Study Application (Version 1.22)

1.0 General Information

***Please enter the full title of your study:**

A Pilot Study: Celecoxib Inhibition of Aromatase Expression and Inflammation in Adipose Tissue of Obese Postmenopausal Women

***Please enter the study short title:**

The Celecoxib study

Is this Study using Subject Management?

(•) Yes ( ) No

2.0 Add Lab/Dept(s)

2.1 List departments associated with this study:

Primary Dept?	Department Name
(•)	**RUH** - Laboratory of Biochemical Genetics and Metabolism (Breslow)
( )	**RUH** - Rockefeller University Hospital

3.0 Assign key study personnel(KSP) access to the study

3.1 *Please add a Principal Investigator for the study:

Holt, Peter R, MD

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Aleman, Jose O, MD, PhD
Clinical- Co-Investigator
Walker, Jeanne Marie, MSN/NP-C
Clinical- Co-Investigator

B) Research Support Staff

Brassil, Donna, MA, RN, CCRC
Study Coordinator
Dowd, Kathleen, BSN, RN, CCRC
Study Coordinator

Hutt, Richard, RN, BA, CCRC
Study Coordinator

3.3 *Please add a Study Contact:

Brassil, Donna, MA, RN, CCRC
Holt, Peter R, MD
Hutt, Richard, RN, BA, CCRC
Walker, Jeanne Marie, MSN/NP-C

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

4.0 Rockefeller University Conflict of Interest

4.1 Investigator Financial Conflict of Interest All KSP (unless they have done so in the past 12 months) must complete and update promptly a Rockefeller University Significant Financial Interest Disclosure at http://mycoi.rockefeller.edu/. Prompt disclosure means within 30 days of discovering or acquiring a Significant Financial Interest, and as early as possible in the development of this protocol. If a KSP discloses a significant financial interest that may constitute a conflict of interest with respect to the proposed study, he or she must E-mail a copy of the Lay Summary of the study to Teresa Solomon (solomot@rockefeller.edu). Doing so will allow the process of addressing the potential COI to proceed in step with the development of the study protocol. Tardiness or non-compliance with this requirement will very likely cause delay in submission of the study for IRB review. Institutional Conflict of Interest As early as possible the PI or designee preparing this application must log in to https://icoi. rockefel ler.edu/account/login.php, which lists entities in which The Rockefeller University has a direct financial interest. If the proposed study involves any entity on that list the PI or designee must E-mail the entity involved and a copy of the Lay Summary to Ms. Teresa Solomon so that the process of addressing the potential Institutional COI can proceed in step with the development of the study protocol.

5.0 External Personnel

5.1 List external personnel who will be working on the study:

Name	Institution	Telephone	E-mail	Role
No External Personnel has been added to this Study				

6.0 Delegation of Authority

6.1 Enter authorized activities for all Rockefeller University personnel named on the study.

Activity Codes:

1. Informed consent	12. Perform assays	23. Diet design and preparation
2. Inclusion / exclusion criteria	13. Specimen / sample analysis	24. Nutritional assessment and counseling
3. Medical / medication history	14. Lumbar puncture	25. Addition of PABA to food
4. Perform physical exam	15. Femoral line placement	26. Data analysis
5. Skin assessments and photos	16. Central line placement	27. Data review
	17. Insulin clamp	

6. Study drug dispensing	**procedure**	**28. Data management**
7. Study drug administration	**18. Leukapheresis**	**29. Maintain regulatory documents / files**
8. Study drug reconciliation	**19. Sigmoidoscopy**	**30. Complete CRF's**
9. Study drug compliance	**20. Fat biopsy**	
10. Administer study questionnaire(s)	**21. Skin biopsy**	
11. Subject recruitment	**22. Conduct sleep study**	

Add up to three additional authorized activities specific to this study:

31:	
32:	
33:	

Activity Codes Continued:

34. Behavioral Testing
35. Bod Pod
36. Bone Marrow Aspiration
37. Neuropsychological Testing
38. Conduct Focus Group
39. Conduct Smell Study
40. Genetic Counseling
41. Apply EEG Electrodes
42. Olfactometer Test
43. Study Participant Teaching
44. Resting Energy Expenditure
45. Source Document Review & Correction
46. Medical Photography
47. Write/Sign LIP orders

Enter delegation of authority for Rockefeller University Key Study Personnel:

Name	Title	Authorized Activities	Start Date	End Date
Holt, Peter R, MD	PI	1, 2, 3, 4, 26, 27, 28	03/26/2013	12/08/2017
Aleman, Jose O, MD, PhD	co-I	1, 2, 3, 4, 26, 27, 28	03/26/2013	12/08/2017
Walker, Jeanne Marie, DNP, ANP-BC	co-I	1, 2, 3, 4, 20, 26, 27, 28	03/26/2013	12/08/2017
Brassil, Donna, MA, RN, CCRC	coordinator	1, 2, 8, 28, 29	03/26/2013	12/08/2017
Stanwix, Jenny E., BS,CCRC	coordinator	1, 2, 8, 28, 29	03/26/2013	05/27/2015
Dowd, Kathleen, BSN, RN, CCRC	coordinator	1, 2, 8, 28, 29	03/26/2013	12/08/2017
Bowles, Nicole,				

PhD	co-I	26, 27	09/04/2014	02/03/2017
Hutt, Richard, RN, BA, CCRC	Coordinator	29	01/22/2016	12/08/2017

Enter delegation of authority for additional Rockefeller University Key Study Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No records have been added				

Enter the authorized activities for External Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No records have been added				

7.0 Study Description

7.1 * Lay Summary

Please provide a summary of your study in lay language. The summary should be no more than a half page (500 words or less) and should contain a clear statement of the rationale for the study.

Inflammation of fat stores is emerging as an important factor in the complications of obesity including type 2 diabetes and in the development and outcome of breast and colon cancers. This inflammation increases the amount of a substance, prostaglandin, which then can stimulate other factors that lead to obesity complications. Prostaglandin (PGE-2) is converted into another prostaglandin (PGE-M) which is excreted in the urine in amounts that reflect the amount of prostaglandins in the body. Inflammation in fat stores also increases the amount and activity of aromatase, an enzyme whose action results in increased estrogen and its metabolites in fat tissues, the blood, and the urine. Increased estrogen is important in postmenopausal obese women in whom the incidence and the spread of breast cancer is increased by estrogen. In addition, inflammation in fat tissues of obese women results in the formation of a characteristic histologic structure called the "crown-like structure" which reflects the death of adipose tissue cells surrounded by accumulated pro-inflammatory cells called macrophages.

Prostaglandins in the body are inhibited by a class of medicines called non-steroidal anti-inflammatory drugs which include aspirin and Advil (with potential bleeding side effects) but also by Celebrex which increases bleeding very little. This medicine is being used by patients with arthritis conditions. We plan to provide Celebrex before and after collecting blood, urine, and abdominal fat tissue (by biopsy) to examine how effective the medicine may be in reducing inflammation, crown-like structures in fat tissue, the enzyme aromatase, PGE-M in the urine and estrogen in blood and urine. Volunteer subjects will be expected to stay in the hospital for about 3 weeks taking Celebrex for approximately 10 days while eating a diet similar to what they consumed before coming into the hospital for the study. The study plans to find out whether Celebrex may be potentially useful to decrease inflammation in fat tissues and thereby lower the production of substances such as estrogens that may increase the risk of developing breast cancer and lead to a poor outcome of the disease.

7.2

*** Public Health Impact Statement**

Provide a brief plain language statement (100 words or less) of the value of the research proposed and its potential impact on population health. Additional instructions located in Help.

Post-menopausal breast cancer is a common disease in the Western world. Celecoxib as an NSAID would be expected to reduce inflammation in adipose tissue including in the breast. Reduction of such inflammation should lower the risk of breast cancer. No directed study of NSAID effect on inflamed adipose tissue has been performed in humans previously for breast cancer therapy. This study has the potential to further future breast cancer treatment.

7.3

*** Submission Request Category**

Please indicate:

Expedited Review

8.0

Screening for Expedited Review

8.1

Studies that may be reviewed by expedited review fall into 7 categories described in detail in 46CFR 8392. These include drawing of blood within prescribed limits, collection of samples such as saliva, mucosal and skin cells by scraping, and excreta or sweat. Data may be collected by physical sensors such as weighing, EKG, EEG, MRI, moderate exercise and strength testing, and body composition assessment. Collection of data from voice, video or image recordings obtained in research. Research on perception, cognition, social behavior employing surveys, interviews, focus groups and oral history.

Research may be conducted on data, documents, records or specimens that have or will be collected solely for non-research purposes in the course of medical treatment or diagnosis.

Note: Protocols that studies that involve a drug that requires an IND, or that involve greater than minimal risk to subjects or that involve the use of X-rays or microwaves are not eligible for an expedited review.

* Based on the above information, does your research study qualify for an "expedited" review?

- (●) Yes
- ( ) No
- ( ) Not Sure

9.0

Clinical Trial Registration

9.1

Clinical Trial Registration

The types of studies listed below must be registered at **www.ClinicalTrials.gov**

- ○ Study involves testing of FDA regulated drugs or biologics (See HELP)
- ○ Study is funded by the NIH, and meets the definition of a "clinical trial" (see HELP)
- ○ Study meets the ICMJE definition of a "clinical trial" (See HELP)
- ◉ None of the above

If you selected 1, 2, or 3, you must register your trial with ClinicalTrials.gov through the Rockefeller University institutional account. Please contact the Clinical Research Support Office x7408 for assistance.

10.0

Study Overview/Summary

10.1 * Who initiated this study?

Please specify one:

- ◉ Principal Investigator Initiated
- ○ Industry Initiated
- ○ Other

If other, please specify:

10.2 * This study in collaboration with:

- ○ Weill Cornell Medical College
- ○ Memorial Sloan-Kettering Cancer Center
- ◉ Both Weill Cornell Medical College and Memorial Sloan-Kettering Cancer Center
- ○ Neither Weill Cornell Medical College nor Memorial Sloan-Kettering Cancer Center

Please note: If any of the first three options is checked, you will be prompted to attach the **Tri-Institutional Study Specific Financial Disclosure** and the **IRB of Record** forms later on in the submission. Links to these forms can be found in the Help link to the right.

10.3 * Are other institutions involved in the study?

- ○ 1. No
- ○ 2. Yes, and a federal, industry or private organization is administratively coordinating the study.
- ◉ 3. Yes, however, a federal, industry or private organization is not administratively coordinating the study.

If #3 was selected above, please provide the following for each involved institution:

Name of Other Institution	Date of Approval by Other Institution	Date of Pending Approval by Other Institution	Date of Expiration at Other Institution
WCMC	03/10/2014		03/05/2015
MSKCC	04/23/2013		

10.4 * Is this a multi-center trial?

○ Yes ◉ No

10.5 * Who (What) is to be studied?

☑ Human Subjects - including coded samples and/or data with links to Identifiers
☐ Deidentified Samples - unable to be linked to identifiers by receiver
☐ Data Only - unable to be linked to identifiers

10.6 *Study Type:

◉ Interventional
○ Observational

10.7 The initial date of IRB approval was:

04/04/2013

10.8 * What is the expected duration of the study?

3 years

10.9 * Are any of the following agents to be used in the study?

Check all that apply:

☐ Drug FDA Approved
☑ Approved Drug for Off-Label Purpose
☐ Investigational New Drug
☐ Biologic Agents
☐ Nutritional Supplements
☐ Placebo
☐ Vaccines
☐ No Agents

10.10 * Are investigational devices to be used in the study?

○ Yes ◉ No

If Yes, please specify:

○ A Significant Risk Device
○ A Non-significant Risk Device

10.11 Special Research Procedures

Does the study propose to directly involve participants in the following special research procedures?

- ☐ Recombinant DNA
- ☐ Gene Therapy

If either item is checked, please see Help for details.

10.12 * Radioactive Isotopes Involved

Will subjects be exposed to any radiation other than routine x-rays solely for clinical care purposes?

- ○ Yes
- ◉ No

11.0 Interventional

11.1 *Interventional, please specify:

- ◉ Open Label
- ○ Single Blind
- ○ Double Blind
- ○ Other

If Other, specify:

12.0 Objectives and Rationale

12.1 * Overview

Briefly state the ***purpose of this study***. Give enough background and rationale to provide both scientists and lay members of the IRB and ACCTS with the basis for exposing human subjects to the risks involved.

Obesity increases the risk for the development of and the progression to metastasis of numerous malignancies including hormone receptor-positive breast cancer in postmenopausal women (1). Medications that suppress the biosynthesis of estrogen or block its actions decrease the risk of hormone receptor-positive breast cancer (2). In obese women, inflammation manifested as crown-like structures (CLS), is associated with NF-κB-dependent induction of proinflammatory mediators including TNF-α, IL-1β, IL-6 and COX-2-derived PGE_2 in breast white adipose tissue (3). Moreover, increased levels of aromatase, the rate-limiting enzyme for estrogen synthesis, are found in association with elevated levels of proinflammatory mediators in breast white adipose tissue (4). This finding is consistent with extensive evidence that proinflammatory mediators, including PGE_2, induce aromatase expression (5-6). Importantly, we have evidence that it is common for inflammation to occur in both breast and abdominal subcutaneous white adipose tissue, in parallel, in obese women making abdominal subcutaneous white adipose tissue a useful surrogate tissue to study.

If reductions in subcutaneous adipose tissues of the inflammatory markers to be studied and aromatase levels directly correlate with reduced urinary excretion of PGE-M, an index of prostaglandin activity in the body, then this will support direct effects of Celecoxib upon adipose tissue inflammation as a mechanism and also will underlie the use of urinary PGE-M determinations as a biomarker reflecting changes in adipose tissue inflammation.

The potential use of celecoxib in modulating aromatase activity is supported by epidemiologic evidence that chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs), prototypic inhibitors of PGE_2 synthesis, decrease levels of circulating estrogens and reduce the risk of breast cancer (7). In addition, increasing numbers of studies have suggested that other complications of obesity including cardiovascular disease and type 2 diabetes mellitus are related to inflammatory activity in adipose tissue.

We plan to study circulating levels of estradiol and estrogen metabolites and the urinary excretion of estrogen metabolites to establish whether this dose of celecoxib, by reducing aromatase, actually alters estrogen metabolism as hypothesized if adipose tissue inflammation is reduced. Direct demonstration of such a change in estradiol and estrogen metabolism should point to the importance of reducing adipose tissue inflammation in obese post-menopausal women in order to reduce the risk and the spread of estrogen receptor positive breast cancer in such patients.
Obesity is associated with elevated levels of urinary PGE-M, a biomarker that reflects increased systemic levels of PGE_2. We hypothesize that treatment with celecoxib, a selective COX-2 inhibitor, will reduce levels of PGE_2 and aromatase in inflamed abdominal subcutaneous white adipose tissue of obese postmenopausal women. This concept is supported by preclinical evidence that celecoxib suppressed PGE_2 levels and aromatase activity in the mammary glands of obese mice (Fig. 1). Celecoxib also suppressed the elevated levels of urinary PGE-M found in obese mice (Fig. 2). Based on this constellation of findings, we speculate that celecoxib-mediated decreases in levels of urinary PGE-M will correlate with reduced levels of PGE_2 and aromatase expression in abdominal subcutaneous white adipose tissue of obese postmenopausal women. Celecoxib is the preferred agent for these studies because it does not have the anti-platelet activity that traditional NSAIDs possess. Hence, biopsies of abdominal subcutaneous white adipose tissue can be done without a medication-related increased risk of bleeding.
The results of this study could be important for highlighting the potential benefit of NSAIDs for reducing the risk of hormone receptor-positive breast cancer in obese postmenopausal women, a growing segment of the population.

Significance
The use of NSAIDs has been associated with a reduced risk and spread of colorectal cancer. Most epidemiological studies suggest that use of NSAIDs also is associated with a reduced risk and spread of breast cancer although the protective effects are more modest. We speculate that this class of medication like others will be effective in some but not all individuals to reduce breast cancer risk. In particular, we hypothesize that these agents will be of benefit if used chronically in the up to 75% of obese postmenopausal women who demonstrate white adipose tissue inflammation and CLS. If Celecoxib suppresses levels of inflammation and aromatase in abdominal white adipose tissue which is likely to mirror what occurs in breast white adipose tissue, this would suggest that chronic use of NSAIDs is likely to reduce the risk and spread of hormone receptor-positive breast cancer in this growing segment of the population. Importantly, if reduction in urinary PGE-M reflects reduction in adipose tissue inflammation this would be a useful non-invasive marker for this property in future studies.

We additonally plan to study the fecal microbiota of 5 of the 10 participants being studied.

Studies on metabolic diseases such as obesity during the past few years have included important consideration of the impact of changes in the colonic microbiome. Indeed, several of our recent studies at The Rockefeller University Hospital have included a collection and storage of fecal specimens for later analysis. We, in collaboration with Dr. Dannenberg at Cornell have established a relationship with Dr. Eric Pamer at MSKCC who is willing to perform analysis on specimens that were collected immediately before and after 10% weight loss in obese volunteers (PHO 785).

Our metabolic studies usually have been performed in small groups of subjects who are studied while consuming a preselected diet before and after an intervention.

As we plan similar studies, it has become evident that we do not know how soon after admission to RU and initiating a Bionutrition Department provided diet should fecal specimen collection be initiated as a stable baseline before starting the intervention. Previously, we only have used 3 days before the intervention based on scant data in the literature. We now believe that it is very important to determine how long it takes under the condition of our studies at RUH to establish reasonable fecal microbiota stability.

Available information suggests that there are 3 predominant microbe enterotypes described initially in 2011 (20). Studies in 5 subjects consuming either a high fat/low fiber or a low fat/high fiber diet in a single study suggested that the distinct differences between individual subjects generally were maintained over 10 days after an abrupt change in the 1^{st} 24 hours. No switching in the primary 3 enterotypes was detected within 1 week of the diets (21).

In a study of Malawi twins, discordant for kwashiorkor, administration of a therapeutic food supplement resulted in modest but non significant changes in the fecal microbiota in 2 weeks (22).

A much quoted study by Faith et al evaluated the stability of the fecal microbiome up to 5 years showing that up to 60% of the individual species remained stable (23). However, weight loss impaired microbiota stability in studies performed before and after 8 weeks of a low calorie diet.

In our present studies, we had taken fecal samples 2-3 days after the RUH admission and the start of a diet designed by our Bionutrition Department that mimicked each subject's pre-study diet and then initiated the intervention. However, on the basis of the available information, we do not know how long to administer such a diet before taking the initial fecal sample prior to the medical intervention such as Celecoxib. The present proposed study will determine whether the fecal microbiota is stable after 3 or 7 days or needs 14 or more days. This information will guide our procedures in future similar studies.

12.2 * Engaging Stakeholders: Describe any plans to engage other stakeholders (Scientists, practitioners, patients, advocacy groups, etc.) for hypothesis generation, or feasibility purposes.

Dr. Andrew Dannenberg who will perform several analyses of adipose tissue pertaining to effects of Celecoxib on the aromatase enzyme. Dr. Bokulich and Dr. Blaser who will perform microbiome studies that aim to determine whether Celecoxib alters fecal microbiota composition and whether a self-selected diet mimicking a subject's pre-study long-term diet will keep fecal microbiota composition constant.

12.3 * Hypothesis

Describe the ***research hypothesis*** in a single sentence.

Celecoxib, an inhibitor of cyclooxygenase-2 (COX-2) will reduce urinary excretion of PGE-M, and suppress levels of prostaglandin E_2 (PGE_2) and aromatase in inflamed abdominal subcutaneous adipose tissue in grade 2-3 obese postmenopausal women.

12.4 * Aim(s)

Indicate how you will ***address the hypothesis*** (e.g., to compare groups, to estimate a parameter, to ascertain feasibility). Since the sample size determination is usually based on the primary aim only, the primary aim should be sufficient to justify the study.

To determine whether oral administration of celecoxib 200 mg BID to grade 2-3 obese postmenopausal women will significantly reduce the excretion of PGE-M in the urine.

12.5 * Primary Outcome(s)

Indicate which ***variable(s)*** will be assessed to judge the primary specific aim. Give measurement units, if applicable.

PGE-M in urine will be significantly reduced

12.6 * Secondary Outcome(s)

Indicate which ***additional variable(s)*** will be assessed to judge the secondary outcome(s). Give measurement units, if applicable.

Crown-like structures in subcutaneous adipose tissue

PGE_2 in subcutaneous adipose tissue

aromatase in subcutaneous adipose tissue biopsies and crown-like structures in subcutaneous adipose tissue

Circulating levels of TNF-α, IL-6, IL-8, and MCP-1.

Levels of circulating serum estradiol and selected estrogen metabolites in serum and urine

Determination of the length of time to achieve stability of fecal microbiota

Serum endocannabinoid concentration at baseline (Days 3 and 14) , Day 13 & 24, and Outpatient End of study visit

12.7 * Methods and Procedures

Please provide a description of the laboratory and clinical analyses and procedures that will be performed. Include the role of external collaborators and consultants when appropriate.

This is a pilot study of 10 grade 2-3 (BMI between 35-50) obese postmenopausal women to determine if treatment with Celecoxib 200 mg bid for 10+/-1 days leads to reduced levels of abdominal subcutaneous white adipose tissue PGE_2, and aromatase activity in association with decreased levels of urinary PGE-M. Previous studies (17) have shown that this interval is sufficient to achieve steady state circulating levels of the drug and to significantly suppress urinary PGE-M levels.
Two screening visits will take place in the OPRC and the remainder of the study will be an in-patient study in which the participants may leave RUH for periods of time during the day, unless it is a "testing" day. Patients will be given a 3-day rotating diet based on their regular diet as reported and reviewed with the bionutrition department.
5 out of the 10 participants recruited will be asked to be admitted to the Rockefeller University Hospital IPU 11 days earlier (2 weeks prior to Celecoxib administration) for a total of 24 inpatient days in order to determine stabilization time for fecal microbiota. 4 additional stool samples will be collected at Days 0,3, 7, and11, +/- 1 day.

Screening Visit #1
Informed consent
Medical History and Physical exam
EKG
Waist measurement
Distribution of 3-day food diary
HIV POCT
Subjects will be instructed to fast 10 hours prior to their next visit for fasting labs.
Subjects will be instructed to discontinue taking over the counter medications (OTCs). Those subjects which require medication for relief of pain will be advised to use only Tylenol and given a week's supply.

Screening visit #2
Return of 3 day food diary
Fasting labs to include- CBC/DIff, ESR, Comprehensive Metabolic Panel, Thyroid Stimulating Hormone, lipid profile, hsCRP, PT/PTT/INR, serum estradiol
Bionutrition consult to review the 3 day food diary and determine subject's "usual diet"
A clinic meal will be provided after labs are drawn.
Dispense Tylenol 325 mg #30, 2 tablets by mouth as needed for pain.
Eligibility will be determined following lab results. Subjects will be scheduled for admission within 1-4 weeks of their screening. If greater than 1 month has passed from screening, safety labs (CBC/DIFF, CMP, PT/PTT/INR) will be re-drawn prior to admission.

Inpatient Admission
Day 0
Admit to RUH at approximately 11 AM
Study diet lunch and dinner
Day 1
Usual diet
Day 2
Spot urine for PGE-M
24 hour urine for testing of the following: PGE-M, estrogen metabolites, creatinine, volume
stool sample +/- 1 day
NPO after 9 pm except water
Day 3
Fasting research labs- TNF-α, IL6, IL8, MCP-1, insulin, serum estradiol and estrogen metabolites, serum endocannabinoids
MSKCC labs: CBC, ESR, CMP, hsCRP, PT/PTT/INR, lipid panel, estradiol
Spot urine for PGE-M after completion of 24-hr urine collection
Fat biopsy
Start Celecoxib 200 mg PO BID
NPO after 9 pm except water
Day 4
Bod Pod

Continue Celecoxib 200 mg PO BID
Day 5
Usual diet
Continue Celecoxib 200 mg PO BID
Day 6
Usual diet
Continue Celecoxib 200 mg PO BID
Day 7
Usual diet
Continue Celecoxib 200 mg PO BID
Day 8
Usual diet
Continue Celecoxib 200 mg PO BID
Day 9
Usual diet
Continue Celecoxib 200 mg PO BID
Day 10
Usual diet
Continue Celecoxib 200mgPO BID
Day 11
Usual diet
Continue Celecoxib 200mg PO BID
Day 12
Spot urine for PGE-M
24 hour urine for testing of the following: PGE-M, estrogen metabolites, creatinine, volume
stool specimen +/- 1 day
Continue Celecoxib 200 mg PO BID
NPO after 9 pm except water

Day 13
Celecoxib 200 mg PO in AM
Fasting research lab: TNF-α, IL6, IL8, MCP-1, insulin, serum estradiol and estrogen metabolites, celecoxib level, serum endocannabinoids
MSKCC labs: CBC, ESR, CMP, PT/PTT/INR, hsCRP, lipid panel, estradiol
Spot urine for PGE-M after completion of 24 hour urine collection
Fat biopsy
Usual diet
Discharge from RUH
Dispense Tylenol 325mg #30 tablets.
Upon discharge, tylenol will be provided 325 mg PO #30 (to be taken PRN)
Subjects will be instructed not to take any NSAIDs until their next visit. Tylenol will be provided to reinforce the need to avoid the use of NSAIDs for intercurrent mild discomfort such as intercurrent headaches or influenza-like symptoms and to substitute tylenol. This precaution is taken to prevent distortion of urine PGE-M to be collected 10 days after cessation of Celecoxib administration.
Out-Patient Visit:
End of study visit (7-11 days after discharge)
Spot urine collection for PGE-M
Research labs: serum estradiol and estrogen metabolites, serum endocannabinoids
MSKCC labs: hsCRP, estradiol
Stool collection- Patients will be given a room in the inpatient unit in order to provide a stool specimen at this visit.
Clinic breakfast
For the 5 participants being admitted 2 weeks prior to Celecoxib administration, the inpatient schedule is as follows:
Day 0
Usual diet
Stool sample +/- 1 day
Day 1
Usual diet
Day 2
Usual diet
Day 3
Stool sample +/- 1 day
Usual diet
Day 4
Usual diet
Day 5
Usual diet
Day 6

Usual diet
Day 7
Stool sample +/- 1 day
Usual diet
Day 8
Usual diet
Day 9
Usual diet
Day 10
Usual diet
Day 11
Usual diet
Stool sample (+/- 1 day)
Day 12
Usual diet
Day 13
Spot urine for PGE-M
24 hour urine for testing of the following: PGE-M, estrogen metabolites, creatinine, volume
NPO after 9 pm except water
Usual diet
Day 14
Usual diet
Fasting research labs- TNF-α, IL6, IL8, MCP-1, insulin, serum estradiol and estrogen metabolites, serum endocannabinoids
MSKCC labs: CBC, ESR, CMP, hsCRP, PT/PTT/INR, lipid panel, estradiol
Spot urine for PGE-M after completion of 24-hr urine collection
stool sample +/- 1 day
Fat biopsy
Start Celecoxib 200 mg PO BID
NPO after 9 pm except water
Day 15
Bod Pod
Usual diet
Continue Celecoxib 200 mg PO BID
Day 16
Usual diet
Continue Celecoxib 200 mg PO BID
Day 17
Usual diet
Continue Celecoxib 200 mg PO BID
Day 18
Usual diet
Continue Celecoxib 200 mg PO BID
Day 19
Usual diet
Continue Celecoxib 200 mg PO BID
Day 20
Usual diet
Continue Celecoxib 200 mg PO BID
Day 21
Usual diet
Continue Celecoxib 200 mg PO BID
Day 22
Usual diet
Continue Celecoxib 200 mg PO BID
Day 23
Spot urine for PGE-M
24 hour urine for testing of the following: PGE-M, estrogen metabolites, creatinine, volume
stool specimen +/- 1 day
Continue Celecoxib 200 mg PO BID
NPO after 9 pm except water
Day 24
Celecoxib 200 mg PO in AM
Fasting research lab: TNF-α, IL6, IL8, MCP-1, insulin, serum estradiol and estrogen metabolites, celecoxib level, serum endocannabinoids
MSKCC labs: CBC, ESR, CMP, PT/PTT/INR, hsCRP, lipid panel, estradiol
Spot urine for PGE-M after completion of 24 hour urine collection
Fat biopsy
Usual diet
Discharge from RUH

Dispense Tylenol 325mg #30 tablets.
Out-Patient Visit:
End of study visit (7-11 days after discharge)
Spot urine collection for PGE-M
Research labs: serum estradiol and estrogen metabolites, serum endocannabinoids
MSKCC labs: hsCRP, estradiol
Stool collection- Patients will be given a room in the inpatient unit in order to provide a stool specimen at this visit.
Clinic breakfast
Methodology for Microbiota Analysis of Stool specimens
Approximately 5 grams of feces will be collected immediately after a bowel movement and rapidly frozen at -80° C.
For each fecal specimen, DNA will be extracted using a phenol-chloroform extraction technique with bead beating for mechanical disruption. The isolated DNA will be purified and then PCR amplified using modified universal primers for the V4-V5 portion of the 16s ribosomal RNA gene. The purified PCR products will be pooled and then barcoded following the Illumina TruSeq Sample Preparation protocol. The library will then be sequenced using the Illumina MiSeq sequencing platform.
The sequence data will be screened and filtered using Mothur before each sequence is classified using a modified inhouse database containing sequences from GreenGenes 99 and retrieved 16S sequences from Genbank. The relative abundance of the microbiota will be represented by the percentages of the classified taxa sequences out of the total sequences present in the sample. In addition to the classification of the raw sequences, sequences that fall into an operation taxonomic unit (OTU) with 97% similarity will also be classified.
Additionally, the biodiversity of the microbiota of a sample will be surveyed using the Shannon Diversity Index. The comparison of the biodiversity between samples will be measured by unweighted UNIFRAC distances and visually represented by the Principal Components Analysis. A LDA Effect Size (LEfSe) analysis can be completed to look for specific bacteria that may contribute to any differences seen between groups of samples.

12.8 * Data Analysis

Describe method(s) of data analysis. Include the role of external collaborators as appropriate.

With 10 subjects, we will be able to detect effect sizes larger than 1 with 80% power at 0.05 significance level on a 2-tail test

12.9 * Explain the rationale for the choice of statistical measures and the number of subjects proposed for the study, including the power calculations when applicable.

In a study including women across the BMI spectrum, the effect size for the pre vs post differences in PGE-M excretion was found to be 0.64 for current smokers, 1.06 for former smokers and 0.68 for non-smokers (17).

Mice data shows that baseline levels of PGE-M are twice as high in obese than lean mice and the reduction on PGE-M is 70% higher in obese mice. Based on this, we will power our study to detect and effect size of 1 in the decrease of PGE-M levels with treatment. Studies in obese mice have shown an almost 3-fold increase in excretion of PGE-M compared to lean mice (AJ Dannenberg unpublished observations).

To test if the measurement of PGE-M in the urine will decrease after administration of Celecoxib 200 mg BID a paired t-test will be used.

A similar approach will be used to test the secondary outcomes including PGE-2 in adipose tissue, cytokine levels (log-transformed), and estrogen metabolites. Decrease in outcomes will be correlated to identify which variable correlates with the primary outcome.

12.10 * Will samples be coded?

(•) Yes ( ) No

If Yes, Please describe coding scheme consistent with GCP. If samples will not be coded, please provide justification for this proposed departure from GCP practice.

Samples will be coded without subject identifiers with a random number.

13.0 Subjects of Study

13.1 Specify age range of subjects:

* Minimum Age:

40

Maximum Age:

70

Please note: If age of subjects indicated is less than 18 years old, you will be prompted to attach a Pediatric Assent form later on in the submission process. A link to the Pediatric Assent form can be found in the Help link to the right, or this form can be downloaded later on in the submission process.

13.2 * Indicate the gender(s) of the subjects:

- [x] Female
- [ ] Male

13.3 * Indicate projected enrollment by race and ethnicity. See Help for disease/volunteer population demographics.

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	5	0	0	5
Not Hispanic or Latino	5	0	0	5
Unknown (individuals not reporting ethnicity)	0	0	0	0
Ethnic Category: Total of All Subjects*	10	0	0	10
Racial Categories				
American Indian/Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	5	0	0	5
White	5	0	0	5
More Than One Race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of All Subjects*	10	0	0	10

13.4 * Will subjects of a specific racial/ethnic group be excluded from participation?

○ Yes ◉ No

If Yes, please specify:

☐ Caucasian
☐ African-American
☐ Hispanic
☐ Asian
☐ Other

Reason for the exclusion:

○ The condition being studied does not occur in the selected group(s)
○ Other

If Other, please specify:

13.5 Gender/Minority Exclusion Justification

All research involving human subjects should be designed and conducted to include members of both genders and members of minority groups, unless a rationale and justification is provided. Please provide such justification below:

This study is looking at post-menopausal women, therefore men will not qualify.

13.6 Vulnerable Populations

Indicate whether any of the following populations will be included in the study:

☐ Children
☐ Pregnant Women
☐ Cognitively Impaired Persons
☑ RU Employees
☐ RU Students
☐ Fetal Tissue or Embryonic Stem Cells
☐ Induced Pluripotent Stem Cells
☐ Other:

If you checked any of the above, give a brief explanation of the need to use these particular individuals:

If the subject is a Rockefeller University employee, does she/he work within the Laboratory of the Principal Investigator or Co-Investigator(s)?

○ Yes
◉ No
○ N/A

If the subject is a Rockefeller University student, does she/he work within the Laboratory of the Principal Investigator or Co-Investigator(s)?

○ Yes
◉ No
○ N/A

13.7 *What is the total number of evaluable participants you plan to enroll at Rockefeller University

Hospital over the course of the entire study?

10

13.8 * What is the total number of participants who will need to sign consent *at Rockefeller University Hospital over the course of the entire study* to result in the desired number of evaluable subjects?

15

13.9 * What is the total number of participants you plan to sign consent *at Rockefeller University Hospital in the next year?*

0

13.10 * What will be the total number of evaluable participants *at all sites over the course of the entire study?*

15

13.11 Inclusion Criteria

Please list subject inclusion criteria:

Order Number	Criteria
1	Postmenopausal woman defined as: 24 consecutive months without a menstrual period and currently not taking any medication known to induce amenorrhea.
3	Body Mass Index of 35-50
4	Stable weight defined as (+/- 5 %) of body weight for at least three months
5	40-70 years of age
6	Fluent in English

13.12 Exclusion Criteria

Please list subject exclusion criteria:

Order Number	Criteria
1	Known hypersensitivity to celecoxib, sulfonamides, aspirin, or NSAIDs
1	Known peptic ulcer disease
2	Hypertension BP > 150/90 (on 2 occasions after resting)
2	Fasting blood glucose > 165 mg/dL
3	HIV positive
3	Screening creatinine > 2X upper limit of normal
	Screening LFT results > 2x upper limit of normal

4	
5	Smokers (or stopped < 3 months ago)
11	Framingham risk score > 15
12	Evidence of active coronary disease by history and/or EKG
13	Subjects who consume 25 grams of soy protein/day or more than 45 mg of isoflavones /day, for subjects who consume this amount of soy, they may stop for 14 days prior to admission
14	Currently taking NSAIDS, aspirin, (if > once a week, stopped <30 days ago).
14	Consuming > 3 servings of fish or seafood/week
15	Currently taking fish oil, omega-3 supplements or other herbal supplements that exceed GRAS (Generally Recognized as Safe) levels, (if currently taking fish oil/omega-3 supplements, there must be a 30 day washout period)
15	current use of anti-coagulants
17	Currently taking any weight control medication
18	Currently taking thioridazine
18	Currently taking lithium
19	Currently taking any estrogen/progesterone hormones including vaginal cream, e-string, or vaginal tablets
20	Currently taking any medication that can alter fat stores as determined by the principal investigator
21	History of Inflammatory Bowel Disease or other chronic inflammatory disorders
21	History of any malignancy other than non-melanoma skin cancer in the past 5 years
22	History of any bleeding disorder
23	History of cardiovascular disease
25	Diagnosis of asthma
26	Any medical, psychological or social condition that, in the opinion of the Investigator, would jeopardize the health or well-being of the participant during any study procedures or the integrity of the data.

14.0 Study Plan

14.1 * Describe the study plan:

*** What is the total number of outpatient visits for all subjects projected for the next year?**

0

*** What is the average length of each outpatient visit (in hours)?**

0

*** What is the total number of Day Patients visits for all subjects projected for the next year?**

0

*** What is the average length of each Day Patient visit (in hours)?**

0

*** What is the total number of inpatient days for all subjects projected for the next year?**

0

14.2 *Number of Patients per arm

Study Arm	Number of Patients
No records have been added	

15.0 Study Drugs

15.1 * List all the medications, study drugs, biological agents, solutions and supplements needed to conduct the study:

See Help for link to Rockefeller University Research Pharmacy web page for additional information.

View Details	Drug Name		FDA Approved	IND Number
⊟	**Trade Drug Name:**	Celebrex		
	Generic Drug Name:	Celecoxib	Yes	
	Investigational Drug Name:			

Trade Drug Name:	Celebrex
Generic Drug Name:	Celecoxib
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	
Is the Drug FDA Approved:	Yes
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose(s):	
Dosing Frequency:	

15.2 * Will the study involve the use of a placebo?

○ Yes ◉ No

If yes, complete A and B.

A. Is there a proven effective therapy for the condition under study?

○ Yes ○ No

If Yes, please specify:

B. Please give a justification for the use of the placebo.

16.0 Consent Procedure

16.1 * This study will use the following types of informed consent:

- ☑ Informed Consent Form Standard - a standard consent form with instructions for adapting it to your study
- ☐ Consent Form Genetic- a consent form designed for a study where genetic testing (as defined by NYS law) is to be done in the CURRENT study
- ☐ Consent for studies including genome wide sequencing
- ☐ Pediatric Assent Form (To be used in addition to Consent) for Pediatric patients
- ☐ Other (e.g., waivers)

Links to the **Standard Consent, Genetic Testing Consent** and the **Pediatric Assent** forms can be found in the Help link to the right, or these forms can be downloaded later on in the submission process.

16.2 * Indicate the consent process to be used.
(See Help for CCTS SOP)

Describe how the required information is being presented to subjects (consent form, orally, information sheet, etc.). Attach a copy of what is being presented to subjects (usually the ICF and Assent forms).

Prior to the initiation of any study related procedures, the potential subjects will be given a copy of the most recent IRB stamped and approved informed consent to read. Additionally, the PI or study staff member who has been designated to consent will discuss the specifics of the study including but not limited to the purpose of the research, procedures, time commitment, required tasks, test article or device, alternative treatments, benefits, risks, confidentiality etc. in a comprehensible (non-scientific) manner, using language readily understandable by the subject. Subjects will be told that participation is voluntary and that, if they do not consent, they will not be penalized. The person consenting will assure the voluntariness of the subject.

Describe the circumstances under which consent will be obtained, where the process will take place and any waiting period between informing the prospective participant and obtaining consent.

A private, confidential setting will be provided for the potential subject to read and discuss the informed consent free from coercion, undue influence or constraints of time. All subjects will be given a chance to ask questions and express concerns. They will be given the option to take the consent home and discuss it with family, friends, and /or health care providers. After a subject and the person conducting the consenting signs and dates the consent, the subject will be given a copy of the signed informed consent form.
An enrollment note will be written in the source document as to who obtained consent, how, when, were questions asked and answered, and that a copy of the informed consent was given to the subject.

Describe the experience of the investigators designated for this task in the DOA in obtaining consent from subjects.

The following staff, P. Holt, J. Walker, J. Stanwix, K. Dowd, D. Brassil, have extensive experience consenting human subjects for participation in research studies.

J. Aleman has demonstrated competency in consenting subjects for participation in research studies. This competency is based on attending a consenting class which includes regulations, the do's and don'ts and didactic role playing. It also includes observing the consenting process as performed by an experienced consenter and then consenting a subject to participate in a research study while being observed by the experienced consenter.

How will it be determined that the subjects or the subjects' authorized representatives understand the information presented?

The "Teach Back" method will be used in the clinical research setting to ask research participants to repeat or "teach back" the information, concepts and directions that the staff member has attempted to convey to the subject. This method is used to assess comprehension and retention of protocol requirements, adverse event information, risks and benefits, and the subject's rights described in the Informed Consent process.

If English is not the subjects' native language, how will written and/or verbal translation be provided?

For unexpected or isolated subjects who are candidates for this study, but for whom English is not a primary language, a translator provided through Pacific Interpreters will be used to facilitate the explanation of the study.

Will any subjects be cognitively impaired so that they may not have the capacity to give consent?

○ Yes ◉ No

If yes, Describe the procedures to be used to determine the individual subject's capacity to provide consent.

For subjects where it has been determined that they lack the capacity to give consent, describe the provisions for obtaining consent from the subjects' legally authorized representative.

16.3 * Based on the demographics, will this study's subject population require foreign language consent form?

○ Yes ◉ No

If Yes, please list the language(s):

16.4 * This study's consent procedure will require the following waivers: (See Help for additional information.)

○ Waiver of one or more elements of informed consent, 45CFR46.116(d)
○ Waiver of documentation of informed consent, 45CFR46.117(c)
◉ No waiver is requested

If a waiver is requested, please explain:

16.5 * Does this study include videotaping, photography or other electronic recording of human subjects?

○ Yes ◉ No

If Yes, please specify:

17.0 Recruitment and Advertising

For assistance consult CRSO to create a robust Recruitment Plan see Help.

17.1 * What is the plan for recruitment?

The CRSO proposes the following recruitment strategy and services:

Advertisements – The CRSO will place advertisements online (Craigslist.org, Centerwatch.com, etc.) as well as in print (Metro, Daily News, Manhattan Media, etc.). The Volunteer Repository will also be utilized. Centralized Call Management – The CRSO will conduct telephone screenings of selected Volunteer Repository members, and of volunteers who call 1800RUCARES, to facilitate screening efficiently. Based on IRB approved eligibility criteria, potentially eligible candidates pre-screened by CRSO staff will be referred to the study coordinator/investigator for further evaluation. Depending on the demands and appeal of a given study, centralized call management can reduce the burdens on the research team 5-10 fold in terms of the number of volunteers they ultimately interact with. The research team and CRSO will work together on a protocol-specific pre-screening script to optimize the process.

Research Volunteer Repository Database – The investigator has agreed to associate protocol PHO-0807 with RKO-0648, the Research Volunteer Repository Protocol, enabling the CRSO to query the existing volunteer database to identify a list of potential volunteers who have agreed to be contacted for future studies and who meet basic eligibility criteria. The CRSO will contact potential volunteer as allowed to determine interest and will refer eligible and interested volunteers to the study coordinator/investigator. In parallel, the research team will seek and document the granting or denial of permission to contact volunteers about future studies.

17.2 *From the date of final IRB approval, how long will it take to complete enrollment of the study?

- ○ 6 Months
- ◉ 12 Months
- ○ 18 Months
- ○ 24 Months
- ○ More than 2 years (specify in years)

17.3 This Study

- ◉ Involves an intervention or comparison and a defined enrollment target
- ○ Is a natural history study with expected annual enrollment over many years
- ○ Is an exploratory mechanistic study
- ○ Other

17.4 This Study will enroll:

- ◉ Healthy volunteers
- ○ Individuals affected with a specific disease/disorder
- ○ Both

17.5 * Do you plan on using the Research Participant Repository (RKO-0648) ?

◉ Yes ○ No

17.6 * Are you screening or recruiting from or through a record review of an existing patient database of a healthcare provider?

○ Yes ◉ No

17.7 * Please describe how the Recruitment Plan addresses recruitment of the volunteers consistent with the demographics of the condition under study:

In consultations with the CRSO, we plan to recruit subjects using the exisiting volunteer repository as well as print advertisements.

17.8 * **Do you plan to advertise directly to potential volunteers? (As opposed to relying on practitioner referrals or flyers to practitioners)**

(•) Yes ( ) No

17.9 * **Do you plan to use the free, web-based volunteer registry, ResearchMatch.org, as a recruitment tool?**

(•) Yes ( ) No

18.0 Research Participant Repository (RKO-0648)

18.1 This protocol, will be linked with the Research Volunteer Screening/Recruitment Data Repository run by the Recruitment staff and the Clinical Research Support Office (protocol RKO-0648-1008). In order to participate in the generation of the Repository the PI will enter into a Collector/Collaborator agreement regarding the Repository. The role of Collector/Collaborator is to contribute to the Repository the name, contact and demographic information, recruitment referral information, and screening outcome information, as well as appropriate protocol specific screening information, of volunteers who are screened by telephone or in person for entry into the protocol regardless of the screening outcome. In addition to screening volunteers for the PI's current study, verbal consent will be obtained from the volunteers regarding their willingness to be contacted in the future about possible additional research studies. This permission may be obtained by the Recruitment office staff through the central Call Center. If the PI receives calls directly from participants for initial prescreening, then the PI is responsible for collecting the required information and conveying it to the Recruitment staff for data entry. The consent or withholding of permission will be recorded in the Repository as will the name of the person who obtained the permission. A volunteer's permission or declination will not affect their eligibility for my current protocol, or future protocols. The Recruitment staff of the Clinical Research Support Office may gather the Repository information and request the verbal consent of the volunteer for re-contacting on my behalf as part of our recruitment plan. In order to benefit from the Repository, the PI will enter into a Recipient/Collaborator agreement with the Repository. The Recipient/Collaborator may receive from the Repository pre-screened lists of potentially eligible subjects for his/her study as a means to facilitate recruitment. The Recruitment staff will prepare the Repository queries according to the protocol eligibility requirements and available Repository information, and may re-affirm permission to re-contact volunteers as necessary. The PI may use the information and names in the list from the Repository only for the current study and may not save the list to use for a future study of his/her own, nor may he/she share the list with colleagues for other studies."

19.0 Utilization of ResearchMatch.org

19.1 Utilization of ResearchMatch.org for Recruitment

Basic information regarding this tool:

- **ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University. There is no cost for researchers at participating institutions in the ResearchMatch.org Network to use ResearchMatch.org. The Vanderbilt IRB provides oversight for ResearchMatch.org as a recruitment tool and this has been documented within the ResearchMatch.org IRB Letter of Understanding which was executed by Dr. Gotschlich in October, 2009. However, individual requests to use ResearchMatch.org as a recruitment tool must be submitted to this institutions' IRB.**

Registration:

- **This recruitment tool may be utilized once the PI or research staff registers for recruitment access through ResearchMatch.org and the Institutional Liaison provides approval.**
- **The ResearchMatch.org Institutional Liaison will review the study information and evidence of IRB approval. He/she will set the researcher's expiration date to mirror that of the study's IRB approval.**

Search Capability:

- **After being granted recruitment access, the researcher can search for appropriate matches amongst the non-identifiable ResearchMatch.org Volunteer profiles in the system. He/she can enter study inclusion/exclusion criteria in the ResearchMatch.org Search Builder which will yield a list of potential matches to the study's criteria.**

Contacting ResearchMatch.org Volunteers:

- **Once yielding a list of potential matches (ResearchMatch.org Volunteers), the researcher will send out IRB-approved content that will be the initial recruitment message that these volunteers receive about the study through ResearchMatch.org. The study's recruitment message will be inserted into the standard ResearchMatch.org electronic notification that informs possible matched Volunteers that he/she has been identified as a potential match for the study. The secure ResearchMatch.org clearinghouse will route this standard ResearchMatch.org email notification. These potential matching volunteers will have the option of replying yes, no, or not respond through a set of quick links available in this notification to the study announcement. THE CONTACT MESSAGE WILL NOT INCLUDE THE STUDY'S DIRECT CONTACT INFORMATION (e.g. EMAIL, PHONE). By responding yes, the Volunteer has authorized ResearchMatch.org to release his/her contact information to the researcher. The researcher will be responsible for managing this contact information as called for by this IRB-approved study protocol.**

Study Management in ResearchMatch.org:

- **Researchers (and the Liaison) can view information regarding his/her study's status in ResearchMatch.org (e.g. number of volunteers contacted for the study via ResearchMatch.org to date, response rate of volunteers, etc.). ResearchMatch.org will also be collecting aggregate data regarding the status of ResearchMatch.org volunteers within the study. Volunteers consent to this within the ResearchMatch.org Volunteer Agreement. This information will allow the researcher to indicate where the Volunteer currently stands within the recruitment process and thus will help the researcher monitor the utility and effectiveness of using this resource (e.g. Did not contact, Not eligible, Enrolled, Completed, etc.).**

20.0 Potential Benefits to Subjects

20.1 * Will participation in this study provide direct benefits to the subject?

○ Yes ◉ No

20.2 If Yes, describe the potential direct benefits:

There will not be any direct benefit to participants.

21.0 Potential Risks to Subjects

21.1 * Describe any potential risks: physical, psychological, social, legal or other and assess their likelihood and seriousness. Indicate risks both to the subjects and to the embryo or fetus if the subject is or may become pregnant. Please provide the potential risks below:

Potential Risks associated with ingestion of Celecoxib are MI, CVA, hypertension, heart failure, renal failure, GI bleeding, ulcers, anemia, life-threatening skin reactions, life-threatening allergic reactions, liver disease including liver failure, and asthma attacks in people who have asthma.
Other side effects include abdominal pain, constipation, diarrhea, flatus, heartburn, nausea, vomitting, and dizziness.
A metaanalysis of 9 studies that compared Celecoxib with other (over the counter) NSAID showed that serious upper gastrointestinal events occurred at a rate 45% less (18).
A nationwide review of cardiovascular risks for Cox-2 inhibitors revealed no significant risk of myocardial infarction,ischemic stroke or atrial fibrillation for Celecoxib (19)
Potential risks associated with venipuncture include discomfort or pain, ecchymosis, bleeding, phlebitis and infection at the needle insertion site. Additional risks include lightheadedness and a vasovagal response.
Potential risks associated with a fat biopsy include a vaso-vagal response and inflammation, discomfort, pain, bleeding, and a superficial infection at the site. A permanent scar with possible depression will develop at the biopsy site.

22.0 Procedures to Minimize Risks

22.1 * Describe the procedures for protecting against or minimizing any potential risks, and include an assessment of their likely effectiveness. Include a discussion of confidentiality safeguards, where relevant, and arrangements for providing medical treatment, if needed.

Fat Biopsy:
Risks of the fat biopsy will be avoided by having only trained and qualified staff performing the procedure. Subjects will be instructed about signs and symptoms of infection, be given written instructions of wound care and removal of the butterfly dressing, and be provided with the investigator's contact information to call if necessary. A study team member will telephone each subject after discharge to monitor for complications.
Venipuncture:
To protect subjects from risks associated with venipuncture, only trained, skilled staff will perform this procedure.
Celecoxib:
All subjects will be carefully screened according to inclusion/exclusion criteria and judgment of the PI and nurse practitioner. Subjects will be carefully monitored, especially for cardiovascular and GI adverse events throughout the duration of their inpatient stay and will not be receiving Celecoxib after discharge.

23.0 Alternative Methods or Treatments

23.1 * Describe alternative methods or treatments for the disease(s) under study, if any, that were considered and why they will not be used:

There is always the option not to participate in this study.

24.0 Data and Safety Monitoring

This section describes the Data and Safety Monitoring Plan (DSMP) required of each protocol undertaken at the CCTS according to HRPP and NIH policies Notice 98 -084 and Notice 00-038, as cited in Help Sections below. Depending on the level or risk and trial phase, some protocols will need Data and Safety Monitoring Boards.

24.1 * Overall Risk Classification

An estimate of risk is necessary to evaluate the adequacy of the planned monitoring. The HELP section provides guidance in making the risk assessment.

Read the risk definitions and examples of risk in the HELP section and select the risk category that best describes the current study.

If your assessment differs from the definitions the HELP section, describe any factors that modify your judgment of the overall risk in the text box after the risk designation.

- ○ MINIMAL RISK
- ○ LOW RISK
- ◉ MODERATE RISK
- ○ SIGNIFICANT RISK

Please provide any optional description(s):

24.2 Protocols Involving Minors

The chance of direct benefit to the child, or to understanding a disorder not otherwise understood, may be major factors in justifying more than minimal risk in research involving children.

Based on the above definitions, please specify your study's risk classification below:

- ○ NOT GREATER THAN MINIMAL RISK (the risk of daily life to a healthy child living in a safe environment) 45 CFR 46.404
- ○ GREATER THAN MINIMAL RISK WITH DIRECT BENEFIT TO SUBJECT; 45 CFR 46.405
- ○ GREATER THAN MINIMAL RISK, NO DIRECT BENEFIT, BUT BENEFIT TO UNDERSTANDING OF SUBJECT'S DISORDER; 45 CFR 46.406
- ○ RESEARCH NOT OTHERWISE APPROVED PRESENTING OPPORTUNITY TO UNDERSTAND, PREVENT OR ALLEVIATE SERIOUS PROBLEM AFFECTING CHILDREN 45 CFR 46.407 (cannot be approved by IRB; requires public comment)

24.3 DSMB

1. The NIH requires that all SIGNIFICANT RISK protocols have a **Data and Safety Monitoring Board** and provide information about the expertise and independence of that Board
2. Phase III trials require a Data and Safety Monitoring Board,
3. A DSMB may be appropriate for some Phase I and II protocols. (See Help for examples.)
4. It is the investigator's responsibility to report to the IRB, the findings and recommendations of the DSMB as they become available.

Please specify:

- ○ A DSMB is required for this study
- ◉ A DSMB is not required for this study
- ○ Unsure

If a DSMB is required, please indicate why:

- ☐ Significant Risk
- ☐ Study Design - Phase III
- ☐ Study Design - Placebo Controlled
- ☐ Study Design - Multicenter Trial
- ☐ Study Design - Other Factor

If other factor, please specify:

If a DSMB is required, select one:

- ○ An independent DSMB has been constituted; the members, mission charter, schedule for meetings, and a listing of the data to be reviewed by the DSMB will be attached.
- ○ A DSMB has not yet been constituted; the PI will consult the IRB and/or CRSO for assistance in assembling a DSMB.

If a DSMB is not required, but is being constituted for other reasons, please explain:

24.4 * Safety Review

Select one:

- ◉ Safety Review is conducted as follows: Laboratory results for research volunteers will be reviewed in a timely manner, usually within 24 hours of receipt by a licensed practitioner. The potential clinical significance of any abnormal finding will be documented in the medical and research record(s), and an appropriate plan or referral developed. The PI's review of safety issues at research team rounds will be documented in the meeting minutes.
- ○ Protocol Specific

If Protocol Specific, please describe safety review for protocol tests and procedures that require other than routine review. For example, an EKG taken to detect emerging conduction problems might require immediate safety review.

24.5 Monitoring

Monitoring Personnel: See Help Bubble to the right.

Internal Monitoring

The PI or his/her designee shall conduct internal monitoring to assure the safe and proper conduct of the protocol and all the elements list above in monitoring, following the general principles of quality management. The intensity and frequency of internal monitoring will depend on the protocol risk to subjects, the experience of the PI and research team, rate of enrollment, and specific details of the protocol.

Internal monitoring of informed consent and eligibility documentation will be conducted by the research team shortly after enrollment begins. Internal monitoring activities will be documented by logs, meeting minutes or other systematic means.

Specify the research team members who will conduct the internal monitoring of the study (see Help for who may monitor):

For new investigators: Internal monitoring should be conducted at least monthly by new investigators until there are essentially no findings to correct at each review.

External Monitoring

* Is external monitoring planned for this protocol?

- ○ Yes
- ◉ No
- ○ Unsure

If external monitoring is planned, please specify (see Help for who may monitor):

- ○ (Significant Risk) External monitoring will occur at least every six weeks unless there is no enrollment
- ○ (Moderate Risk) External monitoring will occur at least quarterly
- ○ (Low or Minimal Risk) External monitoring will occur at least annually

If external monitoring is planned, please specify the name of the monitor:

☑ Note that copies of external monitoring reports must be supplied to the IRB and the CRSO as soon as they are made available

Additionally, audits of the research records of minimal, moderate or significant-risk protocols may be performed by the CRSO staff on a random basis or as part of a prospectively identified auditing plan.

24.6 Adverse Event Classification

Adverse events are classified by definition, severity, and association with the investigational trial.

Definition of an Adverse Event
Any unfavorable or unintended sign (including abnormal lab findings), symptom or disease temporally associated with the use of a medical treatment or procedure, or protocol, regardless of whether it is considered related to the medical treatment or procedure or protocol.

Definition of a Serious Adverse Event
Any unanticipated event that involves the following:
- o results in death
- o is life-threatening
- o requires hospitalization or prolongs existing hospitalization
- o results in persistent or significant disability/incapacity
- o is any medical event which requires treatment to prevent one of the outcomes listed above

Other events can be classified as "serious adverse events" at the discretion of the PI.

Definition of Anticipated/Expected Adverse Event

Any adverse event, which has been reported in the Investigator's Brochure, package insert, safety reports, clinical protocol, consent form or listed in the NCI agent-specific Expected Adverse Event List[3], is classified as an expected adverse event. The investigator must provide the available data of known adverse events and toxicities that have been associated with the study drug, device, intervention, or procedures. This information helps to define the level of risk of the trial and enables safety monitoring. A minimal risk trial may not have any defined risks and a statement to that effect is sufficient to meet the DSMP requirements.

Definition of an Unanticipated/Unexpected Adverse Event
Any adverse event that is not consistent with the known, predicted possible effects of the research protocol. An unexpected adverse event varies in nature, intensity or frequency from information on the investigational product provided in the Investigator's Brochure, package insert, safety reports, clinical protocol, or listed in the consent form.

Definition of an Unanticipated Problem (UaP)
A UaP is an event or circumstance that meets all the following three criteria: [1] the nature, severity, frequency of the event(s) or information was not expected in the descriptions in the study documents or the characteristics of the subject population being studied; [2] there is a reasonable possibility that the procedures involved in the research caused or are linked in a significant way to the problem; [3]the event or information suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized (including physical, psychological, economic, or social harm.

Grade and Relatedness of Adverse Events:

Adverse Events are graded for severity and scored for relatedness to the protocol, according to a published scale. Several standardized AE Reporting scales are available. (See Help for links to these scales.)

* Please indicate the scale you intend to use:

- ○ CTC v2.0 (http://ctep.info.nih.gov/reporting/ctc.html)
- ○ CTCAE v3.0 (http://ctep.info.nih.gov/protocolDevelopment/electronic_applications/docs/ctcaev3.pdf)
- ◉ CTCAE v4.0 (http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf)

○ AIDS Clinical Trials Group (http://aactg.s-3.com/)
○ Other

If Other, please specify:

24.7 Reporting Adverse Events

All AEs will be reported to the IRB at least annually.

Reporting Serious AEs

☑ Serious Adverse Events, (SAEs) will be reported to the IRB according to policy, within two working days of identification of the SAE.

Select all that apply:

☐ SAEs will be reported to the Sponsor and or ESCROW

SAEs will be reported to the sponsor within how many days of the event?

☐ SAEs will be reported directly to the FDA, per 21 CFR 312

SAEs must be reported directly to the FDA within 7 days of the event by the investigator/sponsor.

☐ SAEs will be reported to another entity

Describe:

Reporting Unanticipated AEs:

Select all that apply:

☑ UAEs will be reported to the IRB

UAEs that are related and greater than moderate severity must be reported to the IRB according to policy, within two working days of identification of the UAE.

☐ UAEs will be reported to the Sponsor

UAE will be reported to the sponsor within how many days of the event?

☐ UAEs will be reported to the FDA, per 21 CRF 312

UAEs will be reported to the FDA, per 21 CRF 312, within 15 days.

☐ UAEs will be reported to another entity

Describe:

24.8 Reporting Unanticipated Problems

☑ Unanticipated problems involving risks to subjects or others severe will be reported to the IRB and the CRSO within five working days.

24.9 CLIA/CLEP

Only laboratory and research tests that are CLIA/CLEP certified or waived may be used to determine eligibility, shared with research volunteers, and used in clinical decision making.

Select if applicable:

☑ This study includes tests that are not CLIA/CLEP certified; the results of such tests will not be used in clinical decision making, or to determine eligibility, or shared with subjects or their health care providers.

24.10 Tissue Repository

Human Tissue and Data Repositories collect, store, and distribute human tissue materials and or data for research purposes. Repository activities involve three components: (i) the collectors of tissue samples\data; (ii) the repository storage and data management center; and (iii) the recipient investigators.

* Select one:

◉ I DO NOT intend to collect, store, and distribute human tissue materials for research purposes

○ I DO intend to collect, store, and distribute human tissue materials for research purposes, therefore this protocol entails the Operation of a Tissue Repository. The IRB requires that the protocol specify the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

If you do intend to collect, store, and distribute human tissue materials, you will be asked to upload the following documents later on in the submission:

- A Sample collection protocol (for tissue collector collaborators to follow) and informed consent document for distribution to tissue collectors and their local IRBs.
- A Certificate of Confidentiality (to protect confidentiality of repository specimens and data).
- A Recipients Agreement describing the commitment of the recipient to preserve the anonymity of the samples shared.

25.0 Toxicity Management and Stopping Rules

25.1 * Describe any drug toxicity or other conditions under which the participation of a subject or the conduct of the study would be stopped in order to maximize safety (e.g., toxicity management and stopping rules):

Subjects may be withdrawn from the study if they meet the following criteria:
any evidence of a cardiac event
LFT 2X ULN
bilirubin 1.5-3.0 X ULN
creatinine 2 X ULN
PT/PTT > ULN
any evidence of bleeding

*** Indicate withdrawal criteria and procedures below:**

A subject will be withdrawn from the study if:
1) she is unable to tolerate the study drug

2) she develops a clinically significant adverse event that is ongoing and which necessitates medication or medical treatment which might affect study results
3) she fails to undergo the scheduled testing within the specified period of time
4) she has persistent non-compliance with the protocol
5) she does not adhere to hospital regulations

26.0 Compensation/Costs

26.1 *Will any compensation be offered to participants in return for their participation, e.g., direct payment, medical care, tests, etc.?

- ○ No
- ◉ Yes (Please describe)

$200 for each fat biopsy
$25 for each in-patient day
$50 for each research blood donation
$50 for each urine collection
$50 for urine sample and return to clinic
$50 for stool sample collected at the final visit

26.2 * Will there be any costs to participants associated with their participation in research?

- ○ Yes
- ◉ No

If so, please explain:

27.0 Bibliography

27.1 * Enter your bibliography below:

1. Cleary MP, Grossmann ME: Minireview: Obesity and breast cancer: the estrogen connection. Endocrinology 150:2537-42, 2009
2. Cuzick J, Forbes JF, Sestak I, et al: Long-term results of tamoxifen prophylaxis for breast cancer--96-month follow-up of the randomized IBIS-I trial. J Natl Cancer Inst 99:272-82, 2007
3. Vogel VG, Costantino JP, Wickerham DL, et al: Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. Cancer Prev Res (Phila) 3:696-706, 2010
4. Goss PE, Ingle JN, Ales-Martinez JE, et al: Exemestane for breast-cancer prevention in postmenopausal women. N Engl J Med 364:2381-91, 2011
5. Morris PG, Hudis CA, Giri D, et al: Inflammation and increased aromatase expression occur in the breast tissue of obese women with breast cancer. Cancer Prev Res (Phila) 4:1021-9, 2011
6. Subbaramaiah K, Morris PG, Zhou XK, et al: Increased levels of COX-2 and prostaglandin E2 contribute to elevated aromatase expression in inflamed breast tissue of obese women. Cancer Discov 2:356-65, 2012
7. Zhao Y, Agarwal VR, Mendelson CR, et al: Estrogen biosynthesis proximal to a breast tumor is stimulated by PGE2 via cyclic AMP, leading to activation of promoter II of the CYP19 (aromatase) gene. Endocrinology 137:5739-42, 1996
8. Subbaramaiah K, Hudis C, Chang SH, et al: EP2 and EP4 receptors regulate aromatase expression in human adipocytes and breast cancer cells. Evidence of a BRCA1 and p300 exchange. J Biol Chem 283: 3433-44, 2008
9. Prosperi JR, Robertson FM: Cyclooxygenase-2 directly regulates gene expression of P450 Cyp19 aromatase promoter regions pII, pI.3 and pI.7 and estradiol production in human breast tumor cells. Prostaglandins Other Lipid Mediat 81:55-70, 2006
10. Subbaramaiah K, Howe LR, Port ER, et al: HER-2/neu status is a determinant of mammary aromatase activity in vivo: evidence for a cyclooxygenase-2-dependent mechanism. Cancer Res 66:5504-11, 2006
11. Brodie AM, Lu Q, Long BJ, et al: Aromatase and COX-2 expression in human breast cancers. J Steroid Biochem Mol Biol 79:41-7, 2001

12. Brueggemeier RW, Quinn AL, Parrett ML, et al: Correlation of aromatase and cyclooxygenase gene expression in human breast cancer specimens. Cancer Lett 140:27-35, 1999
13. Hudson AG, Gierach GL, Modugno F, et al: Nonsteroidal anti-inflammatory drug use and serum total estradiol in postmenopausal women. Cancer Epidemiol Biomarkers Prev 17:680-7, 2008
14. Zhao YS, Zhu S, Li XW, et al: Association between NSAIDs use and breast cancer risk: a systematic review and meta-analysis. Breast Cancer Res Treat 117:141-50, 2009
15. Terry MB, Gammon MD, Zhang FF, et al: Association of frequency and duration of aspirin use and hormone receptor status with breast cancer risk. JAMA 291:2433-40, 2004
16. Gierach GL, Lacey JV, Jr., Schatzkin A, et al: Nonsteroidal anti-inflammatory drugs and breast cancer risk in the National Institutes of Health-AARP Diet and Health Study. Breast Cancer Res 10:R38, 2008
17. Duffield-Lillico AJ, Boyle JO, Zhou XK, et al: Levels of prostaglandin E metabolite and leukotriene E(4) are increased in the urine of smokers: evidence that celecoxib shunts arachidonic acid into the 5-lipoxygenase pathway. Cancer Prev Res (Phila) 2:322-9, 2009
18. Deeks, JJ, Smith LA, Bradley MD: Efficacy, tolerability, and upper gastrointestinal safety of celecoxib for treatment of oestoarthritis and rheumatoid arthritis: systematic review of randomised controlled trials. British Medical Journal 325, 1-8, 2002
19. Bäcl M., Yin L., Ingelsson E.: Cyclooxygenase-2 inhibitors and cardiovascular risk in a nation-wide cohort study after the withdrawal of rofecoxib. European Heart Journal 33, 1928-1933, 2012
20. Arumugam M., et. al.: Enterotypes of the human gut microbiota. Nature 2011 May 12;473(7346):174-80.
21. Wu, G.D. et. al.: Linking Long-Term Dietary Patterns with Gut Microbial Enterotypes. Science 2011, 334, 105.
22. Smith M. et al.: Microbiomes of Malawian Twin Pairs Discordant for Kwashiorkor. Science 2013, 339, 548.
23. Fatih J. J. et. al. The Long-Term Stability of the Human Gut Microbiota. Science 2013, 341.

28.0 Appendices

28.1 Enter your appendices below:

29.0 Funding

29.1 * Do you have sufficient financial resources to support your study?

(•) Yes ( ) No

If No, explain:

Funding is provided by a Sackler grant

29.2 If this study is/was a CTSA-funded pilot, please specify dates of funding:

From date:

To date:

29.3 Specify funding by Rockefeller University, industry sponsor and/or grant:

	Sponsor	Funding
Rockefeller University		
Industry		

Grant		
Pilot Award		

29.4 List grants in which this study is named:

PHS or Non-PHS	Program	Grant Number	Grant Name	From Date	To Date
No records have been added					

30.0 Clinical Services

30.1

- [x] Well/Minimally Ill
- [ ] Moderately Ill
- [ ] Severely Ill
- [ ] Other
- [ ] Not Applicable

If other than Well/Minimally Ill, please describe:

30.2 * Does your study group have special care needs?

○ Yes ◉ No

If Yes, specify:

- [ ] Assistance with ambulation
- [ ] Wound care
- [ ] Assistance with ADL
- [ ] Other

If Other, please describe:

30.3 * Does your study have special equipment needs?

○ Yes ◉ No

If Yes, please describe:

30.4 * Will you require storage space on the clinical units for supplies to conduct this study?

○ Yes ◉ No

If Yes, please describe:

30.5 * Is special training of hospital staff required?

○ Yes ◉ No

If Yes, please describe:

31.0 Pharmacy Services

31.1 * Does the study require Pharmacy Services?

◉ Yes ○ No

If No, please proceed to next section.

31.2 Types of pharmacy services required:

- ☑ Dispensing
- ☐ Randomization
- ☐ Aseptic technique training
- ☐ Other

If Other, please specify:

31.3 Dispensing:

- ☐ Sponsor supplied drugs
- ☐ Investigator supplied drugs
- ☑ Pharmacy supplied drugs
- ☐ Other

If Other, please describe:

31.4 Type of medication(s):

- ☑ Oral
- ☐ Anergy panel
- ☐ Injectable
- ☐ Other

If Other, please specify:

If Injectable, please specify:

- ☐ Monday-Friday 8:30AM-5PM
- ☐ Off-hours [all other days/times]

31.5 Compounding: (including mixing medications)

- ☑ None
- ☐ Capsule
- ☐ Placebo
- ☐ Liquid oral formulation
- ☐ Development of new dosage forms
- ☐ Injectable

☐ Ointment, gel, cream or other external product(s)
☐ Other

If Other, please specify:

32.0 Bionutrition

32.1 * Will study require patient meals?

◉ Yes ○ No

If Yes, please specify:

Standard	☑ Inpatient ☐ Outpatient	
Therapeutic	☐ Inpatient ☐ Outpatient	
Research Diet	☐ Inpatient ☐ Outpatient	
Formula Diet	☐ Inpatient ☐ Outpatient	

Nutrient(s) to be controlled (specify):

32.2 Will meal times be altered?

○ Yes ◉ No

If Yes, please explain:

32.3 Will food be provided to caregiver, parent or significant other?

○ Yes ◉ No

32.4 For metabolic diets, is diet homogenization required for nutrient analysis by independent lab?

○ Yes
○ No
◉ N/A

33.0 Clinical and Translational Research Facilitation Office

33.1 Indicate Clinical and Translational Research Facilitation Office assistance requested and/or received in the development of this study:

Protocol Navigation	☑ Requested ☑ Received
Development of consent(s) with research coordinator	☑ Requested ☑ Received
Creation of source documents	☑ Requested ☐ Received
IRB/ACCTS submission	☑ Requested ☑ Received
Initiation Meeting	☑ Requested ☐ Received
Create and maintain regulatory binder	☑ Requested ☐ Received
Internal monitoring	☑ Requested ☐ Received

	Requested	Received
Provision of research coordinator from the Facilitation Office.	☑	☐
Data entry services	☐	☐
Creation of CRF's	☐	☐
Other	☐	☐

If Other, please explain:

34.0 Clinical Research Support Office Resources (CRSO)

34.1 Indicate CRSO assistance requested and/or received in the development of the study:

	Requested	Received
Data and Safety Monitoring Plan	☐	☐
Informed Consent	☐	☐
Recruitment and Advertising	☑	☑
IND Application	☐	☐
Study Monitoring	☐	☐

If Other, please indicate:

35.0 Research Design and Biostatistics Resources

35.1 Indicate Biostatistics assistance requested and/or received in the development of this study:

	Requested	Received
Development of experimental design	☑	☐
Sample size determination (# of subjects)	☑	☐
Randomization schedule	☐	☐
Data analysis	☐	☐
Development of new statistical techniques for data analysis	☐	☐
Other	☐	☐

35.2 Please select the Biostatistician on this Protocol:

- ○ Joel Correa da Rosa, PhD
- ○ Sandra Garcet, PhD
- ◉ Mayte Suarez-Farinas, PhD
- ○ Knut M Wittkowski, PhD, ScD
- ○ Other

If other please specify:

36.0 Biomedical Informatics Resources

36.1 Indicate BioInformatics assistance requested and/or received in the development of this study:

	Requested	Received
Data storage outside of iRIS	☐	☐
Database other than iRIS /Oracle	☐	☐
Database design	☐	☐
Application design	☐	☐
Software other than iRIS	☐	☐

Special computer hardware	☐	☐
Microarray analysis software	☐	☐
Microarray analysis software training	☐	☐
Pathways analysis software	☐	☐
Other	☐	☐

If Other, explain:

36.2 If you are/will be using microarray analysis software, specify:

- ☐ Genespring
- ☐ Other

If Other, specify:

36.3 If you are/will be using pathway analysis software, specify:

- ☐ Ingenuity
- ☐ Pathways Studio
- ☐ Other

If Other, specify:

37.0 Translational Immunomonitoring Resource Center

37.1 Indicate if you plan or did use the following TTCL resources:

	Plan To Use	Used
Sample handling and preparation for immunological studies	☐	☐
Feasibility determination of markers for immunophenotyping of surface and cytoplasm antigens, functional studies and DNA analysis by flow cytometry	☐	☐
Protocols for flow cytometry and Luminex assays	☐	☐
Training for BD LSR II (flowcytometer) and Luminex instruments	☐	☐
Multiparametric analysis of flow cytometry and Luminex	☐	☐

data		
Other	☐	☐

If Other, explain:

38.0 HIPAA Form

38.1 A study's specific HIPAA form signed by the volunteer is required for institutions that are HIPAA covered entities so that they may communicate Private Health Information (PHI) to the Investigator.

Below, Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University are listed so that that they may report laboratory results and X-ray readings respectively. If you foresee that any other entity may need to provide PHI then add them to the field highlighted in green.

38.2 Name of Study:

A Pilot Study: Celecoxib Inhibition of Aromatase Expression and Inflammation in Adipose Tissue of Obese Postmenopausal Women

38.3 Principal Investigator:

Peter R Holt, MD

38.4 Funding Source[1]:

[1] The funding source does not appear on the final HIPAA form unless the source is an industry sponsor.

Who may obtain, use, and/or disclose your health information?

The following persons and organizations may obtain, use, or disclose health information about you.

- The Principal Investigator(s) listed at the top of this form, and persons who assist the Investigator (s) in carrying out the research
- Each research site for this study, including The Rockefeller University, and the research management and support staff and the medical staff at each site
- Health care providers who have provided in the past, or currently provide, health care services to you
- Laboratories and other persons and organizations that will analyze your health information and/or biological samples as part of this study, including Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University

Other entities that may need to provide PHI:

- Members and staff of the Institutional Review Board and other boards and committees that watch over research at The Rockefeller University
- Members and staff of The Rockefeller University's Office of Sponsored Research
- The sponsor(s) of the research, named above, and persons who watch over the research for the sponsor(s)
- The United States Food and Drug Administration, other government agencies, regulatory entities and Rockefeller University consultants that watch over the safety, effectiveness, and quality of research and/or fund The Rockefeller University Hospital

- Others (as described here):

What information will be obtained, used, or disclosed?

The persons and organizations listed above may obtain, use, and disclose:

- Information about you that is created or collected during the research study (but not including any HIV-related information)
- Health information in your medical records that is relevant to the research study (but not including any HIV-related information)
- **And**, if checked below:

___ HIV-related information (this includes any information indicating that you have had an HIV-related test or have HIV infection, HIV-related illness, or AIDS, as well as information that could indicate you may have been exposed to HIV)
___ Other information (as described here)
_____
_____
_____
_____

- Other information (as described here):

By signing this form, you give permission to the persons and organizations listed above to obtain, use and disclose your health information noted above.

How will your health information be used?

The health information noted above, as well as information shown by the boxes checked above (if any), may be obtained, used, and disclosed to:

In addition, the above named investigators, The Rockefeller University, and the above named sponsors may obtain, use, and disclose your information as needed for your treatment or as permitted by the informed consent form for the research study.

- conduct the research study explained to you during the informed consent process; and
- assure the quality, safety, and effectiveness of the research study

Please note that the persons and organizations listed above may re-use or further disclose your information if they are permitted by law to do so.

What are your rights?

It is your right to refuse to sign this authorization form. If you do not sign this form, you will not be able to participate in the research study. Your health care outside the study will not be affected. The payment for your health care and your health care benefits will not be affected.
If you sign this authorization form, you will have the right to withdraw it at any time except to the extent that the persons and organizations listed above:

- have already taken action based upon your authorization;
- need the previously collected information to complete analysis and reports of data for this research; or
- will continue to use and disclose previously collected information as permitted by the informed consent form signed by you (except as to HIV-related information, for which disclosure to new persons or organizations will not occur unless permitted by federal or state law).

If you withdraw the authorization, you will not be permitted to continue taking part in the research study. This authorization form will not expire unless you withdraw it. If you want to withdraw this authorization, please write to the above named investigators.

You have a right to see and copy your health information described in this authorization form in accordance with The Rockefeller University's policies; in certain circumstances where the integrity of the study will be affected, you will not be able to obtain your health records in this study until the study has been completed.
You will receive a copy of this form after you have signed it.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that such information may not be shared without your approval unless permitted by federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (212) 480-2493 or the New York City Commission of Human Rights at (212) 306-7450. These agencies are responsible for protecting your rights.

Your signature

I have read this form, and all of my questions have been answered. By signing below, I acknowledge that I have read and accept all of the information above.

_____
Signature of participant or participant's legal representative

_____
Date

_____
Printed name of participant

_____
Printed name of legal representative (if applicable)

_____
Representative's relationship to participant

THE STUDY PARTICIPANT OR HIS OR HER PERSONAL REPRESENTATIVE MUST BE PROVIDED WITH A COPY OF THIS FORM AFTER IT HAS BEEN SIGNED.

39.0 End of Application Form

39.1 The study application form is complete. The next step in the submission process is to gather attachments before proceeding to the submission form.

The following submission reports are generated in the Lab/Dept Reports menu, Submission Reports section:

- **Delegation of Authority** (if applicable, and if not previously generated)
- **HIPAA form** (if applicable)
- **CCTS Utilization Report** (required for all submissions)
- **Study Progress Report** (if the study has been managed in iRIS for a minimum of one year, generate the Progress Report from the report menu in iRIS. if the study has not been managed in iRIS for one year, complete the Progress Report located on the IRB website.)

All other required forms can be downloaded from the corresponding sections' help links above or from the IRB website.