

Protocol Cover Page:

(Periop Flare) Perioperative Flare in Rheumatoid Arthritis:
Characterization of Clinical and Biological Features (Old IRB#13146)

NCT Number: N/A

Document date: March 9th 2017



electronic Clinical Application Portal (eCAP)

Date: Thursday, March 9, 2017 12:14:02 PM

ID: 2014-233

View: 1 - Study Identification Information

[Print](#) [Close](#)
[Help](#)

VIEW000072

Study Identification Information

This is the first step in your Human Research Application. You will automatically be guided to the appropriate forms needed to complete your submission.

1.0 Title:

(Periop Flare) Perioperative Flare in Rheumatoid Arthritis: Characterization of Clinical and Biological Features (Old IRB #13146)

* Short Title for EPIC:

Periop Flare (If Not Applicable, please enter N/A)

2.0 Description:

hip/knee/shoulder/elbow

3.0 * Principal Investigator:

Susan Goodman, MD

4.0 Study Contact:

Serene Mirza

5.0

Co-Investigators:

First Name	Last Name	Organization
Phaedra	Agius	New York Genome Center
Dalit	Ashany, MD	Rheumatology
Vivian	Bykerk, MD	Rheumatology
Karmela	Chan, M.D.	Rheumatology
Jonathan	Cheah	Fellows
Giancarlo	Chesi	Fellows
Yurii	Chinenov	Research
Luvana	Chowdhury	Soft Tissue
Susan	Chyou	Research
Ian	Cohn	Research
Joel	Correa da Rosa	Independent
Daisy	Crego	Medicine
Shirin	Dey	Medicine
Edward	DiCarlo, MD	Laboratory Medicine
Laura	Donlin, Ph.D.	Research
Mark	Figgie, MD	Arthroplasty: Hip & Knee
Danny	Flores Castro	Rheumatology
Ellen	Gravallese, MD	University of Massachusetts
Sarah	Grond	Medicine
Sanjay	Gupta	Research

If a name does not appear in Co-Investigators directory, please contact zhouy@hss.edu to have an eCAP account created.

First Name	Last Name	Organization
Anh	Hoang	Rheumatology
Lionel	Ivashkiv, M.D.	Research - Rheumatology
Caroline	Jiang	Rockefeller University
Samantha	Lessard	Tissue Engineering, Regeneration and Repair
Theresa	Lu, MD PhD	Research
Michela	Manni	Research
David	Mayman, MD	Arthroplasty: Hip & Knee
Michael	McNamara	Rheumatology
Douglas	Mintz, MD	Radiology and Imaging
Serene	Mirza	Medicine
Kathryn	Oi	Arthroplasty: Hip & Knee
Dana	Orange, MD	Rheumatology
Miguel	Otero, Ph.D.	HSS
Pantelis	Pavlikis	Neurology
Alessandra	Pemis, MD	Rheumatology
Ed	Purdue, PhD	Arthroplasty: Hip & Knee
Caroline	Reidy	Rheumatology
Edd	Ricker	Research
Cristina	Rozo, Ph.D.	Rheumatology
Keerthi	Sadanala	Research
Rachel	Sealfon	Princeton University
Purva	Singh	Tissue Engineering, Regeneration and Repair
Emily	Stein, MD	Rheumatology
Bethany	Syracuse	Research - Dr. Ivashkiv
Olga	Troyanskaya	Princeton University
Victoria	Yao	Princeton University
Woelsung	Yi, PhD	Research
Xiaoning	Yuan	Rehabilitation
Jian	Zhou	Princeton University

6.0 Other Study Staff/Collaborators:

FirstName	LastName	Organization	Email	Role
There are no items to display				

7.0 * Type of Application:

- ☒ Clinical Research Proposal
- ☐ Expedited Retrospective Chart Review
- ☐ Request for Exemption
- ☐ New Registry
- ☐ Existing Approved Registry

Please click [here](#) to preview Exempt Categories.

Click [here](#) to preview Study Designs.

8.0 Select appropriate funding sources for this study:

Name
Other

Other Funding Sources:

Clinical and Translational Science Center

Note: If the funding source of the study is 'Industry Funded Support', Clinical Research Administration (CRA) will be

notified.

If your study requires CRA review, please upload applicable documents, including sponsor protocol, drug brochure, etc :

Name Version

There are no items to display

[Help](#)

ID: 2014-233

View: 1.1 CRP Information

[Help](#)

CRP Information

- 1.0 **The proposal should be submitted to the appropriate Clinical Review Panel (CRP) for scientific review. If you are unsure of which Clinical Review Panel to select, please contact Barbara Bosco at 212.606.1914**

*

Name

Rheumatology

[Help](#)

ID: 2014-233

View: 1.2 Regulatory Status of Drugs and Devices

[Help](#)

Regulatory Status of Drugs and Devices

- 1.0 **The regulatory status of the drugs or devices in this research proposal is:**

Name

Does not apply to this study

[Help](#)

ID: 2014-233

View: 1.3 Pharmacy Involvement / Impact to EPIC

[Help](#)

Pharmacy Involvement / Impact to EPIC

- 1.0 Is this an inpatient study?
☐ Yes ☒ No

- 2.0 * Will this study have Investigational Drug Service involvement?
(Pharmacy will be purchasing/dispensing any medications being used and/or study requires placebo and patient randomization)
☐ Yes ☒ No

3.0

If the answer to either question is yes, please explain briefly below AND contact Mylinh Duong at 646.797.8410 (duongm@hss.edu) or Nicole Oliva at 646.797.8324 (OlivaN@hss.edu).

[Help](#)

ID: 2014-233

View: 1.4 Study Locations

[Help](#)

Study Locations

1.0 Select the Research Facilities where this study will be conducted:

Facility

HSS

Other

1.1 If Other, please specify:

Hospital, medical offices, operating room, research building in the lab of Dr. Pernis
3RD floor Caspary, Collaborative Research Center, Rockefeller University

2.0 * Is this a multi-Center study?

No

ID: 2014-233

View: 2 Specific Aims or Research Questions

This section will be reviewed by the appropriate Clinical Review Panel. Each of the headings in this section must be addressed.

[Help](#)

Specific Aims or Research Questions

1.0 What is the condition or intervention to be studied?

The condition to be studied is worsening (flare) of rheumatoid arthritis (RA) in patients who have undergone arthroplasty. RA patients undergoing arthroplasty most often have severe, erosive disease. If the rate of flare approaches the estimated 26% rate suggested in a previous study for RA patients after arthroplasty (*Johnson ACR 2011*), this could be of significance in regards to their long term arthroplasty and disease outcomes. Patients who flare may not be able to participate in the post-operative rehabilitation thought necessary for optimal arthroplasty outcomes, and it may be difficult for patients who flare after

*Please click
Here for
example.*

discontinuing immunosuppressant medications for surgery to regain remission or low disease activity. Detailed clinical data collected longitudinally from RA patients with severe erosive disease undergoing arthroplasty in conjunction with further characterization of the molecular profile of blood and operative tissue could provide valuable information to inform best practices for this patient group.

2.0 What is/are the research question(s)/specific aim(s)? Pose very specific questions that can be addressed within the proposed design of the study. Prioritize them in order of importance.

1. To determine the rate of post-operative RA flare within 6 weeks of surgery, defined as
 - a. Worsening of disease activity, defined as an increase in the DAS-28 by 1.2 or by 0.6 if the DAS28 was ≥ 3.2 , OR
 - b. Patient reported worsening, defined as noting they are worse or much worse on the question rating their RA since pre-surgery
 - c. AND one of:
 - i. patient wants/needs retreatment of DMARDs and/or biologics and/or prednisone increase (or Medrol dose pack or equivalent or intra-articular corticosteroid injection)
 - ii. increase in MD global of 2/10
 - iii. increase in patient global of 2/10 (on the OMERACT Preliminary Flare Questions [PFQ])
 - iv. flare severity score of ≥ 10
2. To evaluate the responsiveness of the OMERACT PFQ in patients who flare, as defined as a worsening of DAS-28 by 1.2 or by 0.6 if the DAS28 was ≥ 3.2 OR by patient reported worsening.
3. To determine predictors of post-operative flare within 6 weeks of surgery such as baseline disease activity measures and biomarkers, including molecules in the Rho associated kinase (ROCK) pathway, which are measures of immune system activation
4. a. To assess if variability in physical therapy milestones post-op is associated with flare at 6 weeks
 - b. To assess if variability in physical therapy milestones post-op is associated with patient reported outcome measures at 1 year (for e.g., HAQ, DAS-28, HOOS, KOOS).
5. To evaluate if RA patients who flared within 6 weeks after arthroplasty exhibit an increase in ROCK activation at 6 weeks over and above pre-operative baseline levels, compared with patients who don't flare.
6. To better understand the molecular signature of RA flare and prodrome to RA flare. Blood samples harvested during various states of RA disease activity will be analyzed by RNA sequencing and Luminex® protein array to establish which pathways fluctuate most during disease worsening as well as prodrome to worsening. RA flare and the prodrome to flare will be measured by patient self-report using validated instruments of patient reported prodromal symptoms, patient reported disease activity measures and the OMERACT PFQs.

3.0 What is/are the hypothesis(es)?

1. 26% of RA patients will flare after TJR, defined as
 - a. Post op increases in DAS28 > 1.2 if baselines < 3.2 or > 0.6 if baseline ≥ 3.2 OR
 - b. Are worse or much worse on question rating their RA since pre-surgery AND
 - c. Have at least one of
 - i. Want / need treatment
 - ii. An increase in MD Global of 2/10
 - iii. An increase in Patient Global of 2/10 (according to the definitions noted above)
2. The OMERACT preliminary flare questions (PFQs) will detect patients who flare as defined above.
3. RA patients who flare after TJR have worse baseline pre-operative disease activity (DAS >3.2), worse baseline function (HOOS, KOOS, HAQ, elbow/shoulder surveys) and more likely will have had a history of withdrawing a biological therapy compared to patients who do not flare.
4. RA patients who flare post op will not meet their physical therapy milestones and will have worse HOOS, KOOS, elbow, or shoulder pain and function outcomes 1 year after arthroplasty.
5. RA patients who flare will exhibit enhanced immune activation when baseline levels are compared to levels in patients who flare within 6 weeks of surgery based on increased expression/activation of ROCK, IRF4, IRF5 and IRF8 and decreased expression/activity of their inhibitors (Def6 and SWAP-70). These molecules participate in a biologic pathway that regulates production of pro-inflammatory cytokines, potential mediators of RA flare.
6. There is a discrete set of genes expressed in circulating monocytes in RA patients during flare and prodrome of flare.

4.0 Identify and define the primary outcome and when the outcome will be measured. If measuring change in post-operative function is the most important, that will be your primary outcome.

The primary outcome is rate of RA flare within 6 weeks of surgery as measured by the OMERACT flare questionnaire.

5.0 Identify and define the secondary outcome(s) and when they will be measured (list additional goals one at a time with their corresponding outcomes).

1. The severity and impact of flares, using the OMERACT PFQs in the post arthroplasty setting: PFQs including flare intensity, duration of flare and worsening of domains associated with flare (pain, fatigue, stiffness, patient

- reported tender and swollen joint count, difficulties with coping and participation).
- 2. DAS28 at baseline and post-op week 6, and the change during this interval.
- 3. RAPID 3 weekly for 6 weeks and every 3 months for 1 year after arthroplasty, DAS-28, HOOS, KOOS, shoulder/elbow survey, patient global at baseline, 6 weeks, and 1 year.
- 4. Physical therapy functional milestones (PT questionnaire) at baseline and weekly for 86 weeks.
- 5. Biological markers of immune activation including levels of IRF4, IRF5, IRF8, IBP/Def6, SWAP-70, ROCK1, ROCK2 in synovial tissue taken at surgery. Levels of the same immune biomarkers in the peripheral blood measured pre-operatively, at 6 weeks post-operatively and at one year post-operatively.
- 6. Measurement of discrete set of genes expressed in circulating monocytes in RA patients obtained at baseline and weekly for 6 weeks after surgery in a subset of patients at high risk for flare (based on patients who withdrew biologics)

[Help](#)

ID: 2014-233

View: 2.1 Background

[Help](#)

BACKGROUND - Be sure to answer each question individually

1.0 Explain why these research questions are being asked:

RA patients who undergo arthroplasty have severe erosive disease; preliminary data suggests a flare rate as high as 26% in the post-operative period. This study would confirm the rate of post-operative flare, and evaluate the clinical and biologic factors which predict flare. We would also look at the impact of flare on arthroplasty outcomes (HOOS, KOOS, elbow/shoulder survey) and RA disease status (HAQ, DAS-28, RAPID) and better understand the biology of flare.

Flare after arthroplasty is clinically relevant, as medications are typically withheld at the time of surgery with the aim of diminishing surgical site infections.

However, patients who flare may not be able to adhere to post-operative rehabilitation regimens, leading to worse functional outcomes. In addition, patients who flare may have difficulty achieving remission or low disease activity when medications are re-started, leading to worse disease outcomes. There is little information about the characteristics and outcome of flare in the post-operative period. Better understanding of the incidence and clinical characteristics of post-operative flare and the means to predict who will be most likely to flare could lead to more tailored management strategies and potentially better arthroplasty and disease outcomes.

By gathering longitudinal clinical and biologic data from RA patients and obtaining blood and tissue taken at the time of arthroplasty, we have the ability to better characterize precursors and descriptors of flare by comparing patients who flare to those who do not flare. Moreover, the characteristics and outcomes of flare in the post-operative period may be generalizable to understanding the biology and predictors of flare in RA.

2.0 What is the background of the topic that you believe is important for the reviewer to know in considering this protocol, including prior studies by this research team.

Describe strengths and deficiencies of prior studies; explain how this study fits in. Include references.

While the proportion of total arthroplasties performed on RA patients has decreased, the rates of arthroplasty for RA remains stable (Mertlesman-Vos ACR 2012). In spite of improvements associated with the widespread use of potent disease modifying drugs (1, 2), 30-58% of patients with RA can expect to undergo arthroplasty over the course of their illness (3, 4). Therefore a large number of RA patients are affected by perioperative management decisions.

Little is known about the characteristics or rate of flare in the post-operative period, and little is known about the impact of post-operative flare on either overall disease status or arthroplasty outcome. We have shown that RA patients who undergo THR have worse outcomes at two years in WOMAC pain and function scores compared to OA controls (Goodman EULAR 2013), but the reasons for this disparity are not understood. To minimize risk of infection, biologic agents are discontinued perioperatively. It is not known if increases in flare contribute to worse THR outcomes in RA patients relative to OA patients but post-operative flare needs to be considered as a likely factor. If RA patients who flare are unable to participate in postoperative rehabilitation regimens which are important in optimizing arthroplasty outcomes, they may not achieve optimal outcomes. In particular domains that worsen with flare such as fatigue and difficulty coping and participating, conceivable could contribute to a worse outcome. Paradoxically, while patients with multiple arthritic joints have worse outcomes after arthroplasty compared to patients with a singly affected joint (5), which may explain the worse outcome for RA THR patients, RA TKR patients do equally well as osteoarthritis controls, (Goodman EULAR 2013). Thus factors other than polyarticular joint involvement must be impacting outcomes in RA patients undergoing THR. RA patients who have a prolonged or difficult time in re-establishing low disease activity or remission may have worse arthroplasty outcomes and this may be associated with worsening of the flare domains of joint pain and swelling, reflected by escalation to polyarticular disease (6, 7).

Tools are being developed to define and identify flare. Domains such as worsening of patient global assessment, increasing joint pain and swelling, worsening fatigue and pain; difficulty coping and participating, increased patient-reported specific areas of joint pain and swelling, as well as increased medication use have been identified as important in RA flare in general (8). However, the characteristics of post-operative flare have not been studied or defined. Preliminary data from the CATCH cohort (submitted) suggest flare rates of 19-45% occur as part of the course of disease, depending on the flare definition used, even without withdrawing therapy. Data from the NORDMARD registry (9) using a combination of patient reported worsening and treatment increase was associated with a mean (SD) DAS28 worsening of 1.96 (1.28) indicating that a worsening of the DAS28 of 1.2 or by 0.6 if the baseline is already 3.2 is a valid definition of flare as published by van der Maas et al. (10) and that the two definitions of flare are linked. Further assessments of these definitions of flare are required in different patient populations. Validating a tool to identify flare in the post arthroplasty setting would improve the ability to detect flare earlier and implement means to abrogate the impact of disease worsening to enhance long term outcomes for overall disease as well as for arthroplasty.

If this study confirms the high rate of flare in the post op period using a patient reported tool, we will better understand operative features and clinical and biological predictors of flare which will ultimately enable us to identify modifiable risk factors. The ability to predict which patients are likely to flare would be useful in optimizing overall treatment goals and surgical outcomes. Current clinical algorithms for monitoring disease activity are excellent tools for monitoring disease status, but are not completely adequate for identifying and predicting flare and may

not identify all factors that influence the post-operative course. For instance, if RA patients experience worsening pain, stiffness, and fatigue in the post operative course they may not adhere to or benefit from rehabilitation interventions in the same way that usual arthroplasty patients do. These factors have not been studied in the post-arthroplasty setting.

Collecting specimens longitudinally from a cohort of well characterized RA patients with high likelihood of worsening disease activity and post-operative flare provides a unique opportunity to study the biology of RA worsening in the context of clinical domains associated with RA disease activity and flare. It is well known that deregulation of immune responses plays a major role in many autoimmune diseases like RA. Delineating the molecular mechanisms which control the development, activation and differentiation of immune cells could lead to better understanding of how they become deregulated in disease states including RA, with particular focus on a set of molecules that are important in controlling the activation of immune cells. These molecules include IRF4, IRF5, IRF8, IBP/Def6, SWAP-70, ROCK1, ROCK2, and signaling molecules involved in responsiveness to activation stimuli. We hypothesize that in those RA patients who flare after arthroplasty there will be increased ROCK activation leading to enhanced activity of IRF4 (as well as IRF8 and possibly IRF5) and increased expression of pro-inflammatory cytokines/chemokines such as IL-17, IL-21 and CCL20. By following the levels to of ROCK pathway molecules longitudinally we can determine the relationship of these molecules to states of disease activity.

Patients managed with TNF inhibitors who discontinue the medication provide a unique opportunity to study the biology of flare in RA. An unbiased, bioinformatics approach to patient assessment is a useful strategy for identifying defects in complex pathways that result in RA disease activity. Transcriptomes from purified populations of peripheral blood mononuclear cells (CD4+, CD8+, CD20+, CD14+, CD56+) will be compared from samples harvested from patients who flared to those who did not flare during follow up.

Many patients with RA who flare describe non-specific prodromal symptoms such as intense fatigue and flu-like symptoms. These may represent manifestations of a cytokine storm that is triggered by unknown antecedents. Instruments to measure flare such as the OMERACT PFQs have been very recently developed and validated to provide a new opportunity to correlate molecular findings with clinical signs and symptoms of flare. Patients managed with TNF inhibitors who discontinue the medication perioperatively are most likely to be at increased risk for flare and provide a unique opportunity to study the biology of flare in RA. The goal of this aim is to correlate the clinical phenotype as measured by the OMERACT PFQ, measured weekly with the immunological data. The immunological phenotype will be characterized using RNA sequencing of white blood cell (WBC) to develop a comprehensive molecular profile of RA flare.

Comparison of data collected in patients who flare versus those who do not flare provides a unique opportunity to characterize and understand flare, and define the significance of perioperative flare on arthroplasty and disease outcomes while providing further understanding of the biology and immunology of RA worsening.

1. Pincus T, Sokka T. Quantitative measures for assessing rheumatoid arthritis in clinical trials and clinical care. *Best Pract Res Clin Rheumatol* 2003; Oct;17(5):753-81.
2. Pincus T, Sokka T, Kautiainen H. Patients seen for standard rheumatoid arthritis care have significantly better articular, radiographic, laboratory, and functional

status in 2000 than in 1985. *Arthritis Rheum* 2005; Apr;52(4):1009-19.

3. Massardo L, Gabriel SE, Crowson CS, O'Fallon WM, Matteson EL. A population based assessment of the use of orthopedic surgery in patients with rheumatoid arthritis. *J Rheumatol* 2002; Jan;29(1):52-6.

4. Shourt CA, Crowson CS, Gabriel SE, Matteson EL. Orthopedic surgery among patients with rheumatoid arthritis 1980-2007: a population-based study focused on surgery rates, sex, and mortality. *J Rheumatol* 2012; Mar;39(3):481-5.

5. Perruccio AV, Power JD, Evans HM, Mahomed SR, Gandhi R, Mahomed NN, et al. Multiple joint involvement in total knee replacement for osteoarthritis: Effects on patient-reported outcomes. *Arthritis Care Res (Hoboken)* 2012; Jun;64(6):838-46.

6. Bartlett SJ, Hewlett S, Bingham CO,3rd, Woodworth TG, Alten R, Pohl C, et al. Identifying core domains to assess flare in rheumatoid arthritis: an OMERACT international patient and provider combined Delphi consensus. *Ann Rheum Dis* 2012; Nov;71(11):1855-60.

7. Berthelot JM, De Bandt M, Morel J, Benatig F, Constantin A, Gaudin P, et al. A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: The 'FLARE' instrument. *Ann Rheum Dis* 2011; Nov 9

8. Bykerk V, Lie E, Alten R, et al. Establishing a Core Domain Set to Measure Rheumatoid Arthritis Flares: Report of the OMERACT 11 RA Flare Workshop. *J Rheumatol* 2013 (in press).

9. Lie E, Woodworth TG, Christensen R, Kvien TK, Bykerk V, Furst DE, Bingham CO 3rd, Choy EH, and the OMERACT RA Flare Working Group. Validation of OMERACT preliminary rheumatoid arthritis flare domains in the NOR-DMARD study. *Ann Rheum Dis* 2013, Accepted for publication.

10 van der Maas A, Lie E, Christensen R, Choy E, de Man YA, van Riel P, Woodworth T, den Broeder AA. Construct and criterion validity of several proposed DAS28-based rheumatoid arthritis flare criteria: an OMERACT cohort validation study. *Ann Rheum Dis* 2012;0:1-6. doi:10.1136/annrheumdis-2012-202281

3.0 Identify specific gaps in current knowledge that this study is intended to fill.

This study will confirm the rate of post-operative flare in RA patients undergoing arthroplasty, and will validate the use of a tool to identify flare. We will identify clinical and biologic candidates for further study as predictors of flare. We will then evaluate the relationship between post-operative flare and long-term arthroplasty pain and function, which has never been previously evaluated. In addition, by following the levels of ROCK pathway molecules longitudinally we can determine the relationship of these molecules to states of disease activity, which is not known.

4.0 How will answering these questions change clinical practice, change concepts about the topic or confirm the work of other investigators?

If 26% of RA patients flare in the post-operative period then it would be important to know if these patients have differences in achieving successful outcomes from their arthroplasty surgery both in the short and long term and it would then be important to know what can be done to modify flares. It will also be important to identify predictors of these flares as these might be modifiable risk factors or signaling biomarkers. Validation of these would require a larger study. An understanding of the disease pathogenesis assessed when tissue specimens as

well as serum biomarkers are studied in the perioperative context may also contribute the identification of biomarkers associated with flare. In addition, if biologic precursors and predictors of flare are identified, they could have additional applicability in RA management.

5.0 Is this a pilot study that could lead to a more definitive protocol or different study? ☐ Yes ☒ No

5.1 If you answered No, please explain below:

This is not a pilot study.

6.0 Please upload reference or additional document here (if needed).

Name	Description
There are no items to display	

[Help](#)

ID: 2014-233

View: 2.2 Study Design

[Help](#)

Study Design

1.0 Observational:

Name	Description
Prospective Cohort Study	A prospective evaluation of a cohort of patients with a specific characteristic over time to see if they develop a particular endpoint or outcome based on a stated hypothesis (e.g., establishing a cohort to follow patients undergoing a novel procedure in order to evaluate pre- and post-operative function/pain). These studies are conceived before data is collected.

2.0 Experimental:

Name	Description
There are no items to display	

2.1 If Other, please specify:

2.2 If Randomized Controlled Clinical Trial is selected, please choose one of the following:

Name
There are no items to display

If other, please list name or indicate N/A below:

ID: 2014-233

View: 2.3 Recruitment

[Help](#)

Recruitment

1.0

Check all that apply to describe your study population:

Population

Patients

Vulnerable Populations

There are no items to display

1.1 If Other, please specify:

2.0 Inclusion Criteria: *list characteristics that potential subjects and controls need to have. Use a bullet format, if applicable.*

1. Age > 18

2. Patients with Rheumatoid Arthritis, Osteoarthritis, or Inflammatory Arthritis undergoing **primary total hip replacement surgery, primary total knee replacement surgery, primary total elbow replacement surgery or primary total shoulder replacement surgery**

3. Satisfy ACR/EULAR 2010 classification criteria and/or the 1987 RA criteria (see below) and be diagnosed with RA (unless IA patient or OA control).

Rheumatoid arthritis 1987 criteria:

1. morning stiffness in and around joints lasting at least 1 hour before maximal improvement;
2. soft tissue swelling (arthritis) of 3 or more joint areas observed by a physician;
3. swelling (arthritis) of the proximal interphalangeal, metacarpophalangeal, or wrist joints;
4. symmetric swelling (arthritis);
5. rheumatoid nodules;
6. the presence of rheumatoid factor; and
7. radiographic erosions and/or periarticular osteopenia in hand and/or wrist joints.

*Criteria 1 through 4 must have been present for at least 6 weeks. Rheumatoid arthritis is defined by the presence of 4 or more criteria, and no further qualifications (classic, definite, or probable) or list of exclusions are required.

ACR/EULAR 2010 criteria for the classification of RA:

Table 3. The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

Target population (Who should be tested?): Patients who

- 1) have at least 1 joint with definite clinical synovitis (swelling)*
- 2) with the synovitis not better explained by another disease

Classification criteria for RA (score-based algorithm: add score of categories A-D;

a score of $\geq 6/10$ is needed for classification of a patient as having definite RA

Score

A. Joint involvement

0	1 large joint	
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	>10 joints (at least 1 small joint)	5

B. Serology (at least 1 test result is needed for classification)

0	Negative RF <i>and</i> negative ACPA	
	Low-positive RF <i>or</i> low-positive ACPA	2
3	High-positive RF <i>or</i> high-positive ACPA	

C. Acute-phase reactants (at least 1 test result is needed for classification)

0	Normal CRP <i>and</i> normal ESR
1	Abnormal CRP <i>or</i> abnormal ESR

D. Duration of symptoms

0	< 6 weeks
1	≥ 6 weeks

*The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA. Patients with longstanding disease, including those whose disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.

3.0

Exclusion Criteria: *list characteristics that would cause you to exclude potential subjects and controls.*

Justify any age, ethnicity, language, or gender-based exclusion criteria. *Use a bullet format, if applicable.*

1. Primary diagnosis of any of the following systemic rheumatic diseases (see ICD-9 codes 135.0, 136.1, 274, 279.4, 279.8, 287.0, 446.0, 446.1, 446.2, 446.21, 446.4, 446.7, 447.6, 556, 710.0, 710.2, 710.8, 710.9, 711.1, 711.2, 713.3, 713.7, 716.2, 719.3, 720.1, 725)
2. Diagnosis of or crystalline arthropathy.
3. Unable to understand or read English.
4. Unable to follow the study protocol in a reliable manner.
5. Age < 18.

4.0 Age Range:

>18

5.0 Describe how you will identify and recruit potential subjects for participation in the study.

A Recruitment Flyer will be placed in the dictation cubbies and exam rooms of participating surgeons. If a patient with a possible or previous diagnosis of RA schedules an arthroplasty, members of the surgeon's office will send the patient information to the Research Staff using either the study e-mail address, FlareStudy@hss.edu, or other secure forms of communication. Patients will be identified pre-operatively by their treating surgeon or identified by screening patients' records prior to their pre-operative visit.

Patients will be called prior to coming in to the hospital either for their pre-surgical screening visit or for their surgery, depending on when they were identified as a potential subject. A research assistant/ research team member will describe the study, discuss any questions the patient may have, and evaluate the patient's interest in participating in the study. If the patient is interested in the study, they will then be met in person at their visit to the hospital (pre-surgical screening visit or on their day of surgery) to discuss the study further and be consented.

They will receive a Study Overview Sheet (see attached) either in the office, in the mail, or on the day of surgery. They will have the opportunity to discuss any questions with the research assistant/ research team member who will ensure they meet study criteria (see screening sheet). In addition, patients may be identified and recruited from the Total Joint Replacement Patient Education Class by the research assistant. Finally, research assistants may use PS Reporter, MMF, or Clinstar to identify patients before their pre-surgical screening visit, or prior to their surgical procedure. We will request an IRB approved Waiver of HIPAA Authorization.

6.0 * Please select enrollment type from following drop down list:

Over Course of Study

[Help](#)

ID: 2014-233

View: 2.3 Target Enrollment

[Help](#)

Target Enrollment

- 1.0 * What is the maximum number of subject you plan to enroll in this study at HSS?(Please enter a number)
200
- 2.0 If this is a multi-center study, indicate the projected total subject accrual across all sites.

[Help](#)

ID: 2014-233

View: 2.35 Patient Subjects

[Help](#)

Patients

1.0 Please check the box(es) below that best reflect how patients will be identified and recruited for participation.

How subjects will be identified

- ☒ Potential subjects will be identified after a review of medical records of patients under the care of one or more of the study investigators
- ☒ Medical records and/or other Institution sources (databases, registries, billing records, pathology reports, admission logs) will be reviewed to identify potential participants. May involve access of records by individuals not involved in the patient's care.
- ☒ Potential subjects will be identified by their treating physicians and referred to the researchers. Patients' private and identifiable information will not be shared prior to receiving permission from the patient to do so.
- ☐ Potential subjects will be identified from a registry of individuals interested in research opportunities.
- ☐ Subjects will roll-over from another research study.
- ☐ Potential subjects will self-refer in response to advertisements.

ID: 2014-233

View: 2.6 Interventions and Observations

[Help](#)

Interventions and Observations

1.0 Be specific and describe the Interventions or Observations that will be part of this research project. Include a detailed description of the treatment arms, if applicable.

Clinical Data:

If willing to participate, the RC will complete a study screening form, obtain consent, complete a Research Authorization Form and the patient will complete a pre-operative questionnaire/survey containing questions about their demographic information (race, ethnicity, age, weight), medical history, assessment of their replaced joint function, and symptoms as they relate to their RA (OA and IA patients will not be asked survey questions that apply only to RA patients). We requested an IRB approved Waiver of HIPAA Authorization.

o The questionnaire will include patient demographics, RA characteristics, co-morbid conditions, disease classification, medications, PtGA, SF-12, HAQ, RAPID, joint count homunculus, HOOS/KOOS/elbow/shoulder survey.

The research staff will complete a second survey that will ask about the participant's medical history, and medication history.

o The questionnaire will include Medications, disease duration and classification criteria, assessment for extra-articular disease and co-morbidities, MDGA, DAS28, CDAI

~~OA and IA~~ Patients: We will repeat both questionnaires at 6 weeks after surgery at the time of the participants' regularly scheduled appointment.

RA Patients only:

- We will repeat both questionnaires at 6 weeks and one year after surgery at the time of participants' regularly scheduled appointments.
- Questions about RA will also be asked by telephone or by e-mailing an electronic survey each week for six weeks, and then every three months for the rest of the year.

o The questionnaire will include OMERACT flare questions, RAPID, joint humunculus

All questionnaires can be completed in any of the following ways throughout the course of the study: in person at the hospital, over the phone, via e-mail using a secure survey, or by mailing paper forms to and from the hospital.

Blood sample:

We would like to collect and store serum from participants in this study, which means we will need to increase our day-of-surgery allowed blood draw limit from 50.5 to 56.6mL (well below the IRB cap of 550mL):

- **30mL** whole blood in green top heparin tubes (3 tubes, 10mL each, for PBMC isolation)
- **8.5mL** speckle top tube (1 tube, to be spun by research assistant and aliquotted for freezing at -80)
- **2.5mL** for PAXgene tubes (1 tube, to be frozen by the research assistant)
- If not ordered at Pre-Surgical Screening, **3mL** lavender top for erythrocyte sedimentation rate (as marker of inflammatory levels)
- If not ordered at Pre-Surgical Screening, **5mL** into gold serum separator tube for c-reactive protein levels (as marker of inflammatory levels)
- If not available in medical record, **10mL** for combined Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibody (ACPA, also known as anti-CCP)
- *We will no longer be collecting PAX gene tubes day-of-surgery, which were 2.5mL each*

$30 + 8.5 + 2.5 + 3 + 5 + 10 = 59 \text{ mL}$, which is 3.99 tablespoons

IA and RA patients only:

For follow-up visits, we would like to add serum collection, in addition to the whole blood we are already collecting. We would like to increase our 6-week follow-up and 1-year follow-up visit blood draw limit from 28mL to 36.5mL (well below the IRB cap of 550mL):

- **20mL** whole blood in green top heparin tube (2 tubes, 10mL each, for PBMC isolation)
- **8.5mL** speckle top tube (1 tube, to be spun by research assistant and aliquotted for freezing at -80)
- If not ordered by treating physician, **3mL** lavender top for erythrocyte sedimentation rate (as marker of inflammatory levels)
- If not ordered by treating physician, **5mL** into gold serum separator tube for c-reactive protein levels (as marker of inflammatory levels)

$20 + 8.5 + 3 + 5 = 36.5 \text{ mL}$, which is 2.47 tablespoons

- All: In the event that a participant is hospitalized at Hospital for Special Surgery or one of its affiliates at any time between their enrollment on the day of surgery and their 6-week follow-up appointment with their surgeon, we may ask for an additional blood draw of 2 tablespoons (20 ccs) of blood to take place at the time of their routine morning blood draw.
- If for any reason routine lab work is not required at the participants' study visits, we would still require 2 tubes of blood for study purposes and would make arrangements to do so. All samples will be de-identified.
- If for any reason subjects are unable to provide blood at their 6-week or 1-year follow-ups (for example, if the subject was too busy, the line at phlebotomy was too long, or the subject simply did not schedule a 1-year follow-up), we will contact the subject and ask them if they would like to have the blood drawn by Apex Laboratory, Inc, a mobile laboratory capable of visiting patients to draw blood in their homes. If they express interest, we will sent them a new informed consent form, cover letter, and prepaid return envelope. When we recieve the signed consent form, we will call the subject to coordinate an Apex Laboratory visit date. Apex will call the patient to coordinate the proper time to arrive, and will draw a maximum of 1.5 tablespoons of blood for ESR and CRP blood tests. The results of these tests will be communicated to the study research assistant through Apex's HIPAA-compliant web-based platform.

Surgical sample:

- During surgery, the subjects' surgeon will take samples of the tissue removed as part of their surgery from their joint. Specifically for THR, the femoral head will be collected intra-operatively from standardized anatomic sites, (fovea and capsular reflection). For TKR, tissue samples of the patella cartilage, distal femur and proximal tibia, and synovium from the suprapatellar pouch will be collected intra-operatively.
- We collect and analyze this tissue to learn more about the cellular activity that occurs with RA flare. Tissue will be processed first in pathology: sample saved in OCT and 2 slides stained with H&E. Slides will be scored according to a modified Scanzello scoring system. Synovial tissue and PBMCs will be processed according the standard operating procedures established by the AMP network. Cellular samples will be analyzed at HSS, and shared with the AMP network for additional specialized technical analytics to explore markers and pathways expressed in tissue and cells, using (but not limited to) those being explored in the AMP network such as RNA-Seq, ATAC-Seq, CyTOF, FACS.
- We will also photograph the specimen using the Pathology Lab equipment. This photograph will be de-identified before it is used for research purposes. We will also capture de-identified microscopy images of H&E slides prepared from these samples.

2.0 Will you be collecting human fluid or tissue? ☒ Yes ☐ No

If yes, what will you be collecting? ☒ Fluid ☒ Tissue
(Intraoperative and/or outpatient collection)

[Help](#)

ID: 2014-233 View: 2.61 Fluid Specimen Collection

[Help](#)

Fluid Specimen Collection

Please choose form the following and provide requested information.

1.0 ☒ Blood/serum/plasma

Volume:

59 mL (3.99 tablespoons) first visit, 36.5 mL (2.47 tablespoons) for follow-up visits

Timing and Frequency of collection:

During the surgery

Storage requirements:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☒ Additional collection for research purposes

Describe testing and who will do testing:

☐ Urine

Volume:

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

☐ Saliva

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

☐ Synovial Fluid

Volume:

Timing and Frequency of collection:

Site:

Surgical Field: ☐ or **Aspiration:** ☐

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

[Help](#)

ID: 2014-233

View: 2.61 Fluid Specimen Collection - continued

[Help](#)

Fluid Specimen Collection - continued

Please choose from the following and provide requested information.

☐ Other (e.g. cerebral spinal fluid, cheek cells, bronchial lavage, stool, etc)

Describe specimen:

Volume:

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

1.0 Will specimens be sent to an individual or institution outside of HSS? (i.e. external Central Laboratory) ☐ Yes ☐ No

If yes, where/to whom and what testing will be done:

2.0 Is fluid being collected for genetic testing? ☒ Yes ☐ No

If yes, describe testing:

3.0 Is fluid being stored for future testing? ☒ Yes ☐ No

If yes, describe testing:

The samples may be used for testing even after this study has been completed. Further research tests may help us learn more about the disease and response to drugs or treatment. However, future testing on the patient's biological samples may be used for any type of biomedical research, which may or may not be related to the purpose of this study. The results of these future tests will not be shared with the patient.

[Help](#)

ID: 2014-233

View: 2.62 Tissue Specimens Collection

[Help](#)

Tissue Specimens Collection

1.0 Status of Tissue

☐ FRESH

Will frozen tissue be needed? ☐ Yes ☐ No

How will it be delivered to Histopathology? Name/Extension/Beeper #.

☐ FIXED/PARAFFIN EMBEDDED

2.0 ☒ Bone

Site (Specific joint/area):

Femoral head, distal femur, proximal tibia

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☒ Additional collection for research purposes

Describe testing and who will do testing:

Specifically for THR, the femoral head will be collected intra-operatively from standardized anatomic sites, (fovea and capsular reflection). For TKR, tissue samples of the patella cartilage, distal femur and proximal tibia, and synovium from the suprapatellar pouch will be collected intra-operatively.

☐ Bone Marrow

Method of collection: ☐ Biopsy ☐ Aspirate

Site (Specific joint/area):

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

☒ **Cartilage**

Site (Specific joint/area):

Patellar cartilage

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☒ **Additional collection for research purposes**

Describe testing and who will do testing:

☐ **Meniscus**

Site:

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

[Help](#)

ID: 2014-233

View: 2.62 Tissue Specimens Collection - continued

[Help](#)

Tissue Specimens Collection - continued

☐ **Retrieved Device for Biomechanical Testing**

Site:

☒ **Synovium**

Site (specific joint/area):

Synovium from the suprapatellar pouch will be collected intra-operatively.

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☒ **Additional collection for research purposes**

Describe testing and who will do testing:

☐ **Other (i.e. punch biopsy, nucleus pulposus/annulus fibrosus, or other collected tissue/biopsies)**

Provide additional information:

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

1.0 Will specimens be sent to an individual or institution outside

of HSS? (i.e. external Central Laboratory) ☐ Yes ☐ No

If yes, where/to whom and what testing will be done:

2.0 Is tissue being collected for genetic testing? ☐ Yes ☒ No

If yes, describe testing:

3.0 Is tissue being stored for future testing? ☐ Yes ☐ No

If yes, describe testing:

[Help](#)

ID: 2014-233

View: 2.7 Data Collection

[Help](#)

Data Collection

1.0 Indicate what data will be collected.

PARTICIPANT INTAKE

New form location
1. Interest in electronic surveys
2. Symptom onset
3. Date of diagnosis
4. Ethnicity
5. Race
6. Highest level of completed education
7. Current employment status
8. # other people at home
9. Personal income
10. Smoking history
11. Alcohol
12. Relative with RA/PsA/OA/broken hip
13. Other diseases in family

14. Rheumatologist contact info
15. Modified Charlson/SANGA comorbidity index

Day-of-surgery allowed blood draw is 58.5mL (well below the IRB cap of 550mL):

- **30mL** whole blood in green top heparin tubes (3 tubes, 10mL each, for PBMC isolation)
- **8.5mL** speckle top tube (1 tube, to be spun by research assistant and aliquotted for freezing at -80)
- **2.5mL** for PAXgene tubes (1 tube, to be frozen by the research assistant)
- If not ordered at Pre-Surgical Screening, **3mL** lavender top for erythrocyte sedimentation rate (as marker of inflammatory levels)
- If not ordered at Pre-Surgical Screening, **5mL** into gold serum separator tube for c-reactive protein levels (as marker of inflammatory levels)
- If not available in medical record, **10mL** for combined Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibody (ACPA, also known as anti-CCP)

$30 + 8.5 + 2.5 + 3 + 5 + 10 = 59 \text{ mL}$, which is 3.99 tablespoons

Follow-up visit collection is 36.5mL (well below the IRB cap of 550mL):

- **20mL** whole blood in green top heparin tube (2 tubes, 10mL each, for PBMC isolation)
- **8.5mL** speckle top tube (1 tube, to be spun by research assistant and aliquotted for freezing at -80)
- If not ordered by treating physician, **3mL** lavender top for erythrocyte sedimentation rate (as marker of inflammatory levels)
- If not ordered by treating physician, **5mL** into gold serum separator tube for c-reactive protein levels (as marker of inflammatory levels)

$20 + 8.5 + 3 + 5 = 36.5 \text{ mL}$, which is 2.47 tablespoons

Peripheral blood analysis (research assistant, Dr. Pernis lab): After blood is collected PBMCs (or SFMCs) will be isolated. Normally the yield is 1-2M/ml. Thus 40 ml should yield between 40-80M of PBMCs. An aliquot of the PBMCs will be directly assayed for ROCK activation, immune cell subsets and T cell function. Another aliquot will be cultured to assess ROCK activation and T cell function after stimulation by measuring molecules such as IRF4, IRF5, IRF8, IRF9, IRF10, IRF11, IRF12, IRF13, IRF14, IRF15, IRF16, IRF17, IRF18, IRF19, IRF20, IRF21, IRF22, IRF23, IRF24, IRF25, IRF26, IRF27, IRF28, IRF29, IRF30, IRF31, IRF32, IRF33, IRF34, IRF35, IRF36, IRF37, IRF38, IRF39, IRF40, IRF41, IRF42, IRF43, IRF44, IRF45, IRF46, IRF47, IRF48, IRF49, IRF50, IRF51, IRF52, IRF53, IRF54, IRF55, IRF56, IRF57, IRF58, IRF59, IRF60, IRF61, IRF62, IRF63, IRF64, IRF65, IRF66, IRF67, IRF68, IRF69, IRF70, IRF71, IRF72, IRF73, IRF74, IRF75, IRF76, IRF77, IRF78, IRF79, IRF80, IRF81, IRF82, IRF83, IRF84, IRF85, IRF86, IRF87, IRF88, IRF89, IRF90, IRF91, IRF92, IRF93, IRF94, IRF95, IRF96, IRF97, IRF98, IRF99, IRF100, IRF101, IRF102, IRF103, IRF104, IRF105, IRF106, IRF107, IRF108, IRF109, IRF110, IRF111, IRF112, IRF113, IRF114, IRF115, IRF116, IRF117, IRF118, IRF119, IRF120, IRF121, IRF122, IRF123, IRF124, IRF125, IRF126, IRF127, IRF128, IRF129, IRF130, IRF131, IRF132, IRF133, IRF134, IRF135, IRF136, IRF137, IRF138, IRF139, IRF140, IRF141, IRF142, IRF143, IRF144, IRF145, IRF146, IRF147, IRF148, IRF149, IRF150, IRF151, IRF152, IRF153, IRF154, IRF155, IRF156, IRF157, IRF158, IRF159, IRF160, IRF161, IRF162, IRF163, IRF164, IRF165, IRF166, IRF167, IRF168, IRF169, IRF170, IRF171, IRF172, IRF173, IRF174, IRF175, IRF176, IRF177, IRF178, IRF179, IRF180, IRF181, IRF182, IRF183, IRF184, IRF185, IRF186, IRF187, IRF188, IRF189, IRF190, IRF191, IRF192, IRF193, IRF194, IRF195, IRF196, IRF197, IRF198, IRF199, IRF200, IRF201, IRF202, IRF203, IRF204, IRF205, IRF206, IRF207, IRF208, IRF209, IRF210, IRF211, IRF212, IRF213, IRF214, IRF215, IRF216, IRF217, IRF218, IRF219, IRF220, IRF221, IRF222, IRF223, IRF224, IRF225, IRF226, IRF227, IRF228, IRF229, IRF230, IRF231, IRF232, IRF233, IRF234, IRF235, IRF236, IRF237, IRF238, IRF239, IRF240, IRF241, IRF242, IRF243, IRF244, IRF245, IRF246, IRF247, IRF248, IRF249, IRF250, IRF251, IRF252, IRF253, IRF254, IRF255, IRF256, IRF257, IRF258, IRF259, IRF260, IRF261, IRF262, IRF263, IRF264, IRF265, IRF266, IRF267, IRF268, IRF269, IRF270, IRF271, IRF272, IRF273, IRF274, IRF275, IRF276, IRF277, IRF278, IRF279, IRF280, IRF281, IRF282, IRF283, IRF284, IRF285, IRF286, IRF287, IRF288, IRF289, IRF290, IRF291, IRF292, IRF293, IRF294, IRF295, IRF296, IRF297, IRF298, IRF299, IRF300, IRF301, IRF302, IRF303, IRF304, IRF305, IRF306, IRF307, IRF308, IRF309, IRF310, IRF311, IRF312, IRF313, IRF314, IRF315, IRF316, IRF317, IRF318, IRF319, IRF320, IRF321, IRF322, IRF323, IRF324, IRF325, IRF326, IRF327, IRF328, IRF329, IRF330, IRF331, IRF332, IRF333, IRF334, IRF335, IRF336, IRF337, IRF338, IRF339, IRF340, IRF341, IRF342, IRF343, IRF344, IRF345, IRF346, IRF347, IRF348, IRF349, IRF350, IRF351, IRF352, IRF353, IRF354, IRF355, IRF356, IRF357, IRF358, IRF359, IRF360, IRF361, IRF362, IRF363, IRF364, IRF365, IRF366, IRF367, IRF368, IRF369, IRF370, IRF371, IRF372, IRF373, IRF374, IRF375, IRF376, IRF377, IRF378, IRF379, IRF380, IRF381, IRF382, IRF383, IRF384, IRF385, IRF386, IRF387, IRF388, IRF389, IRF390, IRF391, IRF392, IRF393, IRF394, IRF395, IRF396, IRF397, IRF398, IRF399, IRF400, IRF401, IRF402, IRF403, IRF404, IRF405, IRF406, IRF407, IRF408, IRF409, IRF410, IRF411, IRF412, IRF413, IRF414, IRF415, IRF416, IRF417, IRF418, IRF419, IRF420, IRF421, IRF422, IRF423, IRF424, IRF425, IRF426, IRF427, IRF428, IRF429, IRF430, IRF431, IRF432, IRF433, IRF434, IRF435, IRF436, IRF437, IRF438, IRF439, IRF440, IRF441, IRF442, IRF443, IRF444, IRF445, IRF446, IRF447, IRF448, IRF449, IRF450, IRF451, IRF452, IRF453, IRF454, IRF455, IRF456, IRF457, IRF458, IRF459, IRF460, IRF461, IRF462, IRF463, IRF464, IRF465, IRF466, IRF467, IRF468, IRF469, IRF470, IRF471, IRF472, IRF473, IRF474, IRF475, IRF476, IRF477, IRF478, IRF479, IRF480, IRF481, IRF482, IRF483, IRF484, IRF485, IRF486, IRF487, IRF488, IRF489, IRF490, IRF491, IRF492, IRF493, IRF494, IRF495, IRF496, IRF497, IRF498, IRF499, IRF500, IRF501, IRF502, IRF503, IRF504, IRF505, IRF506, IRF507, IRF508, IRF509, IRF510, IRF511, IRF512, IRF513, IRF514, IRF515, IRF516, IRF517, IRF518, IRF519, IRF520, IRF521, IRF522, IRF523, IRF524, IRF525, IRF526, IRF527, IRF528, IRF529, IRF530, IRF531, IRF532, IRF533, IRF534, IRF535, IRF536, IRF537, IRF538, IRF539, IRF540, IRF541, IRF542, IRF543, IRF544, IRF545, IRF546, IRF547, IRF548, IRF549, IRF550, IRF551, IRF552, IRF553, IRF554, IRF555, IRF556, IRF557, IRF558, IRF559, IRF560, IRF561, IRF562, IRF563, IRF564, IRF565, IRF566, IRF567, IRF568, IRF569, IRF570, IRF571, IRF572, IRF573, IRF574, IRF575, IRF576, IRF577, IRF578, IRF579, IRF580, IRF581, IRF582, IRF583, IRF584, IRF585, IRF586, IRF587, IRF588, IRF589, IRF590, IRF591, IRF592, IRF593, IRF594, IRF595, IRF596, IRF597, IRF598, IRF599, IRF600, IRF601, IRF602, IRF603, IRF604, IRF605, IRF606, IRF607, IRF608, IRF609, IRF610, IRF611, IRF612, IRF613, IRF614, IRF615, IRF616, IRF617, IRF618, IRF619, IRF620, IRF621, IRF622, IRF623, IRF624, IRF625, IRF626, IRF627, IRF628, IRF629, IRF630, IRF631, IRF632, IRF633, IRF634, IRF635, IRF636, IRF637, IRF638, IRF639, IRF640, IRF641, IRF642, IRF643, IRF644, IRF645, IRF646, IRF647, IRF648, IRF649, IRF650, IRF651, IRF652, IRF653, IRF654, IRF655, IRF656, IRF657, IRF658, IRF659, IRF660, IRF661, IRF662, IRF663, IRF664, IRF665, IRF666, IRF667, IRF668, IRF669, IRF670, IRF671, IRF672, IRF673, IRF674, IRF675, IRF676, IRF677, IRF678, IRF679, IRF680, IRF681, IRF682, IRF683, IRF684, IRF685, IRF686, IRF687, IRF688, IRF689, IRF690, IRF691, IRF692, IRF693, IRF694, IRF695, IRF696, IRF697, IRF698, IRF699, IRF700, IRF701, IRF702, IRF703, IRF704, IRF705, IRF706, IRF707, IRF708, IRF709, IRF710, IRF711, IRF712, IRF713, IRF714, IRF715, IRF716, IRF717, IRF718, IRF719, IRF720, IRF721, IRF722, IRF723, IRF724, IRF725, IRF726, IRF727, IRF728, IRF729, IRF730, IRF731, IRF732, IRF733, IRF734, IRF735, IRF736, IRF737, IRF738, IRF739, IRF740, IRF741, IRF742, IRF743, IRF744, IRF745, IRF746, IRF747, IRF748, IRF749, IRF750, IRF751, IRF752, IRF753, IRF754, IRF755, IRF756, IRF757, IRF758, IRF759, IRF760, IRF761, IRF762, IRF763, IRF764, IRF765, IRF766, IRF767, IRF768, IRF769, IRF770, IRF771, IRF772, IRF773, IRF774, IRF775, IRF776, IRF777, IRF778, IRF779, IRF780, IRF781, IRF782, IRF783, IRF784, IRF785, IRF786, IRF787, IRF788, IRF789, IRF790, IRF791, IRF792, IRF793, IRF794, IRF795, IRF796, IRF797, IRF798, IRF799, IRF800, IRF801, IRF802, IRF803, IRF804, IRF805, IRF806, IRF807, IRF808, IRF809, IRF810, IRF811, IRF812, IRF813, IRF814, IRF815, IRF816, IRF817, IRF818, IRF819, IRF820, IRF821, IRF822, IRF823, IRF824, IRF825, IRF826, IRF827, IRF828, IRF829, IRF830, IRF831, IRF832, IRF833, IRF834, IRF835, IRF836, IRF837, IRF838, IRF839, IRF840, IRF841, IRF842, IRF843, IRF844, IRF845, IRF846, IRF847, IRF848, IRF849, IRF850, IRF851, IRF852, IRF853, IRF854, IRF855, IRF856, IRF857, IRF858, IRF859, IRF860, IRF861, IRF862, IRF863, IRF864, IRF865, IRF866, IRF867, IRF868, IRF869, IRF870, IRF871, IRF872, IRF873, IRF874, IRF875, IRF876, IRF877, IRF878, IRF879, IRF880, IRF881, IRF882, IRF883, IRF884, IRF885, IRF886, IRF887, IRF888, IRF889, IRF890, IRF891, IRF892, IRF893, IRF894, IRF895, IRF896, IRF897, IRF898, IRF899, IRF900, IRF901, IRF902, IRF903, IRF904, IRF905, IRF906, IRF907, IRF908, IRF909, IRF910, IRF911, IRF912, IRF913, IRF914, IRF915, IRF916, IRF917, IRF918, IRF919, IRF920, IRF921, IRF922, IRF923, IRF924, IRF925, IRF926, IRF927, IRF928, IRF929, IRF930, IRF931, IRF932, IRF933, IRF934, IRF935, IRF936, IRF937, IRF938, IRF939, IRF940, IRF941, IRF942, IRF943, IRF944, IRF945, IRF946, IRF947, IRF948, IRF949, IRF950, IRF951, IRF952, IRF953, IRF954, IRF955, IRF956, IRF957, IRF958, IRF959, IRF960, IRF961, IRF962, IRF963, IRF964, IRF965, IRF966, IRF967, IRF968, IRF969, IRF970, IRF971, IRF972, IRF973, IRF974, IRF975, IRF976, IRF977, IRF978, IRF979, IRF980, IRF981, IRF982, IRF983, IRF984, IRF985, IRF986, IRF987, IRF988, IRF989, IRF990, IRF991, IRF992, IRF993, IRF994, IRF995, IRF996, IRF997, IRF998, IRF999, IRF1000, IRF1001, IRF1002, IRF1003, IRF1004, IRF1005, IRF1006, IRF1007, IRF1008, IRF1009, IRF1010, IRF1011, IRF1012, IRF1013, IRF1014, IRF1015, IRF1016, IRF1017, IRF1018, IRF1019, IRF1020, IRF1021, IRF1022, IRF1023, IRF1024, IRF1025, IRF1026, IRF1027, IRF1028, IRF1029, IRF1030, IRF1031, IRF1032, IRF1033, IRF1034, IRF1035, IRF1036, IRF1037, IRF1038, IRF1039, IRF1040, IRF1041, IRF1042, IRF1043, IRF1044, IRF1045, IRF1046, IRF1047, IRF1048, IRF1049, IRF1050, IRF1051, IRF1052, IRF1053, IRF1054, IRF1055, IRF1056, IRF1057, IRF1058, IRF1059, IRF1060, IRF1061, IRF1062, IRF1063, IRF1064, IRF1065, IRF1066, IRF1067, IRF1068, IRF1069, IRF1070, IRF1071, IRF1072, IRF1073, IRF1074, IRF1075, IRF1076, IRF1077, IRF1078, IRF1079, IRF1080, IRF1081, IRF1082, IRF1083, IRF1084, IRF1085, IRF1086, IRF1087, IRF1088, IRF1089, IRF1090, IRF1091, IRF1092, IRF1093, IRF1094, IRF1095, IRF1096, IRF1097, IRF1098, IRF1099, IRF1100, IRF1101, IRF1102, IRF1103, IRF1104, IRF1105, IRF1106, IRF1107, IRF1108, IRF1109, IRF1110, IRF1111, IRF1112, IRF1113, IRF1114, IRF1115, IRF1116, IRF1117, IRF1118, IRF1119, IRF1120, IRF1121, IRF1122, IRF1123, IRF1124, IRF1125, IRF1126, IRF1127, IRF1128, IRF1129, IRF1130, IRF1131, IRF1132, IRF1133, IRF1134, IRF1135, IRF1136, IRF1137, IRF1138, IRF1139, IRF1140, IRF1141, IRF1142, IRF1143, IRF1144, IRF1145, IRF1146, IRF1147, IRF1148, IRF1149, IRF1150, IRF1151, IRF1152, IRF1153, IRF1154, IRF1155, IRF1156, IRF1157, IRF1158, IRF1159, IRF1160, IRF1161, IRF1162, IRF1163, IRF1164, IRF1165, IRF1166, IRF1167, IRF1168, IRF1169, IRF1170, IRF1171, IRF1172, IRF1173, IRF1174, IRF1175, IRF1176, IRF1177, IRF1178, IRF1179, IRF1180, IRF1181, IRF1182, IRF1183, IRF1184, IRF1185, IRF1186, IRF1187, IRF1188, IRF1189, IRF1190, IRF1191, IRF1192, IRF1193, IRF1194, IRF1195, IRF1196, IRF1197, IRF1198, IRF1199, IRF1200, IRF1201, IRF1202, IRF1203, IRF1204, IRF1205, IRF1206, IRF1207, IRF1208, IRF1209, IRF1210, IRF1211, IRF1212, IRF1213, IRF1214, IRF1215, IRF1216, IRF1217, IRF1218, IRF1219, IRF1220, IRF1221, IRF1222, IRF1223, IRF1224, IRF1225, IRF1226, IRF1227, IRF1228, IRF1229, IRF1230, IRF1231, IRF1232, IRF1233, IRF1234, IRF1235, IRF1236, IRF1237, IRF1238, IRF1239, IRF1240, IRF1241, IRF1242, IRF1243, IRF1244, IRF1245, IRF1246, IRF1247, IRF1248, IRF1249, IRF1250, IRF1251, IRF1252, IRF1253, IRF1254, IRF1255, IRF1256, IRF1257, IRF1258, IRF1259, IRF1260, IRF1261, IRF1262, IRF1263, IRF1264, IRF1265, IRF1266, IRF1267, IRF1268, IRF1269, IRF1270, IRF1271, IRF1272, IRF1273, IRF1274, IRF1275, IRF1276, IRF1277, IRF1278, IRF1279, IRF1280, IRF1281, IRF1282, IRF1283, IRF1284, IRF1285, IRF1286, IRF1287, IRF1288, IRF1289, IRF1290, IRF1291, IRF1292, IRF1293, IRF1294, IRF1295, IRF1296, IRF1297, IRF1298, IRF1299, IRF1300, IRF1301, IRF1302, IRF1303, IRF1304, IRF1305, IRF1306, IRF1307, IRF1308, IRF1309, IRF1310, IRF1311, IRF1312, IRF1313, IRF1314, IRF1315, IRF1316, IRF1317, IRF1318, IRF1319, IRF1320, IRF1321, IRF1322, IRF1323, IRF1324, IRF1325, IRF1326, IRF1327, IRF1328, IRF1329, IRF1330, IRF1331, IRF1332, IRF1333, IRF1334, IRF1335, IRF1336, IRF1337, IRF1338, IRF1339, IRF1340, IRF1341, IRF1342, IRF1343, IRF1344, IRF1345, IRF1346, IRF1347, IRF1348, IRF1349, IRF1350, IRF1351, IRF1352, IRF1353, IRF1354, IRF1355, IRF1356, IRF1357, IRF1358, IRF1359, IRF1360, IRF1361, IRF1362, IRF1363, IRF1364, IRF1365, IRF1366, IRF1367, IRF1368, IRF1369, IRF1370, IRF1371, IRF1372, IRF1373, IRF1374, IRF1375, IRF1376, IRF1377, IRF1378, IRF1379, IRF1380, IRF1381, IRF1382, IRF1383, IRF1384, IRF1385, IRF1386, IRF1387, IRF1388, IRF1389, IRF1390, IRF1391, IRF1392, IRF1393, IRF1394, IRF1395, IRF1396, IRF1397, IRF1398, IRF1399, IRF1400, IRF1401, IRF1402, IRF1403, IRF1404, IRF1405, IRF1406, IRF1407, IRF1408, IRF1409, IRF1410, IRF1411, IRF1412, IRF1413, IRF1414, IRF1415, IRF1416, IRF1417, IRF1418, IRF1419, IRF1420, IRF1421, IRF1422, IRF1423, IRF1424, IRF1425, IRF1426, IRF1427, IRF1428, IRF1429, IRF1430, IRF1431, IRF1432, IRF1433, IRF1434, IRF1435, IRF1436, IRF1437, IRF1438, IRF1439, IRF1440, IRF1441, IRF1442, IRF1443, IRF1444, IRF1445, IRF1446, IRF1447, IRF1448, IRF1449, IRF1450, IRF1451, IRF1452, IRF1453, IRF1454, IRF1455, IRF1456, IRF1457, IRF1458, IRF1459, IRF1460, IRF1461, IRF1462, IRF1463, IRF1464, IRF1465, IRF1466, IRF1467, IRF1468, IRF1469, IRF1470, IRF1471, IRF1472, IRF1473, IRF1474, IRF1475, IRF1476, IRF1477, IRF1478, IRF1479, IRF1480, IRF1481, IRF1482, IRF1483, IRF1484, IRF1485, IRF1486, IRF1487, IRF1488, IRF1489, IRF1490, IRF1491, IRF1492, IRF1493, IRF1494, IRF1495, IRF1496, IRF1497, IRF1498, IRF1499, IRF1500, IRF1501, IRF1502, IRF1503, IRF1504, IRF1505, IRF1506, IRF1507, IRF1508, IRF1509, IRF1510, IRF1511, IRF1512, IRF1513, IRF1514, IRF1515, IRF1516, IRF1517, IRF1518, IRF1519, IRF1520, IRF1521, IRF1522, IRF1523, IRF1524, IRF1525, IRF1526, IRF1527, IRF1528, IRF1529, IRF1530, IRF1531, IRF1532, IRF1533, IRF1534, IRF1535, IRF1536, IRF1537, IRF1538, IRF1539, IRF1540, IRF1541, IRF1542, IRF1543, IRF1544, IRF1545, IRF1546, IRF1547, IRF1548, IRF1549, IRF1550, IRF1551, IRF1552, IRF1553, IRF1554, IRF1555, IRF1556, IRF1557, IRF1558, IRF1559, IRF1560, IRF1561, IRF1562, IRF1563, IRF1564, IRF1565, IRF1566, IRF1567, IRF1568, IRF1569, IRF1570, IRF1571, IRF1572, IRF1573, IRF1574, IRF1575, IRF1576, IRF1577, IRF1578, IRF1579, IRF1580, IRF1581, IRF1582, IRF1583, IRF1584, IRF1585, IRF1586, IRF1587, IRF1588, IRF1589, IRF1590, IRF1591, IRF1592, IRF1593, IRF1594, IRF1595, IRF1596, IRF1597, IRF1598, IRF1599, IRF1600, IRF1601, IRF1602, IRF1603, IRF1604, IRF1605, IRF1606, IRF1607, IRF1608, IRF1609, IRF1610, IRF1611, IRF1612, IRF1613, IRF1614, IRF1615, IRF1616, IRF1617, IRF1618, IRF1619, IRF1620, IRF1621, IRF1622, IRF1623, IRF1624, IRF1625, IRF1626, IRF1627, IRF1628, IRF1629, IRF1630, IRF1631, IRF1632, IRF1633, IRF1634, IRF1635, IRF1636, IRF1637, IRF1638, IRF1639, IRF1640, IRF1641, IRF1642, IRF1643, IRF1644, IRF1645, IRF1646, IRF1647, IRF1648, IRF1649, IRF1650, IRF1651, IRF1652, IRF1653, IRF1654, IRF1655, IRF1656, IRF1657, IRF1658, IRF1659, IRF1660, IRF1661, IRF1662, IRF1663, IRF1664, IRF1665, IRF1666, IRF1667, IRF1668, IRF1669, IRF1670, IRF1671, IRF1672, IRF1673, IRF1674, IRF1675, IRF1676, IRF1677, IRF1678, IRF1679, IRF1680, IRF1681, IRF1682, IRF1683, IRF1684, IRF1685, IRF1686, IRF1687, IRF1688, IRF1689, IRF1690, IRF1691, IRF1692, IRF1693, IRF1694, IRF1695, IRF1696, IRF1697, IRF1698, IRF1699, IRF1700, IRF1701, IRF1702, IRF1703, IRF1704, IRF1705, IRF1706, IRF1707, IRF1708, IRF1709, IRF1710, IRF1711, IRF1712, IRF1713, IRF1714, IRF1715, IRF1716, IRF1717, IRF1718, IRF1719, IRF1720, IRF1721, IRF1722, IRF1723, IRF1724, IRF1725, IRF1726, IRF1727, IRF1728, IRF1729, IRF1730, IRF1731, IRF1732, IRF1733, IRF1734, IRF1735, IRF1736, IRF1737, IRF1738, IRF1739, IRF1740, IRF1741, IRF1742, IRF1743, IRF1744, IRF1745, IRF1746, IRF1747, IRF1748, IRF1749, IRF1750, IRF1751, IRF1752, IRF1753, IRF1754, IRF1755, IRF1756, IRF1757, IRF1758, IRF1759, IRF1760, IRF1761, IRF1762, IRF1763, IRF1764, IRF1765, IRF1766, IRF1767, IRF1768, IRF1769, IRF1770, IRF1771, IRF1772, IRF1773, IRF1774, IRF1

cells will be viably frozen for future validation of RNA seq data. Plasma will be used for measurement of cytokines and other inflammatory proteins.

Tissue analysis (research assistant, surgeon): Special attention will focus on obtaining samples of tissues from standardized anatomic locations, representing entheses, joint margins and synovial lining, and synovial tissue will be collected intra-operatively from standardized anatomic sites, (fovea and capsular reflection). The tissue specimens obtained from these locations will be taken directly to the Histopathology lab and divided into three aliquots. As discussed with Dr. DiCarlo, all processing in Pathology will be performed by the study Research Assistant under the direct supervision of the study pathologist or representative.

- a. The first aliquot will be frozen and sectioned for staining with H&E for tissue identification and for any later processing that might require fresh-frozen tissue. The frozen tissue block (minimum 0.5 cm in diameter) will be preserved in the cryomold and taken to Crow lab for storage in freezer (-80°C).
- b. The second aliquot will be stored fresh in a tube with RNAlater and will be brought by a research assistant to The Rockefeller University Collaborative Research Center to be used for RNAsequencing. The sample will be frozen and subsequently thawed and RNA will be extracted using the Trizol Plus RNA purification system (Life Technologies). RNA will be reverse transcribed and a cDNA library will be generated and sequenced on a HighSeq 2500. Data will be processed by filtering, genome mapping with STAR, and raw read counts will then be processed with edgeR for differential gene expression comparing synovial samples from patients who flared to those who did not flare in 6 weeks of follow up.
- c. The third aliquot will be processed in the HSS pathology laboratory for fixation, paraffin embedding and sectioning, and standard of care H+E staining.
- d. The fourth aliquot will be processed in the Ivashkiv and Pernis laboratories to isolate live synoviocyte cells. Specifically, a fragment of synovial lining (~2 cm³ or greater) will be diced into smaller fragments and cells dislodged from the matrix by mechanical force and/or enzymatic digestion. The resulting single cell suspensions will be stained for cell-type specific surface markers and sorted by flow cytometry. In particular, T and B cell, monocyte and fibroblast populations will be collected. Downstream analyses include various next-generation sequencing protocols, which assay for gene expression levels and epigenetic features. The goal of this procedure is to identify cell populations or intracellular pathways found directly within the diseased tissue that associate with other disease parameters
- e. From the remaining tissue, HSS pathology will conduct fixation, paraffin embedding, sectioning, and standard of care histopathologic examination.

At least 2 formalin-fixed paraffin-embedded tissue blocks will be taken and kept in pathology department. (RA will record pathology accession number)

Additional processing of aliquot #1 will include staining for a panel of cytokines known to characterize the presence/recruitment of specific T cell subsets, particularly TH17 and TH1 cells (IL-17, IL-21, IFN γ and CCL20) as well as the activity state of the ROCK pathway (e.g. by staining for pERM a well-established

target of Rock activity and by staining with newly developed antibodies against phosphorylated ROCK2, IRF4 and IRF8). The expression of these molecules will be further confirmed in the second aliquot after extracting RNA and subjecting the samples to QPCR analysis. Staining for the expression/activity these molecules in fresh-frozen tissues will only be performed if staining in the formalin-fixed paraffin-embedded tissues (aliquot #3) is not successful.

Samples will then be brought to the Pernis lab and subjected to immunofluorescence / immunohistochemical analysis to investigate the expression/function of the signaling components that might be implicated in RA pathogenesis. In particular these studies will assess the composition of the inflammatory infiltrates, the activation state of distinct cellular subsets, and the activity of the ROCK pathway. The activation state of distinct cellular subsets, and the activity of the ROCK pathway (e.g. by staining for pERM a target of Rock activity).

PARTICIPANT SURVEY

New form location
1-9: Preliminary Flare Questionnaire
10. Did you have PT this week?
11. Did you miss PT this week?
12-14. RAPID3 (MDHAQ + pain global + PtGA)
15. RADAI pain
16. Aches & pains that feel like you are getting a cold

This information will be completed by whichever method the participant prefers: telephone or using the e-mail survey function on REDCap.

PARTICIPANT OFFICE VISIT

New form location
1. AM stiffness: no/yes à how long?
2. Aerobic exercise
3. Patient-reported disease activity
4. HAQ unusual fatigue or tiredness
5. HAQ difficulty sleeping
6. Replaced/permanently damaged joints

1.

HOOS/KOOS

COORDINATOR INTAKE

New form location
1987 criteria
2010 criteria
1. Enrolled at PSS vs surgery
2. Date of surgery
3. DOB
4. Sex
5. Surgical joint
6. Weight
7. Height
8. ESR
9. CRP
10. ACPA status
11. RF status
12. Intra-op steroids: yes/no
13. Metal implants?
14. MD 28 joint count
15. MD Global
16. NSAID status

17. Opioid use
18. Current steroid use
19. Current methotrexate use
20. Current non-MTX DMARD use
21. Current biologic use
22. Current statin use
23. Current ACE inhibitor use
24. Current ARB inhibitor use
25. Therapies that have been tried & stopped

COORDINATOR OFFICE VISIT FOLLOW-UP

New form location
1. ESR
2. CRP
3. MD 28 joint count
4. Patient-reported disease activity
5. NSAID status
6. Opioid use
7. Current steroid use
8. Current methotrexate use
9. Current non-MTX DMARD use
10. Current biologic use
26. Current statin use
27. Current ACE inhibitor use

28. Current ARB inhibitor use

Whole blood samples (3x 10mL) will be drawn from each subject, for the ROCK analysis conducted at HSS.

Follow-up office visits will be conducted 6-weeks and 1 year post-op.

Home-Visit Blood Tests (in the event that blood was not drawn at routine visits, and with patient consent):

Biologic data (blood draw): ESR and CRP

(Note: Apex will **not** draw "green-top" whole-blood samples for analysis at HSS.)

2.0 Who will collect the data:

Sarah	Grond	
Anh	Hoang	
Uma	Chandrasekaran	Postdoc
Mark	Phillips Figgie, MD	
Daisy	Crego	
Reena	Khianey Maharaj	
Serene	Mirza	
Shirin	Dey	
Alessandra	Pemis, MD	Senior Scientist
Ryan	Cummings	
David	Mayman, MD	
Susan	Goodman, MD	MD
George	Kalliolias, MD PhD	PhD
Edward	DiCarlo, MD	Pathologist
Caroline	Reidy	Manager
Edd	Ricker	
Sanjay	Gupta	Research Associate
Michela	Manni	Post doctoral Fellow
Michael	McNamara	Research Assistant
Vivian	Bykerk, MD	Attending Physician
Woelsung	Yi, PhD	Research Assoc.
Cristina	Rozo, Ph.D.	
Dana	Orange, MD	Assistant Attending
Lisa	Mandl, MD	Physician\Assistant Professor in Medicine

3.0 When the data will be collected? Include timing of visits(either SOC or specifically for the study).

See attached data collection forms including

4.0 From what source:

Medical Records
Radiographic
Patient

Yes Private Office Charts Please specify which private office: Goodman; Alexiades, Bostrom, Cornell, Figgie, Gonzalez Della Valle, Mayman, Pellici, Salvati, Sculco, Su

No Registries Please specify which registry:

☐ Other Please specify:

[Help](#)

ID: 2014-233

View: 2.8 General Methods and Procedures

[Help](#)

General Methods and Procedures

1.0 * Are controls included in the study? Yes

1.1 If yes, describe how they will be matched with the study subjects; state whether the controls will have identical data recorded, or describe any differences compared to the intervention subjects.

The cohort will include RA patients who do not flare and OA patients as our comparator groups.

2.0

* Are all tests Standard of care? No

If not, identify which tests are not standard of care. What source of funds will be used to pay for them (text box below):

None of the experimental tissue or serum sample collection is standard of care. They will be paid for by the Pernis lab and Darnell lab. Radiographs are standard of care.

RF, CRP, ESR, and ACPA- are standard of care, as they may help determine therapy in patients who flare. However, results are not always available on all TJR patients We will apply for funding through the CTSC for missing labs to pay for CRP, ESR, RF and ACPAs.

3.0 * Will surveys/questionnaires be used? Yes

4.0 * Does the study involve randomization? No

5.0 * Does your study included Placebo or No-Treatment Arm? No

6.0 * Does your study included Washout of Previous Medication? No

7.0 Data collection sheet should be created for the study and uploaded:

Name	Version
Research Authorization Form	0.01

[Help](#)

ID: 2014-233

View: 2.83 Surveys and Questionnaires

[Help](#)

Surveys & Questionnaires

1.0 Please add all survey instruments and questionnaires to be used in this study:

Name Standard Instrument Upload Instrument Usage of Instrument
There are no items to display

ID: 2014-233

View: 2.11 Sample Size and Data Analysis

[Help](#)

Sample Size and Data Analysis

If you are uncertain about how to calculate your sample size and determine appropriate data analysis, please contact the Epidemiology and Biostatistics Core at biostats@hss.edu for assistance in completing this section.

1.0 Is this is a case series based only on the patients available using descriptive statistics in lieu of a sample size calculation?

* No

ID: 2014-233

View: 2.11.1 Sample Size

[Help](#)

[Help](#)

Sample Size and Data Analysis

Support estimates with evidence from the literature of prior studies and perform an appropriate sample size calculation.

For hypothesis testing (e.g., the calculation of p-values using statistical tests), you need to estimate your available sample size and calculate the effect size that will be detectable using your proposed statistical analysis plan. This also applies to a case series where you plan hypothesis testing.

1.0 If you have consulted with a statistician, please indicate their name:

Wei-Ti Huang

2.0 Proposed sample size analysis, include the following:

- Student's t-test, ANOVA, chi-square, regression, etc;
- Alpha level;
- Beta or power level;
- Primary outcome variable estimate (mean +/-s.d. for continuous outcome, frequency/percentage for categorical variable);

- **Number of groups being compared (use 1 for paired analysis within the same subjects);**
- **Effect size or change expected between groups;**
- **Resulting number per group**

Sample Size

- The primary outcome is rate of RA flare within 6 weeks of surgery
- Based on data quoted above we have chosen a conservative estimate of flare as 26%.

Ho: within 6 weeks we have a flare rate for RA patients=0.26

Ha: within 6 weeks the flare rate is different from 0.26(=0.1 0.15 0.2)

Power Analysis of One Proportion

Numeric Results for testing H0: P = P0 versus H1: P <> P0

Test Statistic: Exact Test

		Proportion Given H0	Proportion Given H1	Target	
Actual		(P0)	(P1)	Alpha	
Power Alpha	N Beta				
0.8143 0.1857	47	0.2600	0.1000	0.0500	0.0445
0.8036 0.1964	109	0.2600	0.1500	0.0500	0.0387
0.8017 0.1983	394	0.2600	0.2000	0.0500	0.0445

Report Definitions

Power is the probability of rejecting a false null hypothesis. It should be close to one.

N is the size of the sample drawn from the population.

To conserve resources, it should be small.

Alpha is the probability of rejecting a true null hypothesis. It should be small.

Beta is the probability of accepting a false null hypothesis. It should be small.

P0 is the value of the population proportion under the null hypothesis.

P1 is the value of the population proportion under the alternative hypothesis.

Summary Statements

A sample size of 47 achieves 81% power to detect a difference (P1-P0) of -0.1600 using a

two-sided binomial test. The target significance level is 0.0500. The actual significance level

achieved by this test is 0.0445. These results assume that the population proportion under the

null hypothesis is 0.2600.

Power Analysis of One Proportion

Chart Section



We are estimating the rate of the flare rate in RA post-arthroplasty based on previous data. However, if our estimates are wrong, we may be grossly underpowered. Therefore, an interim analysis is planned, when we have collected 25 RA patients to ensure we are adequately powered to detect the primary outcome of flare as previously defined.

- Alpha level: 0.05
- Beta or power level: 0.8 (80%)
- Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable):

The primary outcome is rate of RA flare within 6 weeks of surgery. Since it's a rate, no mean and s.d. are available.

- Number of groups being compared (use 1 for paired analysis within the same subjects):

2 groups: RA – Flare vs. Non-Flare group for secondary outcome.

- Effect size or change expected between groups:

The expected effect size between the flare and non-flare group is 16%, but the interim analysis will be performed after we collect 50 patients.

- Resulting number per group:

47 with effect size 16% (0.25-0.10) overall.

109 with effect size 11% (0.25-0.15) overall.

394 with effect size 6% (0.25-0.20) overall.

- Total sample size required:

47 patients will provide an adequate sample size to evaluate the primary outcome and enable explorations for the secondary outcomes in this study. It is anticipated that 20% will drop out of the study thus we will need to recruit 57 patients to this study to adequately study the primary and secondary outcomes in this study.

References

Chow, S.C.; Shao, J.; Wang, H. 2003. Sample Size Calculations in Clinical Research. Marcel Dekker. New York.

Fleiss, J. L., Levin, B., Paik, M.C. 2003. Statistical Methods for Rates and Proportions. Third Edition. John

Wiley & Sons. New York.

Lachin, John M. 2000. Biostatistical Methods. John Wiley & Sons. New York.

Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd

Edition. Blackwell Science. Malden, Mass.

Zar, Jerrold H. 1984. Biostatistical Analysis (Second Edition). Prentice-Hall. Englewood Cliffs, New Jersey.

3.0

Data Analysis: describe how the primary outcome will be analyzed and what types of statistical calculations will be used. Do the same for each secondary outcome. Reiterate briefly the main analysis to be done, which groups, which variables, possible confounders. Address how possible confounders will be identified and handled in analysis:

For the Primary Outcome:

Descriptive statistics (rates and proportions, frequency distributions, means, medians, standard deviations and inter-quartile ranges) will be used to describe the baseline data. The two-tailed unpaired Student's t test, or Kruskal-Wallis tests will be performed to evaluate differences in continuous variables between groups (Flare vs. non-Flare group), depending on the distribution of the data, and the Scheffe or Bonferroni multiple comparisons test will be used for multiple comparisons. Chi-Square or Fisher's exact test will be utilized here to compare proportions between groups. Logistic regression will be performed for the HOOS and KOOS score to adjust for potential confounders and effect modifiers.

All secondary outcomes are exploratory.

Pending the distributions of the data, in aim 2 we will evaluate the standard mean difference or effect size for each domain (WOMAC, DAS-28, Flare questionnaire (pain, Pt global, stiffness, fatigue, coping, participation, Pt reported TJC, SJC) in patients who flare vs. those who do not based on criteria of DAS28 worsening, patient reported worsening, MD global, need to initiate or escalate treatment. We would also explore differences in long term WOMAC scores and biomarkers stratifying by flare and adjusting for unknown confounders including baseline function, age, sex, and co-morbidity score. Standard statistical tests will be used.

In aim 3 we will examine a limited number of predictors of flare within 6 weeks using appropriate statistical methods by using a generalized estimating equation and will adjust for unrecognized confounders/effect modifiers including long term WOMAC scores, baseline function, age, sex, and co-morbidity score, and biomarkers stratifying by flare. Standard statistical tests will be used.

In aim 4 we aim to determine how patients who flare meet physical therapy milestones including walking distance, and ADLs, in comparison to patients who do not flare. The evaluation of meeting physical therapy milestones is exploratory. Physical therapy milestones are routinely evaluated as post-op TJA measures and are done weekly. We will examine the distributions of change for each covariate recorded by physical therapy and compare changes in each domain stratified by flare vs. no-flare.

A potential analytic plan depending on distribution of the final data to assess PT milestones will include:

Physical therapy milestones will be assessed based on the questionnaire and analyzed as outlined below: patient VAS: continuous variable- ranging from 0 ~100, analyzed with T-test or regression

Change will be analyzed by

- 1- ANCOVA and study of change
- 2- GEE and treat delta as our continuous outcome

Walking distance: Ordinal variable - Chi-square, fisher exact

Stairs/Transfers/Activities/Driving/Employed: Nominal- Chi-square, fisher exact

We will also explore whether or not the meeting of PT milestones impacts pain and function at 1 year using the HOOS/KOOS. We will treat PT milestones as a binary and WOMAC outcomes will be analyzed as predictors.

In aim 5 and 6 we will compare levels of serum and tissue biomarkers between RA who flare and RA who do not flare using T-tests or chi-square tests, as appropriate. We will correlate self-report functional scores and biomarkers with the development of flare using Spearman correlations.

After sequencing, the reads will be processed by the New York Genome Center in a dedicated RNA-Seq pipeline, consisting of ribosomal RNA filtering, genome mapping with STAR, various QC metrics obtained with picard tools and transcript quantification with HTSeq-count. The raw read counts will then be processed with one of the Bioconductor package for Differential Gene expression (DESeq, edgeR, or limma/voom).

[Help](#)

ID: 2014-233

View: 2.4 Consent Information

[Help](#)

Consent Information

1.0 Describe how, when, and where the consent process will be initiated:

If possible, before coming in to the hospital (either for a pre-operative visit or their surgery), patients will be called by a research team member to discuss the study and evaluate their interest in participating. Patients who are interested will then be consented prior to surgery by the study research assistant or their treating surgeon, or rheumatologist either in the office, in pre-surgical screening, or in the pre-op holding area. If convenient, patients can additionally review the study protocol with the coordinator over the phone, but they will always be consented in person. The consent will be placed in the patients' hospital chart.

In the event that a potential participant requires a translator and is scheduled to have surgery on a weekend, a co-investigator of the research study can contact the potential participant prior to the day of their surgery and consent the patient over the phone. The Hospital for Special Surgery's Language Services Phone Interpreter or in-house employee will translate the Informed Consent to Participate in a Research Study Involving Genetic Testing, the Short Form Consent, and the Research Authorization Form. The translator would function as the witness to the consenting process. If the participant agrees to enroll, the participant will sign these forms in person on the day of their first study visit.

In the event that patients are unable to give study blood at one of their routine follow-up visits, we will be calling them to ask whether they would consider having Apex Laboratory, Inc. visit them in their home to draw blood for lab tests. If they express interest, an additional consent form will be mailed to them. They will have the opportunity to consider this form at home, and are encouraged to call study coordinators to discuss any questions or concerns. The form is to be completed by patients and mailed back to HSS using and included prepaid envelope.

2.0 Who will obtain informed consent from subjects for this research?

First Name	Middle Name	Last Name	Title
Sarah		Grond	
Anh		Hoang	
Mark	Phillips	Figgie, MD	
Daisy		Crego	
Serene		Mirza	
Shirin		Dey	
David		Mayman, MD	

First Name	Middle Name	Last Name	Title
Susan		Goodman, MD	MD
Michael		McNamara	Research Assistant
Vivian		Bykerk, MD	Attending Physician

[Help](#)

ID: 2014-233

View: 3.0 IRB Application

[Help](#)

IRB Application

1.0 Please provide lay abstract:

The condition to be studied is worsening (flare) of rheumatoid arthritis (RA) in patients who have undergone arthroplasty. RA patients undergoing arthroplasty most often have severe, erosive disease. If the rate of flare approaches the estimated 26% rate suggested in a previous study for RA patients after arthroplasty (*Johnson ACR 2011*), this could be of significance in regards to their long term arthroplasty and disease outcomes. Patients who flare may not be able to participate in the post-operative rehabilitation thought necessary for optimal arthroplasty outcomes, and it may be difficult for patients who flare after discontinuing immunosuppressant medications for surgery to regain remission or low disease activity. Detailed clinical data collected longitudinally from RA patients with severe erosive disease undergoing arthroplasty in conjunction with further characterization of the molecular profile of blood and operative tissue could provide valuable information to inform best practices for this patient group.

2.0 * Requested Review Type:

Expedited

3.0 Ancillary/Impacted Services Review (select all that apply):

Note: Do not confuse the committees below with CRP or Research Service Chief

Ancillary Committees

There are no items to display

4.0 * Is Genetic Testing involved in this study? Yes

ID: 2014-233

View: 3.12 Expedited Qualification

[Help](#)

Expedited Qualification

If you check any of the items below, the study is qualified for EXPEDITED review status under federal guidelines.

1.0 * Select all that apply:

Question

- ☐ 1. Clinical studies of drugs and medical devices only when: (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review). OR (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Question

- ☒ 2. This research involves only the collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from healthy, non-pregnant adults or children where the amount of blood and frequency does not exceed federal regulations for normal clinical care.
- ☐ 3. This research involves prospective collection of biological specimens for research purposes by noninvasive means.
- ☐ 4. This research involves the collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
- ☒ 5. This research involves materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes.
- ☐ 6. Collection of data from voice, video, digital, or image recordings made for research purposes.
- ☒ 7. This research will be performed on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or will employ a survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- ☐ 8. This research involves Continuing Review of study previously approved by the convened IRB
- ☐ 9. This research involves Continuing Review of study which are not conducted under an investigational new drug application or investigational device exemption where categories two through eight do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

ID: 2014-233

View: 3.2 Risk/Benefit Assessment-Risks

[Help](#)

Assessment of Research Procedures

1.0 Describe any potential for direct benefits to participants in this study:

Participants are not expected to benefit personally from this research study. Participation in this study will not provide participants with any therapeutic benefits, nor will it provide them with information regarding whether they are genetically predisposed to developing any known illnesses. This study includes drawing blood for investigational procedures, which may not give participants immediate benefit or any benefit. The knowledge gained may benefit others in the future.

2.0 Describe any potential benefits to society:

Benefits for society may include providing further information about the genetic basis of worsening of rheumatoid arthritis as well as the development of safe and effective therapies for that condition.

ID: 2014-233

View: 3.22 Minimal Risk

[Help](#)

Minimal Risk

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. This includes, but is not limited to, administration of non-invasive data collection measures, collection of blood samples, collection of existing data and observational studies

1.0

Please select the applicable tests with standard wording for risks from the list below:

Name	Description
A blood draw	The risk of participating in this study is the risk of having your blood drawn. The risks of blood drawing include mild pain, bruising, and very rarely infection at the place of the needle insertion.

☒ **Risk of breach of confidentiality, include the following:**

Participation in this research involves the potential risk of a breach of confidentiality of your health information that is stored. HSS tries to minimize those risks by (i) removing some direct identifiers from information stored [i.e. names, social security numbers, medical record numbers]; (ii) securing, in a separate location, and limiting access to information linking codes (i.e., linkage codes) assigned to the registry information with direct participant identifiers; and (iii) limiting access to information stored to HSS investigators.

2.0

*** Is any physical testing being done other than surveys, questionnaires, etc?:**

Yes

2.1 If yes, please list the testing being done and describe any potential risks:

This study involves blood draws. The risks of blood drawing include mild pain, bruising, and very rarely infection at the place of the needle insertion.

[Help](#)

ID: 2014-233

View: 3.3 Informed Consent Determination

[Help](#)

Informed Consent

1.0

Indicate the types of consent that will be involved in this study (check any or all that apply):

Informed Consent Category
Written/signed consent by subject

2.0

Waivers: If you are applying for any waivers of consent (check any or all that apply):

Name
<input type="checkbox"/> Waiver of Consent
<input type="checkbox"/> Waiver of Assent
<input type="checkbox"/> Waiver of Parental Permission
<input type="checkbox"/> Waiver of Written or Signed Consent (i.e. information sheets, telephone consent, verbal script)

3.0 * Will this study include non-english speaking participants?

Yes

4.0 If the study does not include non-english speaking participants, please justify:

We do not have the personnel available to translate the study documents or obtain consent in any languages other than English and Spanish.

5.0 Please provide assurance by checking the box below that the study will make all possible efforts to collect Federally mandated gender, race and ethnicity data for all subjects included in the study.

☒ Agree

☐ This will not be possible for the following reasons:

6.0 Will this study be posted at ClinicalTrials.gov?

☒ Yes ☐ No

If yes, please post at the site upon approval of the study by the IRB. ClinicalTrials.gov requires that listings be updated every 12 months as well as 30 days after Major Amendment approvals of a protocol. For more information about what studies should be posted at the site and when to update a posted study at the site, please visit the following website:

http://www.icmje.org/faq_clinical.html

ID: 2014-233

View: 3.31 Consent Forms & Process of Consent

[Help](#)

Consent Forms & Process of Consent

1.0 Good News! We've prepared several different types of consent form templates with some of the information you have already provided. Please follow the instructions below to complete the process.

[Lay term
Glossary](#)

Instructions:

1.1) Download the applicable consent form(s) to your machine and modify as appropriate. Save the modified documents and upload them in the following question.

 [Assent Form For Adolescent Participation In Research Study](#)

 [Informed Consent To Participate In A Genetic Research Study](#)

 [Informed Consent To Participate In Research](#)

 [Informed Consent To Participate In Research Registry](#)

1.2) Please upload all informed consents, waivers, translated documents, phone recruitment scripts, recruitment ads, brochures, etc to be used in this study.

Name	Modified	Version
FLARE ICF NEWEST.doc	8/24/2016 12:31 PM	0.01

ID: 2014-233

View: 3.32 Non-English Speaking Participants

[Help](#)

Non-English Speaking Participants

- 1.0 * Select the process of how you will explain the study and assure that the Non-English speaking subjects understand the study and their participation in research.**

Translator and Translated Short Form Consent

For example, the use of translators, translated informed consent documents, short forms, and any other methods that would be taken.

- 2.0 * Please indicate the method of translation.**

Note: You may use the Translator Language Line to provide translation in conjunction with the appropriately translated short form document.

If the study will likely include subjects and families for whom English is not the primary language, the consent documents must be translated into the participant's language.

- 3.0 If the research will primarily include subjects who speak a language other than English, the informed consent documents should be translated into that language. Please indicate the language(s) and method of translation.**

ID: 2014-233

View: 3.6 Data Privacy & Confidentiality

[Help](#)

Data Privacy & Confidentiality

- 1.0 How will the data for this study be collected and recorded?**

Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by Dr. Goodman and co-investigators and accessible only to the principal investigator (Dr. Goodman), in

addition to other IRB-approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number) will be maintained in a different password-protected database (REDCap), separately from the data. Immediately following data entry into the password-protected databases, the paper-based data collection instruments will be stripped of all personal identifiers and stored in a locked file cabinet maintained by Dr. Goodman. The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

Presentations and publications that result from this study will NOT contain any individual identifiers other than unique study numbers.

Data will be collected and managed using REDCap (Research Electronic Data Capture), electronic data management tools hosted by the Clinical and Translational Research Center (CTSC) at Weill Cornell Medical College Clinical and Translational Science Center and funded by the NIH. REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry 2) audit trails for tracking data manipulation and export procedure 3) automated export procedures for seamless data downloads to common statistical packages and 4) procedures for importing data from external sources. REDCap will allow us to maintain a HIPAA compliant database for all data.

Any hard copy data will be entered into REDCap by an IRB approved study investigator and then checked for data entry accuracy by a different investigator.

2.0 Select Data Recording Identifiers used on this study:

Name

De-identified

2.1 If Other is selected, please specify:

3.0 Where will the research data be stored? Please specify the physical location and how it will be secured to protect confidentiality:

Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by Dr. Goodman and co-investigators and accessible only to the principal investigator (Dr. Goodman), in addition to other IRB-approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number) will be maintained in a different password-protected database (REDCap), separately from the data. Immediately following data entry into the password-protected databases, the paper-based data collection instruments will be stripped of all personal identifiers and stored in a locked file cabinet maintained by Dr. Goodman. The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

4.0 Who, other than the specified study team, will have access to the study records or data? Specify their name, role, and affiliation.

Do not list study personnel

*already listed in
Section 1:*

The information about participant's samples and clinical data will be stored in a password protected database. This will be used by the research team and those others as approved by the Hospital for Special Surgery Institutional Review Board. The research team includes and is not limited to collaborating scientists at: (i)The Hospital for Special Surgery, (ii)Rockefeller University, and (iii) other centers that are part of the NIH-funded AMP (Accelerating Medicines Partnership) Study. The AMP study is examining the role of proteins and genes involved in the biology of inflammation and bone formation in RA.

5.0 If coded or identified data will be released, specify the persons/agencies to whom the information will be released. Please also indicate the provisions that will be taken to assure that the transmission of the data will maintain confidentiality:

6.0 Describe what will happen to the data or data set when the study is completed. Please indicate your plans for the destruction of identifiers at the earliest opportunity consistent with the conduct of the research and/or clinical needs, if applicable:

The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

7.0 If audio/video recordings or photographs will be used, specify your plans for deidentifying or anonymizing the material and when it will be destroyed:

8.0 Describe the data management software that will be used. Identify who will enter the data, and what data quality control measures will be used, such as dual entry, validation checks and locked fields. Insure that your plans are consistent with HIPAA regulations. Contact Ms. Andrea Ansorge with any questions related to HIPAA regulations and research.

Data will be collected and managed using REDCap (Research Electronic Data Capture), electronic data management tools hosted by the Clinical and Translational Research Center (CTSC) at Weill Cornell Medical College Clinical and Translational Science Center and funded by the NIH. REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry 2) audit trails for tracking data manipulation and export procedure 3) automated export procedures for seamless data downloads to common statistical packages and 4) procedures for importing data from external sources. REDCap will allow us to maintain a HIPAA compliant database for all data.

Any hard copy data will be entered into REDCap by an IRB approved study investigator and then checked for data entry accuracy by a different investigator.

9.0

Describe the measures that will be used to preserve confidentiality and rights of subjects.

Below is Hospital for Special Surgery standard accepted practice. By completing this information, you attest that you will follow this procedure for preserving the confidentiality and rights of the subject. You can use the following standard, approved statement.

9.1 If the HSS statement does not apply, please revise it accordingly.

Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by Dr. Goodman and co-investigators and accessible only to the principal investigator (Dr. Goodman), in addition to other IRB-approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number) will be maintained in a different password-protected database (REDCap), separately from the data. Immediately following data entry into the password-protected databases, the paper-based data collection instruments will be stripped of all personal identifiers and stored in a locked file cabinet maintained by Dr. Goodman. The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

Presentations and publications that result from this study will NOT contain any individual identifiers other than unique study numbers.

ID: 2014-233

View: 3.61 Certificate of Confidentiality

[Help](#)

Certificate of Confidentiality

Certificates of Confidentiality constitute an important tool to protect the privacy of research study participants. They are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative or other proceeding, whether at the federal, state or local level.

Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to participants.

For more information, go to the following website:

<http://grants.nih.gov/grants/policy/coc/index.htm>

- 1.0 * Will a Certificate of Confidentiality be obtained for this study?
No

[Help](#)

ID: 2014-233

View: 3.7 HIPAA

[Help](#)

HIPAA

The Healthcare Insurance Portability and Accountability Act (HIPAA) prohibits the use of a person's Protected Health Information without a valid authorization.

1.0 * Will this study record any information which can identify the participants of this study?

Yes

2.0 * Will this study record information that if released, could reasonably place participants at risk of criminal or civil law suits?

No

3.0 * Will this study obtain or review information related to the respondent's medical records or health?

Yes

4.0

[HIPAA Waiver
Flow Chart](#)

Select the option(s) which fits this study:

Name

Self reported medical information

Waiver of authorization requested (Full / Partial / Alteration)

ID: 2014-233

View: 3.71 Waiver of HIPAA Authorization

[Help](#)

Waiver of HIPAA Authorization

Pursuant to the Privacy Regulations of HIPAA, an IRB is **only** permitted to approve a waiver of individual subjects' authorization if it finds and documents specific criteria relevant to the protection of subject privacy.

1.0

I am seeking:

☐ A **full waiver** of subject authorization to use and disclose health information during the course of the research study.

☒ A **partial waiver** of subject authorization to use and disclose health information only for the purpose of:

Pre-operative identification and recruitment through the use of PS Reporter, MMF, Clinstar, or other patient records and from the Total Hip/Total Knee Replacement Patient Education Class. Information

such as e-mail addresses, and phone numbers will be collected post-operatively.

☐ The following alteration to the authorization requirements:

- 2.0 *** Who will have access to the health information needed for the study? Please identify each person by name or category. Example include: the investigator, the research staff, co-investigators and their research staffs, and all research monitors.**

All co-investigators approved on the IRB protocol

- 3.0 *** Please describe the risks to privacy presented by the research and whether the research presents more than minimal risk of harm to subjects' privacy. Include a description of what identifiers will be reviewed, collected, and stored; who will have access to identified information; how access to study data is controlled; who will monitor access to study data; and where data will be stored:**

Patient files will be reviewed to determine the presence of rheumatoid arthritis. Identifiers that will be reviewed: name, address, telephone number, medical record number, date of birth, type of procedure, operating surgeon, race/ethnicity, laterality, zip code, admission date, gender.

Subject information will only be accessible to study co-investigators as listed on the IRB protocol. All information will be stored in locked file cabinets and password protected computer files to which only the approved research personnel have access. Access to the study data will be monitored by the Principal Investigator, Dr. Susan Goodman.

- 4.0 *** Can the research be practicably carried out without the waiver?** ☐ Yes ☒ No

If it is impracticable to obtain individual authorization, please describe **why**:

The waiver is necessary in order for the investigators to identify and recruit potential subjects with rheumatoid arthritis.

- 5.0 *** Can the research be practicably carried out without access to and use of identified health information?** ☐ Yes ☒ No

If it is impracticable to conduct this research without access to identified health information, please describe **why**:

Patients' health information must be viewed in order to determine if they meet the inclusion criteria to be eligible for the study.

6.0 * What is your plan to protect identifiers from improper use and disclosure?

The data listed in this waiver will be maintained in locked file cabinets and in password-protected computer files to which only the approved research personnel have access. All research personnel with access to information covered by this waiver are informed of the IRB, HIPAA, and ethics regulations governing research involving human subjects and are under the supervision of the Principal Investigator.

7.0 * Will the patient identifiers be destroyed at the earliest opportunity? ☒ Yes ☐ No

If **yes**, describe the plan for destroying identifiers (e.g. how, by whom, and when identifiers will be destroyed):

Any page containing patient identifiers will be destroyed by Dr. Goodman at the earliest opportunity upon completion of the study.

If **no**, indicate the health or research justification for retaining the identifiers:

8.0 * Explain how PHI will be acquired and used:

A Recruitment Flyer will be placed in the dictation cubbies and exam rooms of participating surgeons. If a patient with a possible or previous diagnosis of RA schedules an arthroplasty, members of the surgeon's office will send the patient information to the Research Staff using either the study e-mail address, FlareStudy@hss.edu, or other secure forms of communication. Patients will be identified pre-operatively by their treating surgeon or identified by screening patients' records prior to their pre-operative visit. They will receive a Study Overview Sheet (see attached) either in the office, in the mail, or on the day of surgery. They will have the opportunity to discuss any questions with the research assistant/ research team member who will ensure they meet study criteria (see screening sheet). In addition, patients may be identified and recruited from the Total Hip /Total Knee Replacement Patient Education Class by the research assistant. Finally, research assistants may use PS Reporter, MMF, or Clinstar to identify patients before their pre-surgical screening visit, or prior to their surgical procedure. We will request an IRB approved Waiver of HIPAA Authorization.

9.0 Explain how PHI will be protected during this study:

☐ Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by the PI and accessible only to the principal investigator, in addition to other IRB approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number, etc...) will be maintained in a different password protected database maintained by to which only will have access.



Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by Dr. Goodman and co-investigators and accessible only to the principal investigator (Dr. Goodman), in addition to other IRB-approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number) will be maintained in a different password-protected database (REDCap), separately from the data. Immediately following data entry into the password-protected databases, the paper-based data collection instruments will be stripped of all personal identifiers and stored in a locked file cabinet maintained by Dr. Goodman. The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

10.0 * Justify your need to collect PHI on this study:

The waiver is necessary in order for the investigators to identify and recruit potential subjects with rheumatoid arthritis.

Patients' health information must be viewed in order to determine if they meet the inclusion criteria to be eligible for the study.

[Help](#)

ID: 2014-233

View: 3.72 HIPAA PHI Identifiers

[Help](#)

PHI Identifiers

1.0

Identify the types of PHI collected:

Name



Questionnaires or Interviews



Billing Information or Databases



Mental Health Records



Data Registry



Hospital or Medical Records



Biological Samples



DNA Samples

Name

☐ Other

1.1 If Other, please specify the type of PHI collected:

2.0

Select all the PHI Identifiers that apply:

Identifiers

Names

All geographic subdivisions smaller than a state:

Telephone Numbers

E-mail Addresses

Medical Record numbers

All elements of dates (except year) for dates related to an individual:

ID: 2014-233

View: 3.8 Data Safety Monitoring Plan

[Help](#)

Data Safety Monitoring Plan

1.0 * Check the one box below that most accurately reflects the plan for data and safety monitoring for this study.

The study will be monitored only by the study investigators and/or sponsor.

1.1 If Other, Please specify your plan for data safety and monitoring for the study. If no DSMB required, Please specify why:

2.0 Describe the clinical criteria for withdrawing an individual subject from the study due to safety or toxicity concerns:

3.0 Summarize any pre-specified criteria for stopping or changing the study protocol due to safety concerns.

4.0 * Are there any plans to perform an interim efficacy analysis:
No

4.1 If you answered Yes, please describe the plans to conduct an interim analysis.

ID: 2014-233

View: SF - Final Page

[Help](#)

Final Page

You have completed your application!

Please hit "Continue" to finish the HSS Clinical Trial Form.

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must press the "SUBMIT STUDY" button in My Activities for this Study ID:2014-233.

You can track the ongoing status of your submission by logging into the study workspace.

Please feel free to contact the IRB with any questions or concerns.

ID: 2014-233

View: 9.45 HSS Clinical Trial Directory Info

Help

HSS Clinical Trial

The Clinical Trial Registry is posted on the HSS main page to highlight research (including retrospective studies) being conducted at HSS. This same language, once approved by the IRB, can then be used on flyers if you so choose, to post in an effort to recruit subjects.

- 1.0 Title:** (Periop Flare) Perioperative Flare in Rheumatoid Arthritis: Characterization of Clinical and Biological Features (Old IRB #13146)

- 2.0 PI: Susan Goodman, MD**

- ### 3.0 Co-Investigators:

First Name	Middle Name	Last Name	Title
Jonathan		Cheah	
Samantha		Lessard	
Sarah		Grond	
Theresa		Lu, MD PhD	Principal Investigator
Anh		Hoang	
Kathryn		Oi	
Mark	Phillips	Figgie, MD	
Daisy		Crego	
Douglas		Mintz, MD	
Luvana		Chowdhury	
Laura		Donlin, Ph.D.	
Joel		Correa da Rosa	
Serene		Mirza	
Danny		Flores Castro	
Ian		Cohn	
Shirin		Dey	
Yurii		Chinenov	Fellow
Xiaoning		Yuan	
Purva		Singh	
Rachel	Sima	Sealfon	
Giancarlo		Chesi	
Miguel		Otero, Ph.D.	
Phaedra		Agius	
Ellen		Gravallese, MD	
Alessandra		Pemis, MD	Senior Scientist
Keerthi	Caroline	Sadanala	Research Technician
Dalit		Ashany, MD	MD
David		Mayman, MD	
Emily		Stein, MD	
Lionel		Ivashkiv, M.D.	
Susan		Chyou	Research Technician
Edward		DiCarlo, MD	Pathologist
Pantelis		Pavlakis	Clinical Fellow

First Name	Middle Name	Last Name	Title
Ed		Purdue, PhD	Associate Scientist
Karmela		Chan, M.D.	
Bethany		Syracuse	
Caroline		Reidy	Manager
Jian		Zhou	
Edd		Ricker	
Sanjay		Gupta	Research Associate
Olga		Troyanskaya	
Michela		Manni	Post doctoral Fellow
Michael		McNamara	Research Assistant
Vivian		Bykerk, MD	Attending Physician
Woelsung		Yi, PhD	Research Assoc.
Cristina		Rozo, Ph.D.	
Caroline		Jiang	
Dana		Orange, MD	Assistant Attending
Victoria		Yao	

4.0

Posting date:

Name

Upon IRB approval

☐ Post on this date:

5.0

Condition:

Arthritis

☐ Other:6.0 **State the summary including number of patients, enrollment period and duration of follow-up (use lay terms):**

Researchers at Hospital for Special Surgery are trying to learn more about post-operative rheumatoid arthritis (RA) "flare" or worsening of disease. Specifically this study hopes to understand RA flare after total joint replacement surgery and what the result of flaring is over the course of a year. Eligible participants will be asked a lot of questions about their RA, their mobility, etc.; we will also be drawing blood to better understand a subject's recuperation from joint replacement surgery.

We hope to learn how to better manage patients with rheumatoid arthritis when having a joint replacement. For example, if RA patients who flare are unable to participate in post-operative physical therapy and do worse one year after total knee replacement and total hip replacement, perhaps more effective treatment could be developed. The study will also help us to identify early factors that may influence long-term outcomes of joint replacements in RA patients.

Participation in this study will continue over the course of one year, and involves a total of 4 study visits and 9 phone calls as well as several blood draws. The visits and blood draws will, whenever possible, occur at the time of routinely scheduled visits. Subjects will have the opportunity to discuss any questions with the research team members, their surgeon and/or their treating rheumatologist.

7.0 State the inclusion and exclusion criteria (use lay terms):

Inclusion Criteria:

- Age > 18 ~~–75~~
- ~~• No history of anemia~~
- Patients with Rheumatoid Arthritis, Inflammatory Arthritis, or Osteoarthritis undergoing primary total hip, primary total elbow, primary total shoulder, or primary total knee replacement surgery
- Satisfy ACR/EULAR 2010 classification criteria and/or the 1987 RA criteria and be diagnosed with RA (unless IA patient or OA control).
- ~~• RAPID-3 > 6~~
- ~~• Patients are currently (or within one month of enrollment) treated with either Disease-modifying anti-rheumatic drugs ("DMARDs") or biologics.~~
- ~~Aim #6, the following additional inclusion criteria apply:~~
- ~~• Treatment with a TNF-inhibitor at preop visit~~
- ~~• ACPA+~~
- ~~• Patient lives in Manhattan, Brooklyn, Queens, or Bronx~~

Exclusion Criteria:

1. Diagnosis of any other systemic rheumatic disease (see ICD-9 codes 135.0, 136.1, 274, 279.4, 279.8, 287.0, 446.0, 446.1, 446.2, 446.21, 446.4, 446.7, 447.6, 556, 696.0, 710.0, 710.2, 710.8, 710.9, 711.1, 711.2, 713.3, 713.7, 714.0, 715.0, 716.2, 719.3, 720.0, 720.1, 720.2, 720.8, 720.9, 725)
2. Diagnosis of or crystalline arthropathy.
3. Unable to understand or read English.
4. Unable to follow the study protocol in a reliable manner.
5. Age < 18 ~~or > 75~~.
- ~~6. History of anemia by patient report at pre-operative visit.~~
- ~~7. For Aim #6 these apply~~
- ~~• Hgb < 9 on day of discharge~~
- ~~• Peri-operative stress-dose steroids~~

8.0 State the contact information for the study:

Caroline Reidy, MPH
reidvc@hss.edu
646.714.6307

Help



electronic Clinical Application Portal (eCAP)

Date: Thursday, March 9, 2017 12:14:02 PM

ID: 2014-233

View: 1 - Study Identification Information

[Print](#) [Close](#)
[Help](#)

VIEW000072

Study Identification Information

This is the first step in your Human Research Application. You will automatically be guided to the appropriate forms needed to complete your submission.

1.0 Title:

(Periop Flare) Perioperative Flare in Rheumatoid Arthritis: Characterization of Clinical and Biological Features (Old IRB #13146)

* Short Title for EPIC:

Periop Flare (If Not Applicable, please enter N/A)

2.0 Description:

hip/knee/shoulder/elbow

3.0 * Principal Investigator:

Susan Goodman, MD

4.0 Study Contact:

Serene Mirza

5.0

Co-Investigators:

First Name	Last Name	Organization
Phaedra	Agius	New York Genome Center
Dalit	Ashany, MD	Rheumatology
Vivian	Bykerk, MD	Rheumatology
Karmela	Chan, M.D.	Rheumatology
Jonathan	Cheah	Fellows
Giancarlo	Chesi	Fellows
Yurii	Chinenov	Research
Luvana	Chowdhury	Soft Tissue
Susan	Chyou	Research
Ian	Cohn	Research
Joel	Correa da Rosa	Independent
Daisy	Crego	Medicine
Shirin	Dey	Medicine
Edward	DiCarlo, MD	Laboratory Medicine
Laura	Donlin, Ph.D.	Research
Mark	Figgie, MD	Arthroplasty: Hip & Knee
Danny	Flores Castro	Rheumatology
Ellen	Gravallese, MD	University of Massachusetts
Sarah	Grond	Medicine
Sanjay	Gupta	Research

If a name does not appear in Co-Investigators directory, please contact zhouy@hss.edu to have an eCAP account created.

First Name	Last Name	Organization
Anh	Hoang	Rheumatology
Lionel	Ivashkiv, M.D.	Research - Rheumatology
Caroline	Jiang	Rockefeller University
Samantha	Lessard	Tissue Engineering, Regeneration and Repair
Theresa	Lu, MD PhD	Research
Michela	Manni	Research
David	Mayman, MD	Arthroplasty: Hip & Knee
Michael	McNamara	Rheumatology
Douglas	Mintz, MD	Radiology and Imaging
Serene	Mirza	Medicine
Kathryn	Oi	Arthroplasty: Hip & Knee
Dana	Orange, MD	Rheumatology
Miguel	Otero, Ph.D.	HSS
Pantelis	Pavlikis	Neurology
Alessandra	Pemis, MD	Rheumatology
Ed	Purdue, PhD	Arthroplasty: Hip & Knee
Caroline	Reidy	Rheumatology
Edd	Ricker	Research
Cristina	Rozo, Ph.D.	Rheumatology
Keerthi	Sadanala	Research
Rachel	Sealfon	Princeton University
Purva	Singh	Tissue Engineering, Regeneration and Repair
Emily	Stein, MD	Rheumatology
Bethany	Syracuse	Research - Dr. Ivashkiv
Olga	Troyanskaya	Princeton University
Victoria	Yao	Princeton University
Woelsung	Yi, PhD	Research
Xiaoning	Yuan	Rehabilitation
Jian	Zhou	Princeton University

6.0 Other Study Staff/Collaborators:

FirstName	LastName	Organization	Email	Role
There are no items to display				

7.0 * Type of Application:

- ☒ Clinical Research Proposal
- ☐ Expedited Retrospective Chart Review
- ☐ Request for Exemption
- ☐ New Registry
- ☐ Existing Approved Registry

Please click [here](#) to preview Exempt Categories.

Click [here](#) to preview Study Designs.

8.0 Select appropriate funding sources for this study:

Name
Other

Other Funding Sources:

Clinical and Translational Science Center

Note: If the funding source of the study is 'Industry Funded Support', Clinical Research Administration (CRA) will be

notified.

If your study requires CRA review, please upload applicable documents, including sponsor protocol, drug brochure, etc :

Name Version

There are no items to display

[Help](#)

ID: 2014-233

View: 1.1 CRP Information

[Help](#)

CRP Information

- 1.0 **The proposal should be submitted to the appropriate Clinical Review Panel (CRP) for scientific review. If you are unsure of which Clinical Review Panel to select, please contact Barbara Bosco at 212.606.1914**

*

Name

Rheumatology

[Help](#)

ID: 2014-233

View: 1.2 Regulatory Status of Drugs and Devices

[Help](#)

Regulatory Status of Drugs and Devices

- 1.0 **The regulatory status of the drugs or devices in this research proposal is:**

Name

Does not apply to this study

[Help](#)

ID: 2014-233

View: 1.3 Pharmacy Involvement / Impact to EPIC

[Help](#)

Pharmacy Involvement / Impact to EPIC

- 1.0 Is this an inpatient study?
☐ Yes ☒ No

- 2.0 * Will this study have Investigational Drug Service involvement? (Pharmacy will be purchasing/dispensing any medications being used and/or study requires placebo and patient randomization)
☐ Yes ☒ No

well as serum biomarkers are studied in the perioperative context may also contribute the identification of biomarkers associated with flare. In addition, if biologic precursors and predictors of flare are identified, they could have additional applicability in RA management.

5.0 Is this a pilot study that could lead to a more definitive protocol or different study? ☐ Yes ☒ No

5.1 If you answered No, please explain below:

This is not a pilot study.

6.0 Please upload reference or additional document here (if needed).

Name	Description
There are no items to display	

[Help](#)

ID: 2014-233

View: 2.2 Study Design

[Help](#)

Study Design

1.0 Observational:

Name	Description
Prospective Cohort Study	A prospective evaluation of a cohort of patients with a specific characteristic over time to see if they develop a particular endpoint or outcome based on a stated hypothesis (e.g., establishing a cohort to follow patients undergoing a novel procedure in order to evaluate pre- and post-operative function/pain). These studies are conceived before data is collected.

2.0 Experimental:

Name	Description
There are no items to display	

2.1 If Other, please specify:

2.2 If Randomized Controlled Clinical Trial is selected, please choose one of the following:

Name
There are no items to display

If other, please list name or indicate N/A below:

ID: 2014-233

View: 2.3 Recruitment

[Help](#)

Recruitment

[Help](#)

ID: 2014-233

View: 2.35 Patient Subjects

[Help](#)

Patients

1.0 Please check the box(es) below that best reflect how patients will be identified and recruited for participation.

How subjects will be identified

- ☒ Potential subjects will be identified after a review of medical records of patients under the care of one or more of the study investigators
- ☒ Medical records and/or other Institution sources (databases, registries, billing records, pathology reports, admission logs) will be reviewed to identify potential participants. May involve access of records by individuals not involved in the patient's care.
- ☒ Potential subjects will be identified by their treating physicians and referred to the researchers. Patients' private and identifiable information will not be shared prior to receiving permission from the patient to do so.
- ☐ Potential subjects will be identified from a registry of individuals interested in research opportunities.
- ☐ Subjects will roll-over from another research study.
- ☐ Potential subjects will self-refer in response to advertisements.

ID: 2014-233

View: 2.6 Interventions and Observations

[Help](#)

Interventions and Observations

1.0 Be specific and describe the Interventions or Observations that will be part of this research project. Include a detailed description of the treatment arms, if applicable.

Clinical Data:

If willing to participate, the RC will complete a study screening form, obtain consent, complete a Research Authorization Form and the patient will complete a pre-operative questionnaire/survey containing questions about their demographic information (race, ethnicity, age, weight), medical history, assessment of their replaced joint function, and symptoms as they relate to their RA (OA and IA patients will not be asked survey questions that apply only to RA patients). We requested an IRB approved Waiver of HIPAA Authorization.

o The questionnaire will include patient demographics, RA characteristics, co-morbid conditions, disease classification, medications, PtGA, SF-12, HAQ, RAPID, joint count homunculus, HOOS/KOOS/elbow/shoulder survey.

The research staff will complete a second survey that will ask about the participant's medical history, and medication history.

o The questionnaire will include Medications, disease duration and classification criteria, assessment for extra-articular disease and co-morbidities, MDGA, DAS28, CDAI

- All: In the event that a participant is hospitalized at Hospital for Special Surgery or one of its affiliates at any time between their enrollment on the day of surgery and their 6-week follow-up appointment with their surgeon, we may ask for an additional blood draw of 2 tablespoons (20 ccs) of blood to take place at the time of their routine morning blood draw.
- If for any reason routine lab work is not required at the participants' study visits, we would still require 2 tubes of blood for study purposes and would make arrangements to do so. All samples will be de-identified.
- If for any reason subjects are unable to provide blood at their 6-week or 1-year follow-ups (for example, if the subject was too busy, the line at phlebotomy was too long, or the subject simply did not schedule a 1-year follow-up), we will contact the subject and ask them if they would like to have the blood drawn by Apex Laboratory, Inc, a mobile laboratory capable of visiting patients to draw blood in their homes. If they express interest, we will sent them a new informed consent form, cover letter, and prepaid return envelope. When we receive the signed consent form, we will call the subject to coordinate an Apex Laboratory visit date. Apex will call the patient to coordinate the proper time to arrive, and will draw a maximum of 1.5 tablespoons of blood for ESR and CRP blood tests. The results of these tests will be communicated to the study research assistant through Apex's HIPAA-compliant web-based platform.

Surgical sample:

- During surgery, the subjects' surgeon will take samples of the tissue removed as part of their surgery from their joint. Specifically for THR, the femoral head will be collected intra-operatively from standardized anatomic sites, (fovea and capsular reflection). For TKR, tissue samples of the patella cartilage, distal femur and proximal tibia, and synovium from the suprapatellar pouch will be collected intra-operatively.
- We collect and analyze this tissue to learn more about the cellular activity that occurs with RA flare. Tissue will be processed first in pathology: sample saved in OCT and 2 slides stained with H&E. Slides will be scored according to a modified Scanzello scoring system. Synovial tissue and PBMCs will be processed according the standard operating procedures established by the AMP network. Cellular samples will be analyzed at HSS, and shared with the AMP network for additional specialized technical analytics to explore markers and pathways expressed in tissue and cells, using (but not limited to) those being explored in the AMP network such as RNA-Seq, ATAC-Seq, CyTOF, FACS.
- We will also photograph the specimen using the Pathology Lab equipment. This photograph will be de-identified before it is used for research purposes. We will also capture de-identified microscopy images of H&E slides prepared from these samples.

2.0 Will you be collecting human fluid or tissue? ☒ Yes ☐ No

If yes, what will you be collecting? ☒ Fluid ☒ Tissue
(Intraoperative and/or outpatient collection)

[Help](#)

ID: 2014-233 View: 2.61 Fluid Specimen Collection

[Help](#)

Fluid Specimen Collection

Please choose from the following and provide requested information.

1.0 ☒ Blood/serum/plasma

Volume:

59 mL (3.99 tablespoons) first visit, 36.5 mL (2.47 tablespoons) for follow-up visits

Timing and Frequency of collection:

During the surgery

Storage requirements:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☒ Additional collection for research purposes

Describe testing and who will do testing:

☐ Urine

Volume:

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

☐ Saliva

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

☐ Synovial Fluid

Volume:

Timing and Frequency of collection:

Site:

Surgical Field: ☐ or **Aspiration:** ☐

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

[Help](#)

ID: 2014-233

View: 2.61 Fluid Specimen Collection - continued

[Help](#)

Fluid Specimen Collection - continued

Please choose from the following and provide requested information.

☐ Other (e.g. cerebral spinal fluid, cheek cells, bronchial lavage, stool, etc)

Describe specimen:

Volume:

Timing and Frequency of collection:

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ Additional collection for research purposes

Describe testing and who will do testing:

1.0 Will specimens be sent to an individual or institution outside of HSS? (i.e. external Central Laboratory) ☐ Yes ☐ No

If yes, where/to whom and what testing will be done:

2.0 Is fluid being collected for genetic testing? ☒ Yes ☐ No

If yes, describe testing:

3.0 Is fluid being stored for future testing? ☒ Yes ☐ No

If yes, describe testing:

The samples may be used for testing even after this study has been completed. Further research tests may help us learn more about the disease and response to drugs or treatment. However, future testing on the patient's biological samples may be used for any type of biomedical research, which may or may not be related to the purpose of this study. The results of these future tests will not be shared with the patient.

[Help](#)

ID: 2014-233

View: 2.62 Tissue Specimens Collection

[Help](#)

Tissue Specimens Collection

1.0 Status of Tissue

☐ FRESH

Will frozen tissue be needed? ☐ Yes ☐ No

How will it be delivered to Histopathology? Name/Extension/Beeper #.

☐ FIXED/PARAFFIN EMBEDDED

2.0 ☒ Bone

Site (Specific joint/area):

Femoral head, distal femur, proximal tibia

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☒ Additional collection for research purposes

Describe testing and who will do testing:

Specifically for THR, the femoral head will be collected intra-operatively from standardized anatomic sites, (fovea and capsular reflection). For TKR, tissue samples of the patella cartilage, distal femur and proximal tibia, and synovium from the suprapatellar pouch will be collected intra-operatively.

☐ Bone Marrow

Method of collection: ☐ Biopsy ☐ Aspirate

Site (Specific joint/area):

Purpose:

☐ Within SOC

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

☒ **Cartilage**

Site (Specific joint/area):

Patellar cartilage

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☒ **Additional collection for research purposes**

Describe testing and who will do testing:

☐ **Meniscus**

Site:

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

[Help](#)

ID: 2014-233

View: 2.62 Tissue Specimens Collection - continued

[Help](#)

Tissue Specimens Collection - continued

☐ **Retrieved Device for Biomechanical Testing**

Site:

☒ **Synovium**

Site (specific joint/area):

Synovium from the suprapatellar pouch will be collected intra-operatively.

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☒ **Additional collection for research purposes**

Describe testing and who will do testing:

☐ **Other (i.e. punch biopsy, nucleus pulposus/annulus fibrosus, or other collected tissue/biopsies)**

Provide additional information:

Purpose:

☐ **Within SOC**

Describe testing and who will do testing:

☐ **Additional collection for research purposes**

Describe testing and who will do testing:

1.0 Will specimens be sent to an individual or institution outside

of HSS? (i.e. external Central Laboratory) ☐ Yes ☐ No

If yes, where/to whom and what testing will be done:

2.0 Is tissue being collected for genetic testing? ☐ Yes ☒ No

If yes, describe testing:

3.0 Is tissue being stored for future testing? ☐ Yes ☐ No

If yes, describe testing:

[Help](#)

ID: 2014-233

View: 2.7 Data Collection

[Help](#)

Data Collection

1.0 Indicate what data will be collected.

PARTICIPANT INTAKE

New form location
1. Interest in electronic surveys
2. Symptom onset
3. Date of diagnosis
4. Ethnicity
5. Race
6. Highest level of completed education
7. Current employment status
8. # other people at home
9. Personal income
10. Smoking history
11. Alcohol
12. Relative with RA/PsA/OA/broken hip
13. Other diseases in family

Yes Private Office Charts Please specify which private office: Goodman; Alexiades, Bostrom, Cornell, Figgie, Gonzalez Della Valle, Mayman, Pellici, Salvati, Sculco, Su

No Registries Please specify which registry:

☐ Other Please specify:

[Help](#)

ID: 2014-233

View: 2.8 General Methods and Procedures

[Help](#)

General Methods and Procedures

1.0 * Are controls included in the study? Yes

1.1 If yes, describe how they will be matched with the study subjects; state whether the controls will have identical data recorded, or describe any differences compared to the intervention subjects.

The cohort will include RA patients who do not flare and OA patients as our comparator groups.

2.0

* Are all tests Standard of care? No

If not, identify which tests are not standard of care. What source of funds will be used to pay for them (text box below):

None of the experimental tissue or serum sample collection is standard of care. They will be paid for by the Pernis lab and Darnell lab. Radiographs are standard of care.

RF, CRP, ESR, and ACPA- are standard of care, as they may help determine therapy in patients who flare. However, results are not always available on all TJR patients We will apply for funding through the CTSC for missing labs to pay for CRP, ESR, RF and ACPAs.

3.0 * Will surveys/questionnaires be used? Yes

4.0 * Does the study involve randomization? No

5.0 * Does your study included Placebo or No-Treatment Arm? No

6.0 * Does your study included Washout of Previous Medication? No

7.0 Data collection sheet should be created for the study and uploaded:

Name	Version
Research Authorization Form	0.01

[Help](#)

ID: 2014-233

View: 2.83 Surveys and Questionnaires

[Help](#)

Surveys & Questionnaires

Beta is the probability of accepting a false null hypothesis. It should be small.

P0 is the value of the population proportion under the null hypothesis.

P1 is the value of the population proportion under the alternative hypothesis.

Summary Statements

A sample size of 47 achieves 81% power to detect a difference (P1-P0) of -0.1600 using a

two-sided binomial test. The target significance level is 0.0500. The actual significance level

achieved by this test is 0.0445. These results assume that the population proportion under the

null hypothesis is 0.2600.

Power Analysis of One Proportion

Chart Section



We are estimating the rate of the flare rate in RA post-arthroplasty based on previous data. However, if our estimates are wrong, we may be grossly underpowered. Therefore, an interim analysis is planned, when we have collected 25 RA patients to ensure we are adequately powered to detect the primary outcome of flare as previously defined.

- Alpha level: 0.05
- Beta or power level: 0.8 (80%)
- Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable):

The primary outcome is rate of RA flare within 6 weeks of surgery. Since it's a rate, no mean and s.d. are available.

- Number of groups being compared (use 1 for paired analysis within the same subjects):

2 groups: RA – Flare vs. Non-Flare group for secondary outcome.

- Effect size or change expected between groups:

The expected effect size between the flare and non-flare group is 16%, but the interim analysis will be performed after we collect 50 patients.

- Resulting number per group:

First Name	Middle Name	Last Name	Title
Susan		Goodman, MD	MD
Michael		McNamara	Research Assistant
Vivian		Bykerk, MD	Attending Physician

[Help](#)

ID: 2014-233

View: 3.0 IRB Application

[Help](#)

IRB Application

1.0 Please provide lay abstract:

The condition to be studied is worsening (flare) of rheumatoid arthritis (RA) in patients who have undergone arthroplasty. RA patients undergoing arthroplasty most often have severe, erosive disease. If the rate of flare approaches the estimated 26% rate suggested in a previous study for RA patients after arthroplasty (*Johnson ACR 2011*), this could be of significance in regards to their long term arthroplasty and disease outcomes. Patients who flare may not be able to participate in the post-operative rehabilitation thought necessary for optimal arthroplasty outcomes, and it may be difficult for patients who flare after discontinuing immunosuppressant medications for surgery to regain remission or low disease activity. Detailed clinical data collected longitudinally from RA patients with severe erosive disease undergoing arthroplasty in conjunction with further characterization of the molecular profile of blood and operative tissue could provide valuable information to inform best practices for this patient group.

2.0 * Requested Review Type:

Expedited

3.0 Ancillary/Impacted Services Review (select all that apply):

Note: Do not confuse the committees below with CRP or Research Service Chief

Ancillary Committees

There are no items to display

4.0 * Is Genetic Testing involved in this study? Yes

ID: 2014-233

View: 3.12 Expedited Qualification

[Help](#)

Expedited Qualification

If you check any of the items below, the study is qualified for EXPEDITED review status under federal guidelines.

1.0 * Select all that apply:

Question

- ☐ 1. Clinical studies of drugs and medical devices only when: (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review). OR (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Question

- ☒ 2. This research involves only the collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from healthy, non-pregnant adults or children where the amount of blood and frequency does not exceed federal regulations for normal clinical care.
- ☐ 3. This research involves prospective collection of biological specimens for research purposes by noninvasive means.
- ☐ 4. This research involves the collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
- ☒ 5. This research involves materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes.
- ☐ 6. Collection of data from voice, video, digital, or image recordings made for research purposes.
- ☒ 7. This research will be performed on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or will employ a survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- ☐ 8. This research involves Continuing Review of study previously approved by the convened IRB
- ☐ 9. This research involves Continuing Review of study which are not conducted under an investigational new drug application or investigational device exemption where categories two through eight do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

ID: 2014-233

View: 3.2 Risk/Benefit Assessment-Risks

[Help](#)

Assessment of Research Procedures

1.0 Describe any potential for direct benefits to participants in this study:

Participants are not expected to benefit personally from this research study. Participation in this study will not provide participants with any therapeutic benefits, nor will it provide them with information regarding whether they are genetically predisposed to developing any known illnesses. This study includes drawing blood for investigational procedures, which may not give participants immediate benefit or any benefit. The knowledge gained may benefit others in the future.

2.0 Describe any potential benefits to society:

Benefits for society may include providing further information about the genetic basis of worsening of rheumatoid arthritis as well as the development of safe and effective therapies for that condition.

ID: 2014-233

View: 3.22 Minimal Risk

[Help](#)

Minimal Risk

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. This includes, but is not limited to, administration of non-invasive data collection measures, collection of blood samples, collection of existing data and observational studies

1.0

Please select the applicable tests with standard wording for risks from the list below:

Name	Description
A blood draw	The risk of participating in this study is the risk of having your blood drawn. The risks of blood drawing include mild pain, bruising, and very rarely infection at the place of the needle insertion.

☒ **Risk of breach of confidentiality, include the following:**

Participation in this research involves the potential risk of a breach of confidentiality of your health information that is stored. HSS tries to minimize those risks by (i) removing some direct identifiers from information stored [i.e. names, social security numbers, medical record numbers]; (ii) securing, in a separate location, and limiting access to information linking codes (i.e., linkage codes) assigned to the registry information with direct participant identifiers; and (iii) limiting access to information stored to HSS investigators.

2.0

*** Is any physical testing being done other than surveys, questionnaires, etc?:**

Yes

2.1 If yes, please list the testing being done and describe any potential risks:

This study involves blood draws. The risks of blood drawing include mild pain, bruising, and very rarely infection at the place of the needle insertion.

[Help](#)

ID: 2014-233

View: 3.3 Informed Consent Determination

[Help](#)

Informed Consent

1.0

Indicate the types of consent that will be involved in this study (check any or all that apply):

Informed Consent Category
Written/signed consent by subject

2.0

Waivers: If you are applying for any waivers of consent (check any or all that apply):

Name
<input type="checkbox"/> Waiver of Consent
<input type="checkbox"/> Waiver of Assent
<input type="checkbox"/> Waiver of Parental Permission
<input type="checkbox"/> Waiver of Written or Signed Consent (i.e. information sheets, telephone consent, verbal script)

3.0 * Will this study include non-english speaking participants?

Yes

4.0 If the study does not include non-english speaking participants, please justify:

We do not have the personnel available to translate the study documents or obtain consent in any languages other than English and Spanish.

5.0 Please provide assurance by checking the box below that the study will make all possible efforts to collect Federally mandated gender, race and ethnicity data for all subjects included in the study.

☒ Agree

☐ This will not be possible for the following reasons:

6.0 Will this study be posted at ClinicalTrials.gov?

☒ Yes ☐ No

If yes, please post at the site upon approval of the study by the IRB. ClinicalTrials.gov requires that listings be updated every 12 months as well as 30 days after Major Amendment approvals of a protocol. For more information about what studies should be posted at the site and when to update a posted study at the site, please visit the following website:
http://www.icmje.org/faq_clinical.html

ID: 2014-233

View: 3.31 Consent Forms & Process of Consent

[Help](#)

Consent Forms & Process of Consent

1.0 Good News! We've prepared several different types of consent form templates with some of the information you have already provided. Please follow the instructions below to complete the process.

[Lay term
Glossary](#)

Instructions:

1.1) Download the applicable consent form(s) to your machine and modify as appropriate. Save the modified documents and upload them in the following question.

 [Assent Form For Adolescent Participation In Research Study](#)

 [Informed Consent To Participate In A Genetic Research Study](#)

 [Informed Consent To Participate In Research](#)

 [Informed Consent To Participate In Research Registry](#)

[Help](#)

ID: 2014-233

View: 3.7 HIPAA

[Help](#)

HIPAA

The Healthcare Insurance Portability and Accountability Act (HIPAA) prohibits the use of a person's Protected Health Information without a valid authorization.

1.0 * Will this study record any information which can identify the participants of this study?

Yes

2.0 * Will this study record information that if released, could reasonably place participants at risk of criminal or civil law suits?

No

3.0 * Will this study obtain or review information related to the respondent's medical records or health?

Yes

4.0

[HIPAA Waiver
Flow Chart](#)

Select the option(s) which fits this study:

Name

Self reported medical information

Waiver of authorization requested (Full / Partial / Alteration)

ID: 2014-233

View: 3.71 Waiver of HIPAA Authorization

[Help](#)

Waiver of HIPAA Authorization

Pursuant to the Privacy Regulations of HIPAA, an IRB is **only** permitted to approve a waiver of individual subjects' authorization if it finds and documents specific criteria relevant to the protection of subject privacy.

1.0

I am seeking:

☐ A **full waiver** of subject authorization to use and disclose health information during the course of the research study.

☒ A **partial waiver** of subject authorization to use and disclose health information only for the purpose of:

Pre-operative identification and recruitment through the use of PS Reporter, MMF, Clinstar, or other patient records and from the Total Hip/Total Knee Replacement Patient Education Class. Information

such as e-mail addresses, and phone numbers will be collected post-operatively.

☐ The following alteration to the authorization requirements:

- 2.0 *** Who will have access to the health information needed for the study? Please identify each person by name or category. Example include: the investigator, the research staff, co-investigators and their research staffs, and all research monitors.**

All co-investigators approved on the IRB protocol

- 3.0 *** Please describe the risks to privacy presented by the research and whether the research presents more than minimal risk of harm to subjects' privacy. Include a description of what identifiers will be reviewed, collected, and stored; who will have access to identified information; how access to study data is controlled; who will monitor access to study data; and where data will be stored:**

Patient files will be reviewed to determine the presence of rheumatoid arthritis. Identifiers that will be reviewed: name, address, telephone number, medical record number, date of birth, type of procedure, operating surgeon, race/ethnicity, laterality, zip code, admission date, gender.

Subject information will only be accessible to study co-investigators as listed on the IRB protocol. All information will be stored in locked file cabinets and password protected computer files to which only the approved research personnel have access. Access to the study data will be monitored by the Principal Investigator, Dr. Susan Goodman.

- 4.0 *** Can the research be practicably carried out without the waiver?** ☐ Yes ☒ No

If it is impracticable to obtain individual authorization, please describe **why**:

The waiver is necessary in order for the investigators to identify and recruit potential subjects with rheumatoid arthritis.

- 5.0 *** Can the research be practicably carried out without access to and use of identified health information?** ☐ Yes ☒ No

If it is impracticable to conduct this research without access to identified health information, please describe **why**:

Patients' health information must be viewed in order to determine if they meet the inclusion criteria to be eligible for the study.

6.0 * What is your plan to protect identifiers from improper use and disclosure?

The data listed in this waiver will be maintained in locked file cabinets and in password-protected computer files to which only the approved research personnel have access. All research personnel with access to information covered by this waiver are informed of the IRB, HIPAA, and ethics regulations governing research involving human subjects and are under the supervision of the Principal Investigator.

7.0 * Will the patient identifiers be destroyed at the earliest opportunity? ☒ Yes ☐ No

If **yes**, describe the plan for destroying identifiers (e.g. how, by whom, and when identifiers will be destroyed):

Any page containing patient identifiers will be destroyed by Dr. Goodman at the earliest opportunity upon completion of the study.

If **no**, indicate the health or research justification for retaining the identifiers:

8.0 * Explain how PHI will be acquired and used:

A Recruitment Flyer will be placed in the dictation cubbies and exam rooms of participating surgeons. If a patient with a possible or previous diagnosis of RA schedules an arthroplasty, members of the surgeon's office will send the patient information to the Research Staff using either the study e-mail address, FlareStudy@hss.edu, or other secure forms of communication. Patients will be identified pre-operatively by their treating surgeon or identified by screening patients' records prior to their pre-operative visit. They will receive a Study Overview Sheet (see attached) either in the office, in the mail, or on the day of surgery. They will have the opportunity to discuss any questions with the research assistant/ research team member who will ensure they meet study criteria (see screening sheet). In addition, patients may be identified and recruited from the Total Hip /Total Knee Replacement Patient Education Class by the research assistant. Finally, research assistants may use PS Reporter, MMF, or Clinstar to identify patients before their pre-surgical screening visit, or prior to their surgical procedure. We will request an IRB approved Waiver of HIPAA Authorization.

9.0 Explain how PHI will be protected during this study:

☐ Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by the PI and accessible only to the principal investigator, in addition to other IRB approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number, etc...) will be maintained in a different password protected database maintained by to which only will have access.



Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by Dr. Goodman and co-investigators and accessible only to the principal investigator (Dr. Goodman), in addition to other IRB-approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number) will be maintained in a different password-protected database (REDCap), separately from the data. Immediately following data entry into the password-protected databases, the paper-based data collection instruments will be stripped of all personal identifiers and stored in a locked file cabinet maintained by Dr. Goodman. The page containing patient identifiers will be stored separately in a locked file cabinet in Dr. Goodman's office, and will be destroyed at the earliest opportunity upon completion of the study.

10.0 * Justify your need to collect PHI on this study:

The waiver is necessary in order for the investigators to identify and recruit potential subjects with rheumatoid arthritis.

Patients' health information must be viewed in order to determine if they meet the inclusion criteria to be eligible for the study.

[Help](#)

ID: 2014-233

View: 3.72 HIPAA PHI Identifiers

[Help](#)

PHI Identifiers

1.0

Identify the types of PHI collected:

Name



Questionnaires or Interviews



Billing Information or Databases



Mental Health Records



Data Registry



Hospital or Medical Records



Biological Samples



DNA Samples

Name

☐ Other

1.1 If Other, please specify the type of PHI collected:

2.0

Select all the PHI Identifiers that apply:

Identifiers

Names

All geographic subdivisions smaller than a state:

Telephone Numbers

E-mail Addresses

Medical Record numbers

All elements of dates (except year) for dates related to an individual:

ID: 2014-233

View: 3.8 Data Safety Monitoring Plan

[Help](#)

Data Safety Monitoring Plan

1.0 * Check the one box below that most accurately reflects the plan for data and safety monitoring for this study.

The study will be monitored only by the study investigators and/or sponsor.

1.1 If Other, Please specify your plan for data safety and monitoring for the study. If no DSMB required, Please specify why:

2.0 Describe the clinical criteria for withdrawing an individual subject from the study due to safety or toxicity concerns:

3.0 Summarize any pre-specified criteria for stopping or changing the study protocol due to safety concerns.

4.0 * Are there any plans to perform an interim efficacy analysis:
No

4.1 If you answered Yes, please describe the plans to conduct an interim analysis.

ID: 2014-233

View: SF - Final Page

[Help](#)

Final Page

You have completed your application!

Please hit "Continue" to finish the HSS Clinical Trial Form.

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must press the "SUBMIT STUDY" button in My Activities for this Study ID:2014-233.

You can track the ongoing status of your submission by logging into the study workspace.

First Name	Middle Name	Last Name	Title
Ed		Purdue, PhD	Associate Scientist
Karmela		Chan, M.D.	
Bethany		Syracuse	
Caroline		Reidy	Manager
Jian		Zhou	
Edd		Ricker	
Sanjay		Gupta	Research Associate
Olga		Troyanskaya	
Michela		Manni	Post doctoral Fellow
Michael		McNamara	Research Assistant
Vivian		Bykerk, MD	Attending Physician
Woelsung		Yi, PhD	Research Assoc.
Cristina		Rozo, Ph.D.	
Caroline		Jiang	
Dana		Orange, MD	Assistant Attending
Victoria		Yao	

4.0

Posting date:

Name

Upon IRB approval

☐ Post on this date:

5.0

Condition:

Arthritis

☐ Other:6.0 **State the summary including number of patients, enrollment period and duration of follow-up (use lay terms):**

Researchers at Hospital for Special Surgery are trying to learn more about post-operative rheumatoid arthritis (RA) "flare" or worsening of disease. Specifically this study hopes to understand RA flare after total joint replacement surgery and what the result of flaring is over the course of a year. Eligible participants will be asked a lot of questions about their RA, their mobility, etc.; we will also be drawing blood to better understand a subject's recuperation from joint replacement surgery.

We hope to learn how to better manage patients with rheumatoid arthritis when having a joint replacement. For example, if RA patients who flare are unable to participate in post-operative physical therapy and do worse one year after total knee replacement and total hip replacement, perhaps more effective treatment could be developed. The study will also help us to identify early factors that may influence long-term outcomes of joint replacements in RA patients.

Participation in this study will continue over the course of one year, and involves a total of 4 study visits and 9 phone calls as well as several blood draws. The visits and blood draws will, whenever possible, occur at the time of routinely scheduled visits. Subjects will have the opportunity to discuss any questions with the research team members, their surgeon and/or their treating rheumatologist.