations, and conditions of this policy. Investigators are reminded that use of surrogate consent shall apply on a case-by-case basis within the protocol.

1. Identify the vulnerable population: _X__children, ___mentally handicapped, ___pregnant women, ___fetuses, ___prisoners, ___cognitive impairment, ___life-threatening disease, or ___social or ___economically disadvantaged. Address what additional safeguards you will put into place to protect the rights and welfare of this population.

Some of the subjects are expected to be teenagers as this is the typical age range seen for total body irradiation in preparation for bone marrow transplant. An assent form is prepared for these subjects to complement the parental consent. Also the minimum age for this study is set at 14.

2. If you are seeking IRB approval for use of surrogate consent, justify the appropriateness of such use and describe your specific plan for the assessment of the decision-making capacity of the subject(s). **N/A**

RISKS:

1 Address whether there is a possibility of physical, psychological, social or legal injury from participation in this study and assess the likelihood and seriousness of those risks.

The risks associated with study only those from blood draws. Subjects will have approximately 5cc drawn twice; the first 5cc before the first radiation session and the other 5cc 24 hours later. There is a minimal risk of breach of confidentiality as patients will be identified in order to determine their prescription.

2. If the methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used.

N/A

3 Identify your plan for protecting subject privacy and confidentiality.

The subject's identity and diagnosis will only be held electronically in the current radiation oncology database that is used for all patients treated in the radiation oncology department. The blood samples that are drawn will be anonymous and only labeled with study specific numbers.

4. Explain your plan for reporting adverse and serious adverse events to the IRB.

Adverse events will be reported the IRB annually at the time of study renewal. Serious adverse events will be reported to the IRB according to the IRB policies. Serious adverse events will be reported with 5 days of the investigator becoming aware of the event and by using the IRB specific form for reporting serious adverse events and other unanticipated problems.

5. If the study involves the use of placebo, justify why this is appropriate.

N/A

BENEFITS:

1 Address if there is a benefit to individual subjects or to the particular group or class.

This study will help us understand radiation effects, with the ultimate aim of being able to characterize dose in subjects that have been exposed to an unknown amount of radiation.

2. Address if there is no direct benefit to the subject.

There is no direct benefit to the subject.

RISK-BENEFIT RATIO:

1 Address whether the risks to subjects are reasonable in relation to the benefits (note: do not state that the benefits outweigh the risks. Rather, construct a summary assessment of the relative risks (physical, psychological, economical, and legal) to participants versus the potential benefits to participants and society).

We feel that the risk / benefit ratio is positive as the risk to the subject is minimal but the knowledge gained from being able to identify biomarkers following a radiation exposure is significant.

COSTS/COMPENSATION TO SUBJECTS:

1. If the study involves the possibility of added expenses to the subject or to a third party, such as an insurer (e.g., longer hospitalization, extra laboratory tests, travel) address the magnitude of those expenses and how this is justified.

   All the expenses for the blood draw and the sample analysis will be covered by the study team; the subject will not incur any expenses.

2. Describe the amount and type of compensation that will be paid to subjects and how that compensation will be staged/pro-rated.

   No compensation will be offered to the subjects

DISCLOSURE OF PERSONAL AND FINANCIAL INTEREST:

1. Disclose any personal and financial interest in the research as well as the extent of personal and financial interest in the sponsor.

   The researchers do not have financial interest in the results of this research.

WAIVER OF INFORMED CONSENT (if applicable): N/A

If you are requesting waiver or alteration of informed consent, you are required by federal regulations to justify the following four points, for review by the IRB:

1. The research involves no more than minimal risk to the subjects.

2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.

3. The research could not practicably be carried out without the waiver or alteration.

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

TOTAL NUMBER OF COPIES REQUIRED FOR SUBMISSION TO THE IRB ADMINISTRATION:

Original plus 1copy

UNIVERSITY OF CALIFORNIA, DAVIS
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

STUDY TITLE: **Human-based Biodosimetry Using Protein Biomarkers Found In Blood**

INTRODUCTION

This is a research study conducted by Matthew Coleman Ph.D. from the Department of Radiation Oncology. Participating in research is voluntary. You and your child have the right to know about the procedures, risks, and benefits of the research study to you and/or society so that you can make the decision whether or not to participate. This is called informed consent. Please take your time to make your decision and discuss it with your family and friends.

You and your child are being asked to take part in this study because you are about to undergo a course of whole or partial body radiation therapy. The radiation your child has been prescribed is known to create certain proteins (biomarkers) in the blood. We hope to learn more about these biomarkers and how best to detect them in a blood sample. A biomarker is a protein substance that acts as an indicator of a change in a biological state. In order to participate in this study, it will be necessary to give your written consent by signing this form.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to measure biological markers found in the blood following exposure to radiation. Eventually we hope to be able to be able to estimate radiation doses for individuals that are exposed to unknown amounts of radiation, either from accidents or terrorist attacks.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 50 people will take part in this study at UC Davis over the next five years. Up to 150 patients will be recruited at other centers that participate in this study.

BEFORE YOU AND YOUR CHILD BEGIN THE STUDY

We will ask for a brief history of the previous treatments your child has undergone, particularly chemotherapy.

WHAT WILL HAPPEN IF WE TAKE PART IN THIS RESEARCH STUDY?

If you and your child decide to participate in this study, your child will be asked to do the following:

Give a blood sample just prior to their first session of radiation and a second 24 hours later (preceding the second session of radiation). Each sample will be obtained in a standard blood draw from a vein in your hand or arm; approximately 5ml (one teaspoon) will be drawn each time.

The following procedures are part of regular care and may be done even if you do not join the study:
The prescribed radiation therapy treatment will not be altered by participating in this trial.

For IRB Administration Use

APPROVED
by the Institutional Review Board at the University of California, Davis.
SEP 1 - '10 AUG 31 '11
Approved on Expires on

IRB DOCUMENT
VERSION 6/11/2009

Coleman, Matthew
Clean Copy
August 2010

The following procedures are NOT PART OF REGULAR CARE AND WILL ONLY BE DONE IF YOU AND YOUR CHILD JOIN THE STUDY:

Two blood samples will be taken for research purposes.

HOW LONG WILL WE BE IN THE STUDY?

Your child will be asked to participate for two days – the first day of their prescribed radiation dose and the following day. After they are finished giving the blood samples there will no further investigations performed.

CAN WE STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the research Investigator if you are thinking about stopping or decide to stop. The research Investigator will tell you how to stop safely. It is important to tell the research Investigator if you are thinking about stopping so any risks can be managed safely. Another reason to tell the Investigator that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

WHAT SIDE EFFECTS OR RISKS CAN MY CHILD EXPECT FROM BEING IN THE STUDY?

They may have side effects while on this study. Everyone taking part in the study will be watched carefully for any side effects. However, the Investigator does not know all the side effects that may happen. Side effects may be mild or very serious. The research Investigators may give you medicines to help lessen side effects. Risks and side effects related to the biomarkers present in the blood we are studying include:

Your child may experience some discomfort and / or bruising at the blood draw site. There is a small risk of infection associated with a blood draw.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Your child may not benefit from taking part in this research. The information we get from this study should help us to learn more about biomarker proteins that become present in blood following exposure to radiation.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

The alternative is not to take part in this study. If you choose not to take part in this study, your future care will not be affected.

WILL OUR INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information will be kept private. However, we cannot guarantee total privacy. Your personal information may be released if required by law.

If information from the study is published or presented at scientific meetings, your names and other personal information will not be used. The blood samples that your child gives for this study will be kept anonymous

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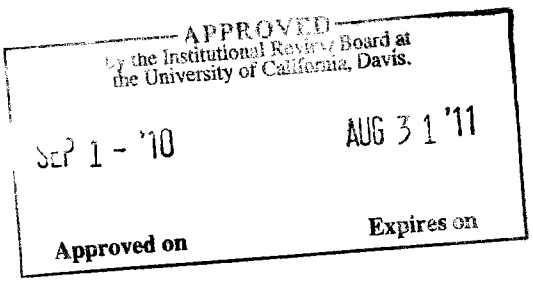

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and only labeled with a study identifier number. All data in this study is held electronically on a password protected secure (internal) network.

Designated University officials, including Institutional Review Board, and the research sponsor BARDA - Biomedical Advanced Research and Development Authority (a government agency) have the authority to review your research records.
If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission.

WHAT HAPPENS IF MY CHILD IS INJURED BECAUSE THEY TOOK PART IN THIS STUDY?

If your child is injured as a direct result of research procedures, they will receive reasonably necessary medical treatment at no cost. The University of California does not provide any other form of compensation for injury. In the case of injury resulting from this study, you and your child do not lose any of your legal rights to seek payment by signing this form.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no charge for you and your child to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department.

WILL WE BE COMPENSATED FOR BEING IN THIS STUDY?

You will not be compensated for being part of this study.

WHAT ARE OUR RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice and completely voluntary. If you decide to take part in this study, you and your child may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care here at UC Davis.

The research investigator may withdraw you from participating in this research if circumstances arise which warrant doing so even if you would like to continue.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study.

DOES THE RESEARCHER HAVE A FINANCIAL INTEREST IN THIS RESEARCH STUDY?

The researchers do not have financial interest in the results of this research.

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WILL SPECIMENS (tissue, blood, urine or other body materials) TAKEN FROM ME BE USED FOR FUTURE RESEARCH PURPOSES?

During the course of the research, the investigator will remove some blood. We would like to keep some of the blood that is left for future research purposes. Your child's specimen(s) will only be used for research purposes. If you and your child agree, these specimen(s) will be kept and used to learn more about radiation induced biomarkers.

If biological specimens, such as blood, tissue, or donated body parts are taken from your child for this study, they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

Your names, address(es), phone number(s) and any other directly identifying information will be removed from the specimen before it is given to another researcher. Because your personal information is not attached to specimens, if you change your mind about sharing specimens later, we may not be able to retrieve it.

If you and your child agree to share the biological specimen(s) collected from your child, please initial here.

_____

Otherwise, your child's specimen will be destroyed at the end of this study.

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit: http://research.ucdavis.edu/IRBAdmin/Participants.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

If you have any questions about this study now, you may contact Prof. Coleman, the Principal Investigator of this study or Dr. Julian Perks, the co- Principal Investigator. They may be contacted in the Department of Radiation Oncology, 4501 X. Street, Sacramento, CA 95817, by writing, or you may call one of the numbers listed below. You can talk to the Investigator about any questions or concerns you have about this study at (in addition to the phone numbers below, a 24 hour emergency number should also be included):

__Matt Coleman _____at phone number___916 703 5022

__Julian Perks _____at phone number___916 734 5869

__24 hour assistance _____at phone number__ 916 734 2011 (ask for the radiation oncologist on call)

For questions about your rights while taking part in this study call the IRB Administration at (916) 703-9151 or write to IRB Administration, CTSC Building, Suite 1400, Room 1429, 2921 Stockton Blvd., Sacramento, CA 95817. The IRB Administration will inform the Institutional Review Board which is a group of people who

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review the research to protect your rights. The IRB Administration has also developed a web site designed to make you familiar with your rights. The web site discusses your basic rights as a research participant, an explanation of the informed consent process, the basic requirement that written consent be in a language understandable to you, and suggested sample questions to ask the research investigator regarding your participation in the study. This web site can be accessed at: www.research.ucdavis.edu/IRBAdmin.

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EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant, you have the following rights that include but are not limited to your right to:

1. **Be informed of the nature and purpose of the experiment;**
2. **Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;**
3. **Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment;**
4. **Be given an explanation of any benefits to the subject reasonable to be expected from the experiment, if applicable;**
5. **Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits;**
6. **Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise;**
7. **Be given an opportunity to ask any questions concerning the experiment or the procedures involved;**
8. **Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice;**
9. **Be given a copy of the signed and dated written consent form;**
10. **Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision**

My signature below will indicate that I have decided to participate in this study as a research subject. I have read and understand the information above. I understand that I will be given a signed and dated copy of this consent form and the Bill of Rights.

Signature of Parent / Guardian _____ **Print Name** _____

Date _____

Signature of Person Obtaining Consent _____ **Print Name of Person Obtaining Consent** _____

Date _____

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PARTICIPATION OF MINORS IN RESEARCH

Who are we and why are we meeting you?

I am Dr Julian Perks and I work at the University of California, Davis in the Department of Radiation Oncology.

We want to tell you about a study that involves children and teenagers like yourself. We want to see if you would like to take part in this study.

Why are we doing this study?

We wish to measure biological markers found in the blood following exposure to radiation. Eventually we hope to be able to be able to estimate radiation doses for individuals that are exposed to unknown amounts of radiation, either from accidents or terrorist attacks.

What will happen to you if you on this study?

We will collect blood samples via a needle in your hand or arm, once before you are treated and once or twice after you have started treatment. Before you begin the study you will be asked to give a brief history of previous treatments you have undergone, particularly chemotherapy.

Will any part of this study hurt?

An IV will be put in your hand or arm using a small needle for each blood draw, this might hurt a little. We will use cream to make it hurt less if you like.

Will you get better if you are on this study?

This study is not related to your treatment and your prescription of radiation will not be altered by being on this study. The blood we collect will help us to assess radiation doses that are given to other people.

Who will know that you are on this study?

Your parents / guardians and your care team will know you are on this study. Other researchers at other institutions will analyze the blood but they will only see the blood and a code number, they will not know any of your personal details.

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Do you have to be on this study?

No, you don't. There is no pressure for you to participate and no one will be angry if you do not want to be on the study, just tell us. Also, if you start the study and you want to stop at any time you are free to do so, again just tell us.

Will specimens (tissue, blood, urine or other body materials) taken from me be used for future research purposes?

During the course of the research, the investigator will remove some blood. We would like to keep some of the blood that is left for future research purposes. Your specimen(s) will only be used for research purposes. If you agree, these specimen(s) will be kept and used to learn more about radiation induced biomarkers.

If biological specimens, such as blood, tissue, or donated body parts are taken from you for this study, they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

Your name, address, phone number and any other directly identifying information will be removed from the specimen before it is given to another researcher. Because your personal information is not attached to specimens, if you change your mind about sharing specimens later, we may not be able to retrieve it.

If you agree to share the biological specimen(s) collected from you, please initial here.

_____

Otherwise, your specimen will be destroyed at the end of this study.

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit:
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Do you have any questions?

If you have any questions about this study now, you may contact Prof. Coleman, the Principal Investigator of this study or Dr. Julian Perks, the co- Principal Investigator. They may be contacted in the Department of Radiation Oncology, 4501 X. Street, Sacramento, CA 95817, by writing, or you may call one of the numbers listed below. You can talk to the Investigator about any questions or concerns you have about this study at (in addition to the phone numbers below, a 24 hour emergency number should also be included):

__Matt Coleman _____at phone number___916 703 5022

__Julian Perks _____at phone number____916 734 5869

__24 hour assistance _____at phone number__ __916 734 2011
(ask for the radiation oncologist on call).

_____ _____
Signature of participant Print name

_____
Date

_____ _____
Signature of person taking consent Print name

_____
Date

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UNIVERSITY OF CALIFORNIA, DAVIS
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

STUDY TITLE: **Human-based Biodosimetry Using Protein Biomarkers Found In Blood**

INTRODUCTION

This is a research study conducted by Matthew Coleman Ph.D. from the Department of Radiation Oncology. Participating in research is voluntary. You have the right to know about the procedures, risks, and benefits of the research study to you and/or society so that you can make the decision whether or not to participate. This is called informed consent. Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you are about to undergo a course of whole or partial body radiation therapy. The radiation you have been prescribed is known to create certain proteins (biomarkers) in the blood. We hope to learn more about these biomarkers and how best to detect them in a blood sample. A biomarker is a protein substance that acts as an indicator of a change in a biological state. In order to participate in this study, it will be necessary to give your written consent by signing this form.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to measure biological markers found in the blood following exposure to radiation. Eventually we hope to be able to be able to estimate radiation doses for individuals that are exposed to unknown amounts of radiation, either from accidents or terrorist attacks.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 50 people will take part in this study at UC Davis over the next five years. Up to 150 patients will be recruited at other centers that participate in this study.

BEFORE YOU BEGIN THE STUDY

You will be asked to give a brief history of previous treatments you have undergone, particularly chemotherapy.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

If you decide to participate in this study, you will be asked to do the following:

Give a blood sample just prior to your first session of radiation and a second 24 hours later (preceding your second session of radiation). Each sample will be obtained in a standard blood draw from a vein in your hand or arm; approximately 5ml (one teaspoon) will be drawn each time.

The following procedures are part of regular care and may be done even if you do not join the study:
Your prescribed radiation therapy treatment will not be altered by participating in this trial.

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The following procedures are NOT PART OF REGULAR CARE AND WILL ONLY BE DONE IF YOU JOIN THE STUDY:

Two blood samples will be taken for research purposes.

HOW LONG WILL I BE IN THE STUDY?

You will be asked to participate for two days – the first day of your prescribed radiation dose and the following day. After you are finished giving the blood samples there will no further investigations performed.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the research investigator if you are thinking about stopping or decide to stop. The research investigator will tell you how to stop safely. It is important to tell the research investigator if you are thinking about stopping so any risks can be managed safely. Another reason to tell the investigator that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

You may have side effects while on this study. Everyone taking part in the study will be watched carefully for any side effects. However, the investigator does not know all the side effects that may happen. Side effects may be mild or very serious. The research investigators may give you medicines to help lessen side effects. Risks and side effects related to the biomarkers present in your blood we are studying include:

You may experience some discomfort and / or bruising at the blood draw site. There is a small risk of infection associated with a blood draw.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may not benefit from taking part in this research. The information we get from this study should help us to learn more about biomarker proteins that become present in blood following exposure to radiation.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Your alternative is not to take part in this study. If you choose not to take part in this study, your future care will not be affected.

WILL MY INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information will be kept private. However, we cannot guarantee total privacy. Your personal information may be released if required by law.

If information from the study is published or presented at scientific meetings, your name and other personal information will not be used. The blood samples that you give for this study will be kept anonymous and only

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labeled with a study identifier number. All data in this study is held electronically on a password protected secure (internal) network.

Designated University officials, including Institutional Review Board, and the research sponsor BARDA - Biomedical Advanced Research and Development Authority (a government agency) have the authority to review your research records.
If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

If you are injured as a direct result of research procedures, you will receive reasonably necessary medical treatment at no cost. The University of California does not provide any other form of compensation for injury. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no charge for you to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department.

WILL I BE COMPENSATED FOR BEING IN THIS STUDY?

You will not be compensated for being part of this study.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice and completely voluntary. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care here at UC Davis.

The research investigator may withdraw you from participating in this research if circumstances arise which warrant doing so even if you would like to continue.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study.

DOES THE RESEARCHER HAVE A FINANCIAL INTEREST IN THIS RESEARCH STUDY?

The researchers do not have financial interest in the results of this research.

WILL SPECIMENS (tissue, blood, urine or other body materials) TAKEN FROM ME BE USED FOR FUTURE RESEARCH PURPOSES?

During the course of the research, the investigator will remove some blood. We would like to keep some of the blood that is left for future research purposes. Your specimen(s) will only be used for research purposes. If you agree, these specimen(s) will be kept and used to learn more about radiation induced biomarkers.

If biological specimens, such as blood, tissue, or donated body parts are taken from you for this study, they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

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If you agree to share the biological specimen(s) collected from you, please initial here. _____
Otherwise, your specimen will be destroyed at the end of this study.

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit: http://research.ucdavis.edu/IRBAdmin/Participants.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

If you have any questions about this study now, you may contact Prof. Coleman, the Principal Investigator of this study or Dr. Julian Perks, the co- Principal Investigator. They may be contacted in the Department of Radiation Oncology, 4501 X. Street, Sacramento, CA 95817, by writing, or you may call one of the numbers listed below. You can talk to the Investigator about any questions or concerns you have about this study at (in addition to the phone numbers below, a 24 hour emergency number should also be included):

__Matt Coleman _____at phone number___916 703 5022

__Julian Perks _____at phone number___916 734 5869

__24 hour assistance _____at phone number__ 916 734 2011 (ask for the radiation oncologist on call)

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EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

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1. **Be informed of the nature and purpose of the experiment;**
2. **Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;**
3. **Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment;**
4. **Be given an explanation of any benefits to the subject reasonable to be expected from the experiment, if applicable;**
5. **Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits;**
6. **Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise;**
7. **Be given an opportunity to ask any questions concerning the experiment or the procedures involved;**
8. **Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice;**
9. **Be given a copy of the signed and dated written consent form;**
10. **Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision**

My signature below will indicate that I have decided to participate in this study as a research subject. I have read and understand the information above. I understand that I will be given a signed and dated copy of this consent form and the Bill of Rights.

_____ _____

Signature of Subject **Print Name**

_____

Date

_____ _____

Signature of Person Obtaining Consent **Print Name of Person Obtaining Consent**

_____

Date

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Task 9 Radiotherapy Patient Data Sheet

latest author HB

Date of update 110207

Patient and exposure information

Patient id*	Patient Disease and reason for radiation**	Patient Group***	Total dose**** (cGy) (planned)	Dosing details (fractions etc.) (actual dosimetry)	Sample collection time since first radiation (h)	Gender	Age	Chemo	Chemo details (what drug, dose, time etc.)	Time between last chemo and pretreatment sample	Comments on Patient	Smoking	Height (inches)	Weight (Kg)	Cancer type	Cancer location	Cancer stage
T9-D001-0	Cervical cancer	PBI-GI	0 cGy		0	F	63	Yes	Cisplatinum 75 mg.	concurrent		No	65	75.9	squamous cell	cervix	
T9-D001-1			180 cGy PBI	1 fraction day/180 cGy	23.5			Yes									
T9-D003-0	Leukemia	PBI-BDI-GI	0 cGy		0	F	87	Yes	Carboplatin 360 mg, Taxo 90 mg.	Concurrent	Massive tumor, irradiation scheduled just prior to surgery to reduce tumor mass	No	62	55.3	Adenocarinoma	Uterus	4B
T9-D003-1			350 cGy BID	2 fractions day/ 370 cGy	24			Yes									
T9-D004-0	Prostate Cancer	PBI-GI	0 cGy		0	M	74	No	NA	NA		Ex-smoker	67	95	Adenocarcinoma	Prostate	T1C
T9-D004-1			200 cGy PBI	1 fraction day/ 255 cGy	24			No									
T9-D005-0	Prostate Cancer	PBI-GI	0 cGy		0	M	75	No	NA	NA		Ex-smoker	67	92	Adenocarcinoma	Prostate and Seminal Vesicals	T1C
T9-D005-1			200 cGy PIB	1 fraction day/180 cGy	24			No									
T9-S006-0	Leukemia	TBI	0 cGy		0	M	44	Yes	Fludarabine 50 mg daily X3 11/4,5,6 last dose 11/6 Cyclophosphamide 51 mg daily X 2 days 11/5 and 11/6	3 days		No	182.8 cm	109	AML	Bone Marrow	In remission
T9-S006-1			200 cGy	1 fraction day/165 cGy with lung shieldi	24			Yes									
T9-S007-0	Leukemia	TBI	0 cGy		0	F	43	No	Intrathecal Methotrexate 12 mg (no	1 week	Patient was scheduled for TBI-BID but machine broke down prior to the afternoon irradiation	No	64	75.6	ALL	Bone Marrow	In remission
T9-S007-1			300 cGy BID	1 fraction/150 cGy with lung shielding	23			No									
T9-S009-0	Lymphoma	TBI	0 cGy		0	M	38	Yes	Fludarabine 75 mg /day 11/17-11/21 Cytoxan 35mg 1 time 11/17	3 days	Non-myeoablative	Ex-smoker	172 cm	77.8	AML	Bone Marrow	Minimal residual disease inv
T9-S009-1			200 cGy	1 fraction day/200 cGy	24			Yes									
T9-D010-0	Prostate	PBI-GI	0 cGy		0	M	77	No	NA	NA		Ex-smoker	71	95.6	Adenocarcinoma	Prostate fossa	T2NXMX
T9-D010-1			180 cGy PBI	1 fraction day/180 cGy	24			No									
T9-D011-0	Prostate	PBI-GI	0 cGy		0	M	70	No	NA	NA		Ex-smoker	71	95.6	Adenocarcinoma	Prostate fossa	T2NXMX
T9-D011-1			180 cGy PBI	1 fraction day/180 cGy	24			No	NA	NA		Ex-smoker	68	94.5	Prostate	Prostate	T1C

Legend

*** for patient ID**	T9-D	radiotherapy study, UC Davis patient
	T9-S	radiotherapy study, UCSF patient
	"001"	sequential patient number
	"-0"	pre-irradiation
	"-1"	first sample post-irradiation, second sample would be a "2"
****Patient disease and reason**	eg AML. Bone marrow ablation for transplant	
***** patient group**	TBI single	single acute exposure whole body
	TBI-BID	two acute exposures on the same day
	PBI-GI	Partial body, gastrointestinal involvement
	PBI-BM	Partial body, bone marrow
	PBI-CNS	Partial body, central nervous system (brain volume)
******total dose**	xx cGy	total dose delivered between pre and last post samples

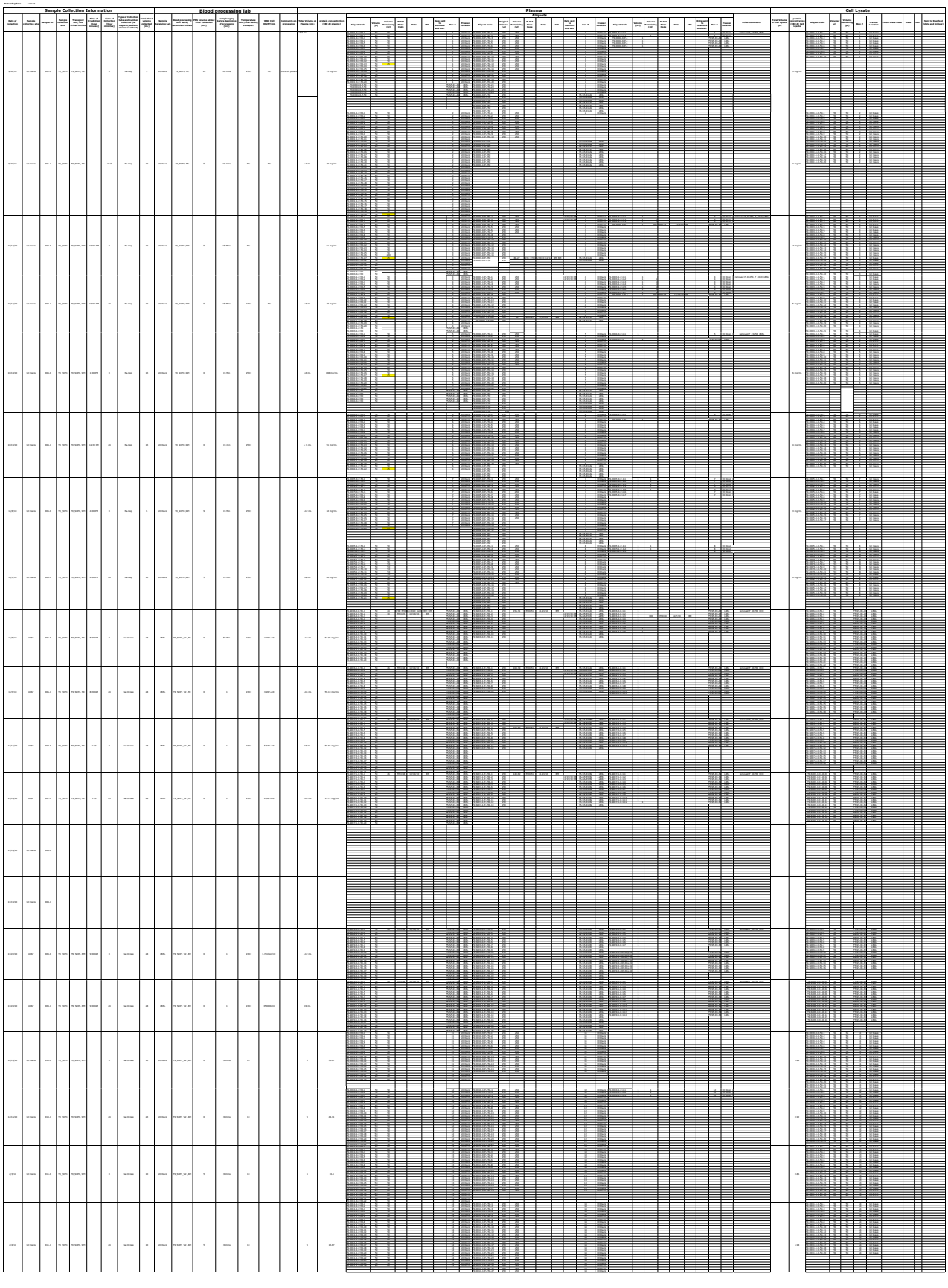
[redacted]

[redacted]

[redacted]

rolving bone marrow

[redacted]



ZOOM IN ON COMPUTER FOR DETAIL

Attachment 4

UCD/LBNL RAPID PROJECT DOCUMENT

Document Title: T9 SOP1 Human plasma and WBC isolation
File Name with date version: T9_SOP1_Plasma_and_WBC_ isolation_101201.doc
Document code: T9_SOP1
Adopted from T7 SOPs 2 and 3

Purpose: Methods for the isolation of human PLASMA and WBC from whole blood collected from radiotherapy patient donors.

Contents:

1. Materials

1. 5-40 mL human peripheral blood collected in sodium citrate vacutainers (BD, 369714). Keep at room temperature (20°C) until used. Process samples within 1 hour of collection.
2. RBC lysis buffer (5Prime, #2900040)
3. Dulbecco's Phosphate-Buffered Saline (PBS) (Sigma, D8537)
4. M-PER mammalian protein extraction reagent (Pierce, 78501)
5. Halt™ Protease Inhibitor Cocktail Kit (Pierce, 78410)
6. Halt™ Phosphatase Inhibitor Cocktail Kit (Pierce, 78420)
7. 70% ethanol
8. Clorox bleach
9. 15 mL conical tube (Corning, 430052)
10. 50 mL conical tube (Corning, 430829)
11. 0.5 mL microcentrifuge tube (Eppendorf, 022431064)
12. 1.5 mL microcentrifuge tube (Eppendorf, 022431021)
13. 1.2 mL cryovial (Corning, 430658)
14. 2.0 mL cryovial (Corning, 430659)
15. Aspiration flask
16. Waste bin
17. Eppendorf 5810 and 5417R centrifuges (with fixed-angle rotor and swinging bucket rotor)
18. -80ºC freezer (Rm. 1107) for plasma and WBC lysate storage
19. Pipet-aid
20. 10 mL serological pipettes

21. Pipettes (20 µL, 200 µL, 1000 µL capacity)
22. Pipette tips (20 µL, 200 µL, 1000 µL capacity)
23. VWR lab marker for labeling conical tubes and flasks
24. Microcentrifuge labels
25. Cryolabels
26. Cryoboxes

2. Reference

1. T9 SOP3 and 4 Human Blood Transport
2. T9 Experiment Log data sheet

3. Isolation of human plasma

All steps indicated under Section 3 to be performed at room temperature within a biosafety cabinet (Room 1204 UCD / Room 278 LBNL) or centrifuged within a secondary enclosure. The Eppendorf 5810 centrifuge is equipped with a secondary enclosure for safe processing (Room 1201 UCD / Room 278 LBNL). All used pipette tips, pipettes, and other waste are to be discarded in a red biohazardous waste bag container within the biosafety cabinet or main laboratory.

1. Decant the irradiated whole blood from each tube into two properly labeled 15 mL conical tubes.
2. Use the *Sorvall T6000D* to centrifuge the tubes at 800xg (or 3,200 rpm), at RT, for 10 minutes.
3. After centrifugation, use a *Pipet-aid* to carefully aspirate most of the plasma layer to within 1 cm of the opaque interface containing white blood cells and transfer to a clean, labeled 50 mL conical tube. Then use a *P1000 pipette* to carefully aspirate remaining plasma and 2 cm of the packed red blood cells below the opaque interface and transfer to a clean conical tube labeled for isolating the WBCs.
4. Use a *P20 pipette* to first aliquot 10 µL plasma into a labeled 0.5 mL microcentrifuge tube for protein concentration measurement. Then use a *Pipet-aid* to aliquot plasma in to the following amounts/tubes 20 X 50 uL, 20 X 250 uL and any additional material in 1 mL per 2.0 mL cryovial. The last cryovial may not contain exactly 1 mL of plasma. If there are less than 1 mL plasma left to aliquot, then transfer this amount into the last vial (which will already contain 1 mL) and document in the log how much plasma is in that last vial (1 mL - 2 mL). Record in the T9 data log the number of aliquot cryovials as well as the amount (mL) in the last vial.
5. From the set aside first aliquot of 10 µL measure the protein concentration as outlined in T9 SOP 2.
6. Store all aliquots in -80ºC freezer until needed for protein concentration measurements and ELISAs. **Avoid freeze/thaw cycles.**

4. Isolation of human WBCs

All steps indicated under Section 5 to be performed at room temperature within a biosafety cabinet or centrifuged within a secondary enclosure. The Eppendorf 5810 centrifuge is equipped with a secondary enclosure for safe processing. All used pipette tips, pipettes, and other waste

are to be discarded in a red biohazardous waste bag container within the biosafety cabinet or main laboratory.

1. To the WBC containing conical tubes add 3 volumes of 37 ^{o}C RBC lysis buffer. Make sure that the blood/WBC ratio to lysis buffer is exactly 1:3, use more conical tubes as needed.
2. Incubate the samples at room tempature for 10 min with mixing on a Nutator.
3. Centrifuge the tubes at 400xg (2,200 rpm), at RT, for 8 minutes.
4. Decant the supernatant and loosen the pellet by flicking or dragging the tube along a rack.
5. Add 10 mL of 37 ^{o}C RBC lysis buffer and repeat starting at step 2.
6. Once supernatant is no-longer pink (2-4 RBC lysis steps), decant the supernatant and resuspend the pellet in 10 mL cold PBS.
7. Remove 100 uL for cell counting.
8. Centrifuge the remaining sample at 400xg (2,200 rpm),, at RT, for 8 minutes.
9. Decant the supernatant, and loosen the pellet by flicking or dragging the tube along a rack.
10. Proceed to WBC lysate preparation.

5. Preparation of WBC lysate *All steps indicated under Section 5 to be performed at room temperature within a biosafety cabinet (Room 1204 UCD / Room 278 LBNL) or centrifuged within a secondary enclosure. The fixed-angle rotor for the Eppendorf 5417R centrifuge is equipped with a secondary enclosure for safe processing. All used pipette tips, pipettes, and other waste are to be discarded in a clear biohazardous waste bag container within the biosafety cabinet.*

1. In a separate tube, dilute Halt™ Protease Inhibitor Cocktail Kit and Halt™ Phosphatase Inhibitor Cocktail Kit 1:100 in M-PER (1 mL of M-PER reagent is required per cell pellet).
2. Add 1 mL M-PER reagent to pelleted WBCs in the 15 mL conical tube. Pipette up and down to mix and transfer the sample to a 1 mL centrifuge tube. Incubate the tube at RT for 10 minutes.
3. Use the *Eppendorf 5804 centrifuge* to remove the cell debris by centrifugation at 14,000 g for 5 minutes.
4. Transfer the cell lysis supernatant to a new 1.5 mL microcentrifuge tube and place on ice until ready for aliquots.
5. Transfer a 10 µL aliquot of the supernatant to a labeled 0.5 mL microcentrifuge tube for protein quantitation (BCA).
6. Transfer remaining supernatant to labeled 1.2 mL cryovials, with 50 µL per vial, for protein quantitation (ELISA) and discard cell debris. In total there should be 20 cryovial tubes of lysate aliquots. The last vial will have less than 50 µL. Record in the T9 data log the number of aliquot vials as well as the amount (µL) in the last vial.
7. From the set aside first aliquot of 10 µL measure the protein concentration as outlined in T9 SOP 2.
8. Store WBC lysate aliquots in -80ºC freezer until needed for protein concentration measurement and ELISAs. **Avoid freeze/thaw cycles.**

6. Freezing of WBC cells for RNA isolation. *All steps indicated under Section 6 to be performed at room temperature within a biosafety cabinet (Room 1204 UCD / Room 278 LBNL) or centrifuged within a secondary enclosure. The fixed-angle rotor for the Eppendorf 5417R centrifuge is equipped with a secondary enclosure for safe processing. All used pipette tips, pipettes, and other waste are to be discarded in a clear biohazardous waste bag container within the biosafety cabinet.*

1. To the WBC-containing conical tubes add 3 volumes of Cold +4 ^{o}C RBC lysis buffer. Make sure that the blood/WBC to lysis buffer ratio is exactly 1:3, use more conical tubes as needed.
3. Incubate the samples at room tempature for 10 min with mixing on a Nutator.
4. Centrifuge the tubes at 400xg (2,200 rpm), at RT, for 8 minutes. You should see a white pellet with a thin red layer on the top.
5. Decant the supernatant and loosen the pellet by flicking or dragging the tube along a rack.
6. Add 10 mL of Cold +4 ^{o}C PBS buffer and centrifuge the tubes at 400xg (2,200 rpm), at +4 ^{o}C, for 8 minutes.
7. Carefully pipet off the PBS and dissolve the cell pellet in 1.2 mL of TRIZOL reagent. Transfer the sample to a clean RNAse free 2.0 mL eppendorf tube and store in -80ºC freezer until RNA isolation

7. Cleanup

1. After each biosafety cabinet use, decontaminate work surface with fresh 10% household bleach.
2. Allow aspiration flask (liquid medical waste + 10% household bleach) to sit for 3 to 20 minutes (depending on the quantity of material) for disinfection. Then pour liquid down the sanitary sewer drain and discard pipettes into the biohazard waste bin. Rinse flask with fresh 10% household bleach.

8. Appendix 1. Labeling format for flasks, tubes, and cryovials

Entry #	Container type	Amount (per sample)	Purpose	Labeling Format	Example
1	Sodium-heparin vacutainer	1-8'	for collected blood (10mL blood / vacutainer)	PIN	123
2	Location sample was taken from	1-8'	for collected blood (10mL blood / vacutainer)	Loc (U or D)	D123
3	Accuspin Histopaque-1077 column	2	separation of human PBMC from RBC	unexposed (0) or Exposed (1)	0 or 1
4	50 mL conical tube	1	aspirated plasma layer	Dose - Plasma	0 - P
5	15 mL conical tube	1	aspirated wbc layer	Dose - WBC (C)	0 - C
6	0.5 mL microcentrifuge tube	1	10 µL plasma aliquot (BCA)	Expt-PIN-Dose-P-PrC	P1-123-0 Gy-P-PrC
7	2.0 mL cryovial	20	50 µL plasma aliquots (ELISA)	Expt-PIN-Dose-P-01 (01..20)	D001-0 P 50 1
8	2.0 mL cryovial	20	250 µL plasma aliquots (ELISA)	Expt-PIN-Dose-P-01 (01..20)	D001-0 P 250 1
9	2.0 mL cryovial	0 - 20	1 mL plasma aliquots (ELISA)	Expt-PIN-Dose-P-01 (01..20)	D001-0 P 1 1
10	1.2 mL cryovial	20	50 - µL WBC lysate aliquots (ELISA)	PIN-bC-01 (01..03)	D001-0 C 50 1

Expt: experiment name and number
PIN: human personal identification number (3 digits)
P: plasma
C: WBC lysate
PrC: protein concentration

Human variations in blood protein after radiation exposures

A. Patient Information needed for inclusion of the patient in the study. Once the patient is consented, the patient will be assigned a de-identified number by Dr. Coleman. The form should be completed and provided to Dr. Coleman along with the consent form at final blood draw.

B. The following are reasons for not enrolling the patients in this study:
1. Patient not between 14 and 80 years of age.
2. Patient cannot be pregnant.

C. Please complete the following questions to help us analyze the biomarker data.

Patient initial: _____

Date of radiotherapy treatment _____

1	Age between 14 - 80	Age _____
	Gender (X)	Male _____ Female-_____
	Height and Weight	**Height** _____ **Weight** _____

2	Does the patient currently have a cold/flu?	Yes No
	Has the patient had a cold or the flu in the last month?	Yes No

3	Does patient currently smoke cigarettes?	1	No, never smoked (less than 100 cigarettes in lifetime)

How many? Cigarettes/day	2 No, ex-smoker (greater than 100 cigarettes in lifetime) 3. Smoked during the past 3 months 4. Yes, currently smokes

4 Is there evidence of disease at time of irradiation?

a. Cancer
Specify: _____

b. Current Stage: _____

C. Current Location: _____

5 Is the patient receiving chemotherapy?	Yes No
If yes, please list 1. Type, 2. Dosage and 3. Frequency	1 _____ _____ 2 _____ _____ 3 _____ _____
Does chemotherapy coincide with radiotherapy?	Yes No

When was the last time patient received chemotherapy prior to this radiation/transplant	
6 Radiation treatment dose?	Total dose: Total fractions: Fractions per day:
Was shielding used?	Yes No
Was this a partial body exposure:	Yes No
For the partial body exposure list the body volume	Body volume:

7 CBC prior to irradiation: Differential white blood count prior to irradiation:	:

8 CBC after irradiation:	:

Differential white blood count after irradiation:	

To ensure the completeness of the information above please list your contact information below:

9	Name:	_____
	Contact phone number or email(s)	(____)_____ Email: _____

LBNL RAPID PROJECT DOCUMENT

Document Title: T9 SOP2 Protein Concentration
File Name with date version: T9_SOP2_protein_conc_101201.doc
Document code: T9_SOP2
Adopted from: T6b_SOP1

Purpose - Method for determining total protein concentration obtained from plasma and PBMCs lysate

Contents:

1.0 Reference:

A. Instructions, pp 1-5, Pierce BCA Protein Assay Kit (Thermo Scientific);
B. see document T6b_SOP1 for vendor pdf

2.0 Materials

A. Pierce BCA protein assay kit (Pierce; 23227)
B. 2 ml centrifuge tubes
C. 96 well ELISA plate
D. Pipette

3.0 Preparation of Diluted Albumin Standards

A. Using the following table as guide, prepare a set of protein standards. Dilute the contents of one Albumin Standard (BSA) ampule into several clean vials, preferably using the same diluent as the samples(s). Each 1 mL ampule of 2.0 mg/mL Albumin Standard is sufficient to prepare a set of diluted standards for the concentration range suggested in Table 1 below. There will be sufficient standard of each concentration to perform three standard curves. Freeze the remaining two vials for each concentration at -20°C for future use.

Table1: BSA Concentrations for Generating Standard Curve

Vial	Volume of M-PER lysis bufffer	Volume and Source of BSA	Final BSA Concentration
9	0	300 µl of Stock	2,000 µg/ml
8	125 µl	375 µl of Stock	1,500 µg/ml
7	325 µl	325 µl of Stock	1,000 µg/ml
6	175 µl	175 µl of vial 8 dilution	750 µg/ml
5	325 µl	325 µl of vial 7 dilution	500 µg/ml
4	325 µl	325 µl of vial 5 dilution	250 µg/ml

3	325 µl	325 µl of vial 4 dilution	125 µg/ml
2	400 µl	100 µl of vial 3 dilution	25 µg/ml
1	400 µl	0	0 µg/ml = Blank

4.0 Preparation of the BCA working reagent (WR)

A. 1. Use the following formula to determine the total volume of WR required:
(# standards + # unknowns) x (# replicates) x (volume of WR per sample) = total WR volume required
Example: for the standard microplate procedure with 3 unknowns and 2 replicates of each sample:
(9 standards + 3 unknowns) x (2 replicates) x (200 uL) = 4800 µL of 4.8 mL WR required.

B. Prepare WR by mixing 50 parts of BCA reagent A with 1 part of BCA reagent B (50:1, Reagent A:B).

Note: When reagent B is first added to reagent A, turbidity is observed that quickly disappears upon mixing to yield a clear, green WR. Prepare sufficient volume of WR base on the number of samples to be assayed. The WR is stable for several days when stored in a closed container at room temperature (RT).

5.0 Protein Concentration Determination

A. Pipette 25 µl of each standard and diluted unknown sample in triplicate in each well of a 96-well plate.
5.A.1 For plasma samples, dilute samples 1:25 with MPER lysis buffer. (4 µl plasma in 96 µl buffer=100 µl total)
5.A.2 For cell lysate samples, dilute samples 1:10 with MPER lysis buffer. (9 µl lysate in 81 µl buffer=90 µl total)

B. Standardized plate design (This is the design all plates should follow; not all wells need to contain sample) [ST=standard, SM=sample]

	1	2	3	4	5	6	7	8	9	10	11	12
A	ST1	ST2	ST3	ST4	ST5	ST6	ST7	ST8	ST9	SM1	SM2	SM3
B	ST1	ST2	ST3	ST4	ST5	ST6	ST7	ST8	ST9	SM1	SM2	SM3
C	ST1	ST2	ST3	ST4	ST5	ST6	ST7	ST8	ST9	SM1	SM2	SM3
D	SM4	SM5	SM6	SM7	SM8	SM9	SM10	SM11	SM12	SM13	SM14	SM15
E	SM4	SM5	SM6	SM7	SM8	SM9	SM10	SM11	SM12	SM13	SM14	SM15
F	SM4	SM5	SM6	SM7	SM8	SM9	SM10	SM11	SM12	SM13	SM14	SM15
G	SM16	SM16	SM16	SM18	SM18	SM18	SM20	SM20	SM20	SM22	SM22	SM22
H	SM17	SM17	SM17	SM19	SM19	SM19	SM21	SM21	SM21	SM23	SM23	SM23

C. Add 200 µl of WR to each well and mix plate thoroughly on a plate shaker for 30 seconds.
D. Cover plate and incubate at 37^{o}C for 30 minutes.

E. Cool plate to room temperature (~5 minutes).
F. Use TECAN Infinite M200 Plate Reader to determine protein concentration at 562nm according to instructions provided in *T6b_SOP2*.

LBNL RAPID PROJECT DOCUMENT

Document Title: T9 SOP3 Human Blood Transport
File Name with date version: T9_SOP3_blood_transport_101201.doc
Document code: T9_SOP3

Purpose: Methods for the transportation of human blood collections from Radiation Oncology Clinic, Cancer Center (Building 93, 4501 X street. Sacramento, CA 95817) to Oak Park Facility and from UCSF to LBNL Potter Street.

Contents:

1. Reference

1. MEDICAL WASTE MANAGEMENT PLAN FOR SCHOOL OF MEDICINE & GBSF UNIVERSITY OF CALIFORNIA, DAVIS.
2. UCD BUA #0923 and LBNL BUA #160
3. IRB document: 201018353-1

2. Materials

1. Personal Protective Equipment: Do not bring/wear a lab coat in the clinic. The following is only worn for removing human samples within the lab: lab coat; eye goggles; latex gloves
2. Primary containers: labeled, sodium citrate vacutainers (BD, 369714), which hold 4.5 mL of human blood per vacutainer. Six vacutainers per adult or four vacutainers per minor.
3. Secondary containers: 50 mL conical tubes and Ziploc bag
4. Tertiary container: break-resistant, leak-proof outer container for secondary container storage (e.g., a Small Coleman-type cooler)
5. Biohazard and transport container labels.
6. High-low recording thermometer.
7. Government/lab personnel vehicle

3. Donor Recruitment and Blood Collection

1. Donors will be recruited and blood will be collected as described in UCD IRB Narrative.
2. Consent and Assent forms are filed in Radiation Oncology with the IRB coordinator Angela Atkinson, located in the Department of Radiation Oncology.

4. Transportation (from Cancer Center clinical facilities to lab)

NOTE: The blood samples are not subject to the shipping regulations of the U.S. Department of Transportation (DOT) Hazardous Material Regulations (HMR) because they are considered non-infectious biological materials (e.g., cells, tissues, blood, plasma, etc.) from humans that are not suspected of having an infectious disease [Ref. 1].
Wear PPE (lab coat, safety glasses and gloves) while processing vacutainers in the lab.

1. At UCD or UCSF Radiation Oncology, the Nursing Station will provide contact information for obtaining human blood samples from consented radiotherapy patients. Ensure that the blood collection vacutainers are properly labeled with the sample PIN number.
2. Place labeled vacutainers into the 50 mL conical tubes. Secure secondary container with its lid.
3. Each 50 mL conical tube must be labeled with the PIN number. Put all 50 mL tubes inside a Ziploc bag. Label the Ziploc bag with information provided in Appendix 1.
4. Reset the high-low thermometer and place the probe in between the 50 ml tubes.
5. Place an absorbent packing material inside the tertiary container to absorb the entire contents of all inner liquid container(s) in the event of a materials leak.
6. Place bagged container into a break-resistant, leak-proof tertiary container (e.g., a sealed Coleman cooler).
7. Label tertiary container with a universal biohazard symbol (human blood is considered Risk Group 2).
8. Record sample PIN, date, time of sample draw and amount of blood collected in the T9 experiment log.
9. Secure tertiary container in vehicle trunk or other location so as to avoid shifting or sliding of the materials.
10. Transport blood samples to Oak Park Facility (Room 1108) or LBNL, 717 Potter Street (Room 109).
11. At destination carefully inspect contents for any damages or leaks. Remove samples and place into the biosafety cabinet. Disinfect secondary container.
14. Isolate plasma and WBCs following T9 SOP1.

5. Appendix 1. Label to be affixed to secondary container for blood transport

Type	**Secondary Container (Ziploc bag)**
Contents	sodium citrate vacutainers (total human blood: mL)
Date	
Sender Name	
Sender Phone	
Destination	
Recipient Name	Matthew Coleman or Wei He
Recipient Phone	

LBNL RAPID PROJECT DOCUMENT

Document Title: T9 SOP4 Human Sample Transport to LBNL
File Name with date version: T9_SOP4_sample_transport_LBNL_101201.doc
Document code: T9_SOP4

Purpose: Methods for the transportation of frozen human WBC lysates and Plasma collections from Radiation Oncology Clinic, Cancer Center (Building 93, 4501 X street. Sacramento, CA 95817) to LBNL, Potter street. Berkeley, CA 94720.

Contents:

1. Reference

1. MEDICAL WASTE MANAGEMENT PLAN FOR SCHOOL OF MEDICINE & UNIVERSITY OF CALIFORNIA, DAVIS.
2. UCD BUA #0923
3. IRB document: 201018353-1

2. Materials

1. Personal Protective Equipment: The following is worn for handling frozen human samples and dry ice within the lab: lab coat; eye goggles; latex gloves
2. Secondary containers: Cryobox and Ziploc bag
3. Tertiary container: break-resistant, leak-proof outer container for secondary container storage (e.g., a Styrofoam-type cooler).
4. 2.0 lb of dry ice
5. Biohazard and transport container labels.
6. Government/lab personnel vehicle

3. WBC/PLASMA Data Log

1. Samples will be logged out of UCD and added to LBNL BARDA logs.

4. Transportation (from UCD clinical facilities to LBNL Potter Street Facility)

NOTE: The blood samples are not subject to the shipping regulations of the U.S. Department of Transportation (DOT) Hazardous Material Regulations (HMR) because they are considered non-infectious biological materials (e.g., cells, tissues, blood, plasma, etc.) from humans that are not suspected of having an infectious disease [Ref. 1].
Wear PPE (lab coat, safety glasses and gloves) while processing and packaging human samples to be transported.

12. Place a call to LBNL point of contact (Helen Budworth (510)486-7445)
27. Place labeled Cryovials into the cryoboxes as secondary container with its lid.
13. Label box corresponding PIN for the tubes. Put the box inside a Ziploc bag. Label the Ziploc bag with information provided in Appendix 1.
14. Place bagged container into a break-resistant, leak-proof tertiary container (e.g., a sealed Styrofoam or Coleman cooler).
15. Cover the boxes in the tertiary container with ~2 lb of crushed dry ice. (Available on 2nd floor of the Oak Park Facility in Dr. Kit Lams' laboratory)
16. Label tertiary container with a universal biohazard symbol (human blood is considered Risk Group 2).
17. Remove PPE and wash hands thoroughly.
18. Record sample PIN, date, amount of samples removed in the T9 experiment log.
19. Secure tertiary container in vehicle trunk so as to avoid shifting or sliding of the materials.
20. Transport samples to LBNL Potter street facility (Bldg 977, Room 109).
21. At destination carefully inspect contents for any damages or leaks. Remove samples and place into -80 C freezer.

5. Appendix 1. Label to be affixed to secondary container for sample transport

Type	**Tertiary Container**
Contents PIN	
Date	
Sender Name	Matthew Coleman or Wei He
Sender Phone	(916) 734-5314
Destination	LBNL, Potter Street, Bldg 977. Berkeley, CA
Recipient Name	Helen Budworth
Recipient Phone	(510)486-7445

LBNL RAPID PROJECT DOCUMENT

Document Title: T9 SOP5 Human Sample Transport to LBNL
File Name with date version: T9_SOP5_blood_transport_LBNL_10212010.doc
Document code: T9_SOP5

Purpose: Methods for the transportation of frozen human WBC lysates and Plasma collections from Radiation Oncology Clinic, Cancer Center (Building 93, 4501 X street. Sacramento, CA 95817) to LBNL, Potter street. Berkeley, CA 94720.

Contents:

1. Reference

1. MEDICAL WASTE MANAGEMENT PLAN FOR SCHOOL OF MEDICINE & UNIVERSITY OF CALIFORNIA, DAVIS.
2. UCD BUA #0923
3. IRB document: 201018353-1

2. Materials

1. Personal Protective Equipment: The following is only worn for handling frozen human samples and dry ice within the lab: lab coat; eye goggles; latex gloves
2. Secondary containers: Cryobox and Ziploc bag
3. Tertiary container: break-resistant, leak-proof outer container for secondary container storage (e.g., a Styrofoam-type cooler).
4. 2.0 lb of dry ice
5. Biohazard and transport container labels.
6. Government/lab personnel vehicle

3. PBMC/PLASMA Data Log

1. Samples will be logged out of UCD and added to LBNL BARDA logs.

4. Transportation (from UCD clinical facilities to LBNL Potter Street Facility)

NOTE: The blood samples are not subject to the shipping regulations of the U.S. Department of Transportation (DOT) Hazardous Material Regulations (HMR) because they are considered non-infectious biological materials (e.g., cells, tissues, blood, plasma, etc.) from humans that are not suspected of having an infectious disease [Ref. 1].
Wear PPE (lab coat, safety glasses and gloves) while processing vacutainers and packaging human samples to be transported.

22. Place a call to LBNL point of contact (Sandya Bhatnagar (510)486-7380)
28. Place labeled Cryovials into the cryoboxes as secondary container with its lid.
23. Label box corresponding PIN for the tubes. Put the box inside a Ziploc bag. Label the Ziploc bag with information provided in Appendix 1.
24. Place bagged container into a break-resistant, leak-proof tertiary container (e.g., a sealed Styrofoam or Coleman cooler).
25. Cover the boxes in the tertiary container with ~2 lb of crushed dry ice. (Available on 2nd floor of the Oak Park Facility in Dr. Kit Lams' laboratory)
26. Label tertiary container with a universal biohazard symbol (human blood is considered Risk Group 2).
27. Remove PPE and wash hands thoroughly.
28. Record sample PIN, date, amount of samples removed in the T9 experiment log.
29. Secure tertiary container in vehicle trunk so as to avoid shifting or sliding of the materials.
30. Transport samples to LBNL Potter street facility (Bldg 977, Room 109).
31. At destination carefully inspect contents for any damages or leaks. Remove samples and place into -80 C freezer.

5. Appendix 1. Label to be affixed to secondary container for sample transport

Type	**Tertiary Container**
Contents PIN 001, 003, 004, 005	1 box of T9 BARDA Plasma samples 001-0:1mL, 5X250 uL, 001-1:1mL, 5X250 uL 003-0:1mL, 5X250 uL, 003-1:10X250 uL 004-0:1mL, 5X250 uL, 004-1:1 mL, 5X250 uL 005-0:1mL, 5X250 uL, 005-1:1 mL, 5X250 uL
Date	
Sender Name	Matthew Coleman or Wei He
Sender Phone	(916) 734-5314
Destination	LBNL, Potter Street, Bldg 977. Berkeley, CA
Recipient Name	Helen Buddworth
Recipient Phone	(510)541-31887