June 29, 2010

Protocol Number: 2010H0110
Protocol Title: BCRF AS A BIOMARKER FOR JOINT DISEASE PROGRESSION, Sudha Agarwal, David C. Flanigan, Kevin V. Hackshaw, Oral Biology
Type of Review: Initial Review – expedited
IRB Staff Contact: Kristen Kalina (614) 292-9804 Kalina.8@osu.edu

Dear Dr. Agarwal,

The Biomedical Sciences IRB APPROVED BY EXPEDITED REVIEW the above referenced research. The Board was able to provide expedited approval under 45 CFR 46.110(b)(1) because the research meets the applicability criteria and one or more categories of research eligible for expedited review, as indicated below.

Date of IRB Approval: June 29, 2010
Date of IRB Approval Expiration: May 24, 2011
Expedited Review Category: 2, 3, 5

In addition; the research has been approved for a waiver of documentation of the consent process and for partial waiver of HIPAA Research Authorization (recruitment purposes only).

If applicable, informed consent (and HIPAA research authorization) must be obtained from subjects or their legally authorized representatives and documented prior to research involvement. The IRB-approved consent form and process must be used. Changes in the research (e.g., recruitment procedures, advertisements, enrollment numbers, etc.) or informed consent process must be approved by the IRB before they are implemented (except where necessary to eliminate apparent immediate hazards to subjects).

This approval is valid for one year from the date of IRB review when approval is granted or modifications are required. The approval will no longer be in effect on the date listed above as the IRB expiration date. A Continuing Review application must be approved within this interval to avoid expiration of IRB approval and cessation of all research activities. A final report must be provided to the IRB and all records relating to the research (including signed consent forms) must be retained and available for audit for at least 3 years after the research has ended.

It is the responsibility of all investigators and research staff to promptly report to the IRB any serious, unexpected and related adverse events and potential unanticipated problems involving risks to subjects or others.

This approval is issued under The Ohio State University’s OHRP Federalwide Assurance #00006378. All forms and procedures can be found on the ORRP website – www.orrp.osu.edu. Please feel free to contact the IRB staff contact listed above with any questions or concerns.

Karla Zadnik, OD, PhD, Chair
Biomedical Sciences Institutional Review Board
1. PROJECT TITLE

BCRF as a biomarker for joint disease progression

2. INSTITUTIONAL REVIEW BOARD

Select the Board to review this research:

- [ ] Behavioral and Social Sciences
- [x] Biomedical Sciences
- [ ] Cancer

Final Board assignment is determined by ORRP.

3. PRINCIPAL INVESTIGATOR (or Advisor) - see Qualifications for service as a PI

<table>
<thead>
<tr>
<th>Name (Last, First, MI):</th>
<th>Degree(s):</th>
<th>University Academic Title:</th>
<th>College (TIU):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agarwal, Sudha</td>
<td>Ph.D.</td>
<td>Professor</td>
<td>Dentistry</td>
</tr>
<tr>
<td>Department Name (TIU):</td>
<td>Oral Biology</td>
<td>Department # (TIU):</td>
<td>21350</td>
</tr>
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<td>4157 Postle Hall</td>
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<td>03133876</td>
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<tr>
<td>305 West 12th Avenue, Columbus, 43210</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>E-mail:</td>
<td><a href="mailto:Agarwal.61@osu.edu">Agarwal.61@osu.edu</a></td>
<td>Fax:</td>
<td>614-247-7475</td>
</tr>
<tr>
<td>Phone:</td>
<td>614-537-6986</td>
<td>Emergency phone:</td>
<td>614-247-6473</td>
</tr>
</tbody>
</table>

4. CO-INVESTIGATOR(S)

Are there any OSU Co-Investigators on this protocol?  
- [x] Yes  Complete Appendix A1
- [ ] No

Signatures of Co-Investigator(s) are required on Appendix A1.

5. KEY PERSONNEL

Are there any OSU key personnel on this protocol?  
- [x] Yes  Complete Appendix A1
- [ ] No

Key personnel are defined as individuals who participate in the design, conduct, or reporting of human subjects research. At a minimum, include individuals who recruit or consent participants or who collect study data.

6. EXTERNAL CO-INVESTIGATOR(S) & KEY PERSONNEL

Are any external (non-OSU) Investigators or key personnel engaged in the OSU research?  
- [ ] Yes
- [x] No  Go to Question #7

“Engaged” individuals are those who intervene or interact with participants in the context of the research or who will obtain individually identifiable private information for research funded, supervised, or coordinated by OSU. See OHRP Engagement Guidance or contact ORRP for more information.

If Yes  Who will provide approval for these external personnel?  
- [ ] OSU IRB  Complete Appendix A2
- [ ] Non-OSU IRB  Provide a copy of the approval(s)
7. ADDITIONAL CONTACT(S)

If further information about this application is needed, specify the contact person(s) if other than the PI (e.g., study or regulatory coordinator, research assistant, etc.).

<table>
<thead>
<tr>
<th>Name (Last, First, MI):</th>
<th>Phone:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flanigan, David</td>
<td>Clinic: (614) 293-3600, Office: (614) 293-2413</td>
</tr>
<tr>
<td>E-mail:</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:David.flanigan@osumc.edu">David.flanigan@osumc.edu</a></td>
<td>Fax: 614-293-8448</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Name (Last, First, MI):</th>
<th>Phone:</th>
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<tbody>
<tr>
<td>Hackshaw, Kevin</td>
<td>(614) 293-8093</td>
</tr>
<tr>
<td>E-mail:</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:Kevin.hackshaw@osumc.edu">Kevin.hackshaw@osumc.edu</a></td>
<td>Fax: (614) 293-5631</td>
</tr>
</tbody>
</table>

All OSU individuals listed on this protocol will have access to information about IRB actions and the completion status of each individual's administrative and training requirements (CITI, COI disclosure). Note: Personal financial information provided in COI disclosures is not included.

8. EDUCATION

Have all OSU investigators and key personnel completed the required web-based course (CITI) in the protection of human research subjects?  

- [X] Yes  
- [ ] No  

Educational requirements (initial and continuing) must be satisfied prior to submitting the application for IRB review. See CITI Training or contact ORRP for more information.

9. FINANCIAL CONFLICT OF INTEREST

Does any OSU investigator (including principal or co-investigator), key personnel, or their immediate family members have a financial interest (including salary or other payments for services, equity interests, or intellectual property rights) that would reasonably appear to be affected by the research, or a financial interest in any entity whose financial interest would reasonably appear to be affected by the research?

- [ ] Yes  
- [X] No  

All OSU investigators and key personnel must have a current COI disclosure form (updated as necessary for the proposed research) filed before IRB review. Examples of financial interests that must be disclosed include (but are not limited to) consulting fees or honoraria; stocks, stock options or other ownership interests; and patents, copyrights and royalties from such rights. For more information, see Office of Research Compliance COI Overview and COI Forms.

10. FUNDING OR OTHER SUPPORT

If the research is federally funded and involves a subcontract to or from another entity, an IRB Authorization Agreement may be required. Contact ORRP for more information.

a. Is the research funded or has funding been requested?

- [ ] Yes  
- [X] No  

   If Yes ➔ Specify sponsor:

Provide a copy of the grant application or funding proposal. The University is required to verify that all funding proposals and grants (new or renewals) have been reviewed by the IRB before funds are awarded.

b. Is any support other than monetary (e.g., drugs, equipment, etc.) being provided for the study?

- [ ] Yes  
- [X] No  

   If Yes ➔ Specify support and provider:

11. OTHER INSTITUTIONAL APPROVALS

Check all that apply and provide applicable documentation. See websites listed below for information on obtaining approvals. IRB review cannot be conducted until required institutional approvals or exemptions are obtained, except as noted.

- [X] None  

  Clinical Research Center (CRC) Scientific Advisory Committee (SAC) – Approval required for research sponsored by the CRC. Final IRB approval will be held pending receipt of SAC approval.
Institutional Biosafety Committee (IBC) – Approval required for research involving biohazards (recombinant DNA, infectious or select agents, toxins), gene transfer, or xenotransplantation.

Comprehensive Cancer Center (CCC) Clinical Scientific Review Committee (CSRC) – Approval or exemption required for cancer-related research.

Maternal-Fetal Welfare Committee – Approval required for some research involving pregnant women and fetuses.

Human Subject Radiation Committee (HSRC) – Approval required for research involving radiologic procedures for research purposes (e.g., non-clinical care X-rays, DEXA or CT scans, nuclear medicine procedures, etc.).

12. LOCATION OF THE RESEARCH

Research to be conducted at locations other than approved performance sites will minimally require a letter of support and may require another IRB's approval if personnel are engaged. See OHRP Engagement Guidance or contact ORRP for more information.

a. List the specific site(s) at which the OSU research will be conducted (include both domestic and international locations).

<table>
<thead>
<tr>
<th>Location Name (or description)</th>
<th>Address (street, city and state, or country)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4010 Postle Hall Laboratories</td>
<td>305 West 12th Avenue, Columbus, 43210</td>
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</table>

b. Are all the sites named above on the OSU list of approved research performance sites? X Yes → Go to Question #13

   If No →  ☐ Domestic sites → Provide a letter of support, as applicable
   ☐ International sites → Complete Appendix U

c. For multi-site research, is the OSU PI the lead investigator or is OSU the lead site? X Yes

   ☐ No → Go to Question #13

   i. Describe the communication between sites that might be relevant to the protection of participants, such as unanticipated problems, interim results, and protocol modifications.

   ii. Describe IRB oversight arrangements for each site (i.e., who is providing IRB review and approval). Provide copies of the non-OSU approvals, as applicable. Contact ORRP if requesting OSU be the IRB of record.

13. EXPEDITED REVIEW

Are you requesting Expedited Review? X Yes → Complete Appendix B

☐ No

14. SUMMARY OF THE RESEARCH

Summarize the proposed research using non-technical language that can be readily understood by someone outside the discipline. Explain briefly the research design, procedures to be used, risks and anticipated benefits, and the importance of the knowledge that may reasonably be expected to result. Use complete sentences (limit 300 words).

Osteoarthritis and osteoporosis constitute the major causes of disability, afflicting more than 60% percent of the population above 40 years of age. Presently, there is a paucity of biomarkers that could provide definitive prognosis of these diseases. Recently, we have identified a protein, BCRF (bone and cartilage regenerative factor) that regulates cartilage and bone growth. BCRF is produced by bone marrow stromal cells and secreted in the blood. BCRF production is inhibited in inflamed cartilage and bone in rats and mice.
Therefore, it is important to examine BCRF levels during inflammation of cartilage and bone in humans. Our Aims are to examine (i) the presence / loss of BCRF in bone and cartilage obtained from healthy or osteoarthritic / osteoporotic cartilage and bone. (ii) Assess the levels of BCRF in the serum samples of healthy and osteoarthritic / osteoporotic / rheumatic disease afflicted patients. Research design: Aim (i) Obtain a small specimen (0.5 cubic mm) of cartilage and/or bone that is discarded during joint surgeries of osteoarthritic / osteoporotic joints, or joints of Healthy patients undergoing surgery due to trauma or fractures. Perform immunohistochemistry (IHC) to examine the presence of BCRF in these specimens. Aim (ii) Obtain blood samples (1 CC) from healthy and osteoarthritic/osteoporotic/rheumatic disease afflicted patients, by requesting one extra small tube of blood, while blood is being collected prior to joint surgeries. Examine serum levels of total BCRF by Enzyme Linked Immunoassays. Risks and Benefits. No risks are involved with the proposed study. Patient identities will not be recorded on any specimens. If we find that BCRF is suppressed in the serum or in inflamed cartilage / bone, this will provide a much needed biomarker to see the progression of osteoarthritis / osteoporosis. The IHC studies by examining the presence/absence of BCRF will then confirm the results of ELISA used in Aim # 2.

15. SCIENTIFIC BACKGROUND & LITERATURE REVIEW
Summarize existing knowledge and previous work that support the expectation of obtaining useful results without undue risk to human subjects. Use complete sentences (limit 300 words).
During a transcriptome-wide analysis of genes regulated by experimental osteoarthritis in rats, we observed that BCRF is drastically suppressed in the inflamed cartilage and bone due to inflammation. The role of this protein in cartilage or bone was not known. We are in the process of writing the manuscript demonstrating that the presence of BCRF is essential for bone remodeling. In the BCRF knockout mice the bone does not remodel. Hence, its absence in inflamed cartilage retards repair/ bone formation. This factor is secreted in the serum, and is present at very low concentrations in the sera of osteoarthritic rats. The next logical step is to examine the presence of BCRF in the inflamed and healthy cartilage and bone. This information will be correlated its absence in the serum to joint/bone diseases such as osteoarthritis, osteoporosis, and rheumatic disorders. We are proposing to obtain these tissues without any risks imposed to patients. These finding will be significantly beneficial to patients by providing a diagnostic tool for the prognosis of the progression of arthritic diseases.

16. RESEARCH OBJECTIVES
List the specific scientific or scholarly aims of the research study.
Aim 1. Examine serum levels of BCRF by ELISA. We have on hand an ELISA test that can measure BCRF levels human / rat / mouse serum (BCRF is a highly conserved molecule).
Aim 2. Examine the presence of BCRF in healthy and inflamed cartilage and bone to correlate its presence in serum with cartilage/bone disease(s).

17. RESEARCH METHODS & ACTIVITIES
a. Identify and describe all interventions and interactions that are to be performed solely for the research study. Distinguish research (i.e., experimental) activities from non-research activities.
No invasive procedures will be performed specifically for the study. For Aim 1, one CC of blood will be collected for ELISA to measure BCRF concentrations in the serum. An extra one small tube for 1 CC of blood will be requested while blood specimen is being taken prior to surgery or for blood analysis/testing. A phlebotomist will draw the blood. For Aim 2, the study will use bone and cartilage fragments (0.5 mm or smaller) that are discarded during joint/bone surgery. We will then examine the presence of BCRF in cartilage and bone specimens by immunohistochemistry. This data will then be correlated with the presence of BCRF in the serum.
No subject identifiers will be used for the specimens collected for the study. A new number, approximate age and disease (osteoporosis/osteoarthritis/healthy) will identify samples.

b. Check all research activities that apply:
- Anesthesia (general or local) or sedation
- Magnetic Resonance Imaging (MRI)
- Audio, video, digital, or image recordings
- Materials that may be considered sensitive, offensive, threatening, or degrading
- Biohazards (e.g., rDNA, infectious agents, select agents, toxins)
- Non-invasive medical procedures (e.g., EKG, Doppler)
- Biological sampling (other than blood)
- Observation of participants (including field notes)
X Blood drawing
☐ Coordinating Center
☐ Data, not publicly available
☐ Data, publicly available
☐ Data repositories ➔ Complete Appendix C
(future unspecified use, including research databases)
☐ Deception ➔ Complete Appendix D & Appendix M1
☐ Devices ➔ Complete Appendix E
☐ Diet, exercise, or sleep modifications
☐ Drugs or biologics ➔ Complete Appendix F
☐ Emergency research
☐ Focus groups
☐ Food supplements
☐ Gene transfer
☐ Genetic testing ➔ Complete Appendix G
☐ Internet or e-mail data collection
☐ Oral history (does not include medical history)
☐ Placebo
☐ Pregnancy testing
☐ Program Protocol (Umbrella Protocol)
☐ Radiation (e.g., CT or DEXA scans, X-rays, nuclear medicine procedures) ➔ Complete Appendix V
☐ Record review (which may include PHI)
☐ Specimen research
☐ Stem cell research
☐ Storage of biological materials ➔ Complete Appendix H
(future unspecified use, including repositories)
☐ Surgical procedures (including biopsies)
☐ Surveys, questionnaires, or interviews (one-on-one)
☐ Surveys, questionnaires, or interviews (group)
☐ Other
 Specify:

18. DURATION
Estimate the time required from each participant, including individual interactions, total time commitment, and long-term follow-up, if any.
No extra time will be required from the patients.

19. NUMBER OF PARTICIPANTS
The number of participants is defined as the number of individuals who agree to participate (i.e., those who provide consent or whose records are accessed, etc.) even if all do not prove eligible or complete the study. The total number of research participants may be increased only with prior IRB approval.

a. Provide the total number of participants (or number of participant records, specimens, etc.) for whom you are seeking OSU IRB approval. 80

b. Explain how this number was derived (e.g., statistical rationale, attrition rate, etc.).

Specimen will be collected from 20 healthy trauma patients undergoing joint surgery (40 to 70 years of age), 20 osteoarthritis patients (40 – 70 years of age), 20 osteoporosis patients (40 – 70 years of age), and 20 patients with other rheumatic diseases such as rheumatoid arthritis/fibromyalgia (40 – 70 years of age). This number of patients would provide enough sample size for statistical analysis.

c. Is this a multi-center study? ☐ Yes ➔ Indicate the total number of participants to be enrolled across all sites: ☐ No

20. PARTICIPANT POPULATION
a. Specify the age(s) of the individuals who may participate in the research:
The Ohio State University Institutional Review Boards - INITIAL REVIEW OF HUMAN SUBJECTS RESEARCH

Age(s): 40 to 70 years of age

- 20 healthy subjects undergoing knee surgery due to trauma (40 to 70 years of age)
- 20 osteoarthritis patients with radiographically confirmed Osteoarthritis (40 – 70 years of age)
- 20 osteoporosis patients undergoing joint surgery (40 – 70 years of age)
- 20 patients with clinically diagnosed rheumatic diseases such as rheumatoid arthritis/fibromyalgia (40 – 70 years of age).

b. Specify the participant population(s) to be included (check all that apply):

- Adults X
- Decisionally Impaired Adults → Complete Appendix W
- Children (< 18 years) → Complete Appendix I
- Healthy Volunteers
- Neonates (uncertain viability/nonviable) → Complete Appendix K
- Non-English Speaking → Complete Appendix J

Pregnant Women/Fetuses → Complete Appendix K
Prisoners → Complete Appendix L
Students from Participant Pools (e.g., REP) Specify:
Unknown (e.g., research using secondary data/specimens, non-targeted surveys, program protocols)

The Ohio State University Institutional Review Boards - INITIAL REVIEW OF HUMAN SUBJECTS RESEARCH

20. CHARACTERISTICS OF THE POPULATION(S) AND EXPLANATION OF RESEARCH REQUIREMENTS

In this study we will be examining the levels of BCRF in serum samples and cartilage/bone tissue to examine the relationship of the levels of BCRF in osteoarthritis (OA). To find any correlations between levels of BCRF and OA, four major types of patients/subjects will be recruited: (i) Healthy subjects undergoing joint surgery due to trauma. These subjects will serve as healthy controls with no disease activity, (ii) OA patients with radiographically confirmed OA, who will be undergoing joint surgery for cartilage repair. (iii) Osteoporosis patients with clinically and radiographically confirmed osteoporosis, (iv) Patients with clinically and symptomatically diagnosed other arthritic diseases such as rheumatoid arthritis or fibromyalgia. Groups (iii) and (iv) will provide the specificity of the BCRF levels in OA versus other joint diseases.

Arthritis is a disease mostly observed in adults. Therefore, in this pilot study we will use specimens from adults of mostly 40 and 75 years of age.

Pregnant women will not be included. Women will be verbally asked if they are pregnant, and if so, they will be advised not to take part in the study.

d. Are any of the participants likely to be vulnerable to coercion or undue influence? X No

If Yes → Describe additional safeguards to protect participants’ rights and welfare.

e. Will pregnant women be excluded from participation in the research? X Yes

If Yes → Explain how the nature of the research requires/justifies their exclusion. Address means of pregnancy screening.

Osteoporosis and osteoarthritis are both influenced by the changes in estrogen levels. Therefore, to exclude the possibility that BRF levels change during pregnancy, we will exclude pregnant women from this study. Women will be verbally asked if they are pregnant, if so, they will be advised not to take part in the study.

21. PARTICIPANT IDENTIFICATION, RECRUITMENT, & SELECTION

a. Provide evidence that you will be able to recruit the necessary number of participants to complete the study.

Drs. Flanigan and Hackshaw routinely treat patients with various forms of arthritis. They treat more than 500 patients per year with osteoarthritis/osteoporosis/ rheumatoid diseases. Therefore, recruiting patients with osteoarthritis (20), osteoporosis (20), rheumatoid arthritis (20) or healthy trauma patients undergoing joint surgery (20) is realistic.
b. Describe how potential participants will be identified (e.g., advertising, individuals known to investigator, record review, etc.). Explain how investigator(s) will gain access to this population, as applicable.

Identification of patients: The patients treated in the clinics of Drs. Hackshaw and Dr. Flanigan will be identified and recruited in this study. (i) Dr. Flanigan routinely treats patients and gets radiographic confirmation of OA, osteoporosis or trauma patients that require joint surgery to repair cartilage or bone. He will identify and recruit subjects undergoing surgery from this pool of patients. Dr. Flanigan will verbally describe the details of the study specified in the script. He will then give at least one week to the patients to decide on the participation in the study. Only those patients willing to participate will be recruited in the study. Once recruited in the study, he will collect small pieces of cartilage/bone that are discarded during surgery from osteoarthritic / osteoporotic / systemically healthy trauma patients. He will also ask for an extra cc of blood when the patients give blood for clinical testing. (ii) Dr. Hackshaw will recruit patients from his clinic. He will identify and recruit patients with clinically diagnosed rheumatoid arthritis or fibromyalgia. He will explain the details of the study to the patients and ask for their consent to participate in the study according to the script. The patients agreeing to consent for participation, will be recruited in the study. He routinely gets blood analysis performed on these patients. At that time he will ask for an additional one cc of blood saved in a separate tube.

We will not advertise to gain access to patient population being recruited. The only patients being treated by Drs. Hackshaw and Dr. Flanigan will be recruited in the study. Dr. Flanigan and Dr. Hackshaw will be provided a table with patient numbers (Sample attached). They will sequentially give the number to the specimen, and note the disease, approximate age and sex of the patient. No other identifiers will be used on the specimens.

c. List the investigator(s) and/or key personnel who will recruit participants and what process will be used to determine participant eligibility.

The Aims are to examine the presence of BCRF in the serum samples from patients with osteoarthritis/osteoporosis/rheumatoid arthritis or healthy trauma patients. Dr. Hackshaw and Dr. Flanigan will identify the patient population to be used in this study. Dr. Flanigan will be collecting tissue and blood from radiographically confirmed OA, osteoporosis or trauma patients undergoing joint surgery to repair cartilage/bone. Dr. Hackshaw, will be recruiting clinically diagnosed patients with rheumatoid arthritis or fibromyalgia. Drs. Flanigan and Hackshaw will determine the extent of arthritic disease in patients and their inclusion in the study. They are Dr. Agarwal’s collaborators and are aware of the Specific Aims of the study in detail. The serum samples /tissue fragments will be identified with disease, sex and age of the patient. All patient identifiers will be removed prior to sending the specimens to the lab for BCRF analysis.

d. Describe the recruitment process; including the setting in which recruitment will take place. Explain how the process respects potential participants’ privacy. Provide copies of proposed recruitment materials (e.g., ads, flyers, website postings, recruitment letters, and oral/written scripts).

Drs. Flanigan will identify patients in the clinic during the routine patient visit for the diagnosis of the disease/problem. Dr. Flanigan’s patients with radiographically confirmed OA, osteoporosis or trauma requiring joint surgery, would be recruited in the study. He will inform the patient of the ongoing study in the language provided in the script. The patient will be asked to let him know of his consent at the time of next appointment. In case the patient agrees to take part in the study, Dr. Flanigan will ask for an extra 1 cc of blood in a separate tube at the time of blood draw prior to surgery. He will also collect a small piece of bone and/or cartilage that are discarded during surgery, for analysis. He will then designate a number to the tube with diagnosis, approximate age and sex of the patient prior to sending it to the lab for BCRF analysis.

Similarly, Dr. Hackshaw’s patient with clinically diagnosed and symptomatic Rheumatoid arthritis/ fibromyalgia will be recruited. He will ask the patient of his possible participation in the study, as described in the script. In case patient agrees, Dr. Hackshaw will ask for 1 cc of blood be collected at the time of blood being drawn for clinical testing. He will then designate a number to the tube with diagnosis, approximate age and sex of the patient prior to sending it to the lab for analysis.

In all cases the privacy and identity of the patient will be kept strictly confidential. No patient identifiers will be used on the specimens.

### 22. INCENTIVES TO PARTICIPATE

Will participants receive compensation or other incentives (e.g., free services, cash payments, gift certificates, parking, classroom credit, travel reimbursement) to participate in the research study? Compensation plans should be pro-rated (not contingent upon study completion) and should consider participant withdrawals, as applicable.

If Yes → Describe the incentive, including the amount and timing of all payments.
23. ALTERNATIVES TO STUDY PARTICIPATION

Other than choosing not to participate, list any specific alternatives, including available procedures or treatments that may be advantageous to the subject.

In case the patients do not choose to participate in the study, at this point there are no alternatives that can be provided to the patients. This is a pilot study. We anticipate that we will be able to recruit sufficient patients in the study from Drs. Hackshaw and Flanigan’s patient populations. In case potential participants do not choose to participate in the study, they will not be included in the study. There are no other alternatives treatments that could be provided to the patients at this time.

24. INFORMED CONSENT PROCESS

a. Indicate the consent process(es) and document(s) to be used in the study. Check all that apply. Provide copies of documents and/or complete relevant appendices, as needed. See Consent for Research for templates or contact ORRP for more information.

- Assent – Form
- Assent – Verbal Script
- Informed Consent – Form
X Informed Consent – Verbal Script
Complete Appendix M2
- Parental Permission – Form
- Parental Permission – Verbal Script
- Translated Consent/Assent – Form(s)
Complete Appendix J
- Waiver or Alteration of Consent Process
Complete Appendix M1
- Informed Consent – Addendum
X Waiver of Consent Documentation
Complete Appendix M2

b. List the investigator(s) and/or key personnel who will obtain consent from participants or their legally authorized representatives.

Drs. Flanigan, Hackshaw and Agarwal will obtain the consent from the patients. Specimen will be collected from 20 healthy trauma patients undergoing joint surgery (40 to 70 years of age), 20 osteoarthritis patients (40 – 70 years of age), 20 osteoporosis patients (40 – 70 years of age), and 20 patients with other rheumatic diseases such as rheumatoid arthritis/fibromyalgia (40 – 70 years of age).

Dr. Flanigan will collect the cartilage/bone pieces from the discarded tissue while they are performing the surgical procedure.

N/A

Although Drs. Hackshaw or Flanigan.

When Drs. Flanigan or Hackshaw identify a patient with OA, osteoporosis, requiring trauma surgery, rheumatoid arthritis, or fibromyalgia, they will ask consent of the patient to participate in the study. At this time, the potential participants (patients scheduled for surgery or patients undergoing therapy) will be provided full information detailed in the script. They will be given a week to decide on the possible participation in the study. In case the participants decide to take part in the study, they will be asked to give 1 cc of blood while they give blood for clinical analysis. Dr. Flanigan will collect the cartilage/bone pieces from the discarded tissue while they are performing the surgical procedure.

N/A

Explain how the possibility of coercion or undue influence will be minimized in the consent process.

N/A

There will not be any coercion or undue influence for participants to take part in the study. The recruitment will be totally voluntary. The participants will be told clearly the details of the study as described in the script for verbal consent. Only those, who are willing to participate, will be included in the study.

f. Will any other tools (e.g., quizzes, visual aids, information sheets) be used during the consent process to assist participant comprehension?

X No

Provide copies of these tools
g. Will any other consent forms be used (e.g., for clinical procedures such as MRI, surgery, etc. and/or consent forms from other institutions)?

\[ \square \text{Yes } \rightarrow \text{Provide copies of these forms} \]
\[ \square \text{No} \]

25. PRIVACY OF PARTICIPANTS

a. Describe the provisions to protect the privacy interests of the participants.

No subject identifiers will be used on the specimens that are collected for the study. A new number will be given to all specimens and a list of the specimen will be provided to their physicians (Drs. Flanigan and Hackshaw). The specimen will be identified as early or late osteoarthritis, early or late osteoporosis, early or late Rheumatic disease, or healthy control, and approximate age of patient in years. No birthdates, names, or any other personal identifiers will be used.

b. Does the research require access to personally identifiable private information?

\[ \square \text{Yes} \]
\[ \square \text{No} \]

\[ \text{If Yes } \rightarrow \text{Describe the personally identifiable private information involved in the research. List the information source(s) (e.g., educational records, surveys, medical records, etc.).} \]

26. CONFIDENTIALITY OF DATA

a. Explain how information is handled, including storage, security measures (as necessary), and who will have access to the information. Include both electronic and hard copy records.

All patient identifiers on the specimens will be removed and destroyed. The tubes will be given a new number that is separate from clinical ID number and the specimen recorded by this number in hard and electronic data collection system. The new number given in the laboratory, with disease and age description, will identify the specimen. The laboratory technician running the test will have access to only new ID number, without patient identifier. Information gained from the tests by Dr. Agarwal will be shared with Drs. Hackshaw and Flanigan. No patient IDs will be used in the publications or any other means of dissemination of information.

b. Explain if any personal or sensitive information that could be potentially damaging to participants (e.g., relating to illegal behaviors, alcohol or drug use, sexual attitudes, mental health, etc.) will be collected.

\[ \square \text{Yes} \]
\[ \square \text{No} \]

\[ \text{N/A} \]

See OSU HRPP policy Privacy and Confidentiality for more information.

c. Will you be obtaining an NIH Certificate of Confidentiality?

\[ \square \text{Yes } \rightarrow \text{Provide a copy before you begin the research} \]
\[ \square \text{No} \]

d. Explain any circumstances (ethical or legal) where it would be necessary to break confidentiality.

\[ \text{N/A} \]

e. Indicate what will happen to the identifiable data at the end of the study. Research-related records should be retained for a period of at least three years after the research has been discontinued (i.e., no further data collection, long term follow-up, re-contact, or analysis of identifiable/coded data.)

\[ \square \text{Identifiers permanently removed from the data and destroyed (de-identified)} \]
\[ \square \text{Identifiable/coded (linked) data are retained} \]
\[ \text{X Identifiable data not collected} \]

27. HIPAA RESEARCH AUTHORIZATION

Will individually identifiable Protected Health Information (PHI) subject to the HIPAA Privacy Rule requirements be accessed, used, or disclosed in the research study?

\[ \text{X We will not be doing anything that is out of the line of normal patient care. (i) We will be collecting pieces of bone/cartilage tissue that is discarded during surgeries, and (ii) We will obtain one extra tube of 1 cc blood, while the patient is giving blood for regular analysis. These patients will be those currently being treated in the clinics. Drs. Flanigan and Hackshaw would be} \]
identifying these patients for the study and provide the samples with a new number, approximate age, sex and disease. No other identifiers will be required for the study. Therefore, if we ask for consent, we will be adding one source of possible disclosure of patient identity.

☐ Yes ➔ Check all that apply:
☐ Written Authorization ➔ Provide a copy of the Authorization Form
X Partial Waiver (recruitment purposes only) ➔ Complete Appendix N
☐ Full Waiver (entire research study) ➔ Complete Appendix N
☐ Alteration (written documentation) ➔ Complete Appendix N

28. REASONABLY ANTICIPATED BENEFITS

a. List the potential benefits that participants may expect as a result of this research study. State if there are no direct benefits to individual participants. Compensations is not to be considered a benefit.

There are no immediate potential benefits that participants may expect as a result of this research study.

b. List the potential benefits that society and/or others may expect as a result of this research study.

The potential benefits that would be realized will be identification of a biomarker that will be able to predict progression/remission of arthritic diseases.

29. RISKS, HARMS, & DISCOMFORTS

a. Describe all reasonably expected risks, harms, and/or discomforts that may apply to the research. Consider the range of risks, including physical, psychological, social, legal, and economic. As applicable, discuss severity and likelihood of occurrence.

No risks involved in the study. No procedure will be performed specifically for this study. (i) We will be collecting pieces of bone/cartilage tissue that is discarded during surgeries, and (ii) We will obtain one extra tube of 1 cc blood, while the patient is giving blood for regular analysis. These patients will be those currently being treated in the clinics.

b. Describe how risks, harms, and/or discomforts will be minimized.

N/A

30. MONITORING

Does the research involve greater than minimal risk (i.e., are the harms or discomforts described in Question #29 beyond what is ordinarily encountered in daily life or during the performance of routine physical or psychological tests)?

☐ Yes ➔ X No

If Yes ➔ Describe the plan to oversee and monitor data collected to ensure participant safety and data integrity. Include the following:

• The information that will be evaluated (e.g., incidence and severity of actual harm compared to that expected);
• Who will perform the monitoring (e.g., investigator, sponsor, or independent monitoring committee);
• Timing of monitoring (e.g., at specific points in time, after a specific number of participants have been enrolled); and
• Decisions to be made as a result of the monitoring process (e.g., provisions to stop the study early for unanticipated problems).

31. ASSESSMENT OF RISKS & BENEFITS

Discuss how risks to participants are reasonable when compared to the anticipated benefits to participants (if any) and the importance of the knowledge that may reasonably be expected to result.

There are no risks to patients. The only risk to healthy subjects may be a small hematoma caused during blood draw. The knowledge gained from this study will be very beneficial to arthritis patients. At this time there are no biomarkers that can predict whether a drug has delayed progression of the disease or that a patient is producing growth factors required for bone repair. This study might be able to provide a biomarker to test the progression / repair of cartilage/ bone in patients with joint diseases.
32. PARTICIPANT COSTS/REIMBURSEMENTS

a. List any potential costs subjects (or their insurers) will incur as a result of study participation (e.g., parking, study drugs, diagnostic tests, etc.).

N/A

b. List any costs to participants that will be covered by the research study.

None.
33. APPLICATION CONTENTS

Indicate the documents being submitted for this research project. Check all appropriate boxes.

☒ Initial Review of Human Subjects Research Application
☒ Appendix A1: OSU Co-Investigators & Key Personnel (questions 4 & 5)
☐ Appendix A2: External (non-OSU) Co-Investigators & Key Personnel (question 6)
☐ Appendix B: Expedited Review – Initial Review (question 13)
☐ Appendix C: Data Repositories (question 17b)
☐ Appendix D: Deception (question 17b)
☐ Appendix E: Devices (question 17b)
☐ Appendix F: Drugs or Biologics (question 17b)
☐ Appendix G: Genetic Testing (question 17b)
☐ Appendix H: Storage of Biological Materials (question 17b)
☐ Appendix I: Children (question 20b)
☐ Appendix J: Non-English Speaking Participants (questions 20b and 24a)
☐ Appendix K: Pregnant Women/Fetuses/Neonates (question 20b)
☐ Appendix L: Prisoners (question 20b)
☐ Appendix M1: Waiver or Alteration of Consent Process (questions 17b & 24a)
☒ Appendix M2: Waiver of Consent Documentation (question 24a)
☐ Appendix N: Waiver of HIPAA Research Authorization (question 27)
☐ Appendix U: Research in International Settings (question 12)
☐ Appendix V: Radiation (question 17b)
☐ Appendix W: Decisionally Impaired Adults (question 20b)
☐ Consent form(s), Assent Form(s), Permission Form(s), and Verbal Script(s), including translated documents (question 24a)
☐ HIPAA Research Authorization Form(s) (question 27)
☐ Data Collection Form(s) involving protected health information (Appendix N)
☐ Recruitment Materials (e.g., ads, flyers, telephone or other oral script, radio/TV scripts, internet solicitations) (question 21d)
☐ Script(s) or Information Sheet(s), including Debriefing Materials (question 24)
☐ Instruments (e.g., questionnaires or surveys to be completed by participants) (question 17b)
☐ Other Committee Approvals/Letters of Support (questions 11 & 12)
☒ Research Protocol
☐ Complete Grant Application or Funding Proposal
☐ Drug Manufacturer’s Approved Labeling/Investigator’s Drug Brochure (Appendix F)
☐ Device Manufacturer’s Approved Labeling (Appendix E)
☐ Other supporting documentation and/or materials

For Multi-Center Clinical Trials supported by DHHS, the submission will also include:
☐ DHHS-approved Sample Informed Consent Document (if one exists)
☐ DHHS-approved Protocol (if one exists)
34. ASSURANCE

PRINCIPAL INVESTIGATOR (or Advisor)

I agree to follow all applicable policies and procedures of The Ohio State University and federal, state, and local laws and guidance regarding the protection of human subjects in research, as well as with professional practice standards and generally accepted good research practice guidelines for investigators, including, but not limited to, the following:

- Perform the research as approved by the IRB under the direction of the Principal Investigator (or Advisor) by appropriately trained and qualified personnel with adequate resources;
- Initiate the research after written notification of IRB approval has been received;
- Obtain and document (unless waived) informed consent and HIPAA research authorization from human subjects (or their legally authorized representatives) prior to their involvement in the research using the currently IRB-approved consent form(s) and process;
- Promptly report to the IRB events that may represent unanticipated problems involving risks to subjects or others;
- Provide significant new findings that may relate to the subjects willingness to continue to participate;
- Inform the IRB any proposed changes in the research or informed consent process before changes are implemented, and no changes will be made until approved by the OSU IRB (except where necessary to eliminate apparent immediate hazards to participants);
- Complete and submit a Continuing Review of Human Subjects Research application before the deadline for review at intervals determined by the IRB to be appropriate to the degree of risk (but not less than once per year) to avoid expiration of IRB approval and cessation of all research activities;
- Maintain research-related records (and source documents) in a manner that documents the validity of the research and integrity of the data collected, while protecting the confidentiality of the data and privacy of participants;
- Retain research-related records for audit for a period of at least three years after the research has ended (or longer, according to sponsor or publication requirements) even if I leave the University;
- Contact the Office of Responsible Research Practices for assistance in amending (to request a change in Principal Investigator) or terminating the research if I leave the University or am unavailable to conduct or supervise the research personally (e.g., sabbatical or extended leave);
- Provide a Final Study Report to the IRB when all research activities have ended (including data analysis with individually identifiable or coded private information); and
- Inform all Co-Investigators, research staff, employees, and students assisting in the conduct of the research of their obligations in meeting the above commitments.

I verify that the information provided in this Initial Review of Human Subjects Research application is accurate and complete.

__________________________
Signature of Principal Investigator (or Advisor)

Sudha Agarwal / david Flanigan / Kevin hackshaw
Printed name of Principal Investigator (or Advisor)

__________________________
Date March 16, 2010

DEPARTMENT CHAIR (or Signatory Official)

As Department Chair (or Signatory Official) for the Principal Investigator, I acknowledge that this research is in keeping with the standards set by our unit and that it has met all Departmental/College requirements for review.

*If the PI or any Co-Investigator is also the Department Chair, the signature of the Dean or other appropriate Signatory Official, such as the Associate Dean for Research, must be obtained.*

__________________________
Signature of Department Chair

Scott Herness
Printed name of Department Chair

__________________________
Date March 16, 2010
**APPENDIX A1**

**OSU Co-Investigators & Key Personnel**

Complete this form to list OSU Co-Investigators and key personnel on the research study. Signatures are required of all OSU Co-Investigators. Use Appendix A2 to list external (non-OSU) Co-Investigators and key personnel.

*Key personnel are defined as individuals who participate in the design, conduct, or reporting of human subjects research. At a minimum, include individuals who recruit or consent participants or who collect study data.*

*All OSU individuals listed on this protocol will have access to information about IRB actions and the completion status of each individual's administrative and training requirements (CITI, COI disclosure). Note: Personal financial information provided in COI disclosures is not included.*

**PI Name: Sudha Agarwal**

<table>
<thead>
<tr>
<th>Name (Last, First, MI):</th>
<th>Degree(s):</th>
<th>University Academic Title:</th>
<th>College (TIU):</th>
<th>Department Name (TIU):</th>
<th>Department # (TIU):</th>
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<tr>
<td>Agarwal, Sudha</td>
<td>Ph.D.</td>
<td>Professor</td>
<td>Dentistry</td>
<td>Oral Biology</td>
<td>21350</td>
<td>03133876</td>
<td>614-537-6986</td>
<td><a href="mailto:Agarwal.61@osu.edu">Agarwal.61@osu.edu</a></td>
</tr>
<tr>
<td>Signature of Co-Investigator</td>
<td></td>
<td>Date March 16, 2010</td>
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Printed name of Co-Investigator Sudha Agarwal

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<tr>
<td>David Flanigan</td>
<td>M.D.</td>
<td>Assistant Professor</td>
<td>Medicine</td>
<td>Orthopedics</td>
<td>Clinic: (614) 293-3600, Office: (614) 293-2413</td>
<td>(614) 293-8093</td>
<td><a href="mailto:David.Flanigan@osumc.edu">David.Flanigan@osumc.edu</a></td>
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<tr>
<td>Signature of Co-Investigator</td>
<td></td>
<td>Date March 16, 2010</td>
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<td>Hackshaw, Kevin V.</td>
<td>M.D.</td>
<td>Associate Professor</td>
<td>Medicine</td>
<td>Immunology/Rheumatology</td>
<td></td>
<td></td>
<td>(614) 293-8093</td>
<td><a href="mailto:Kevin.Hackshaw@osumc.edu">Kevin.Hackshaw@osumc.edu</a></td>
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Signature of Co-Investigator ___________________________ Date ____________

Printed name of Co-Investigator ___________________________

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Printed name of Co-Investigator ___________________________

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Signature of Co-Investigator ___________________________ Date ____________

Printed name of Co-Investigator ___________________________
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<th>Name (Last, First, MI):</th>
<th>Madiai, Francesca</th>
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<td>Department Name:</td>
<td>Rheumatology</td>
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<tr>
<td>E-mail:</td>
<td><a href="mailto:Francesca.madiai@osumc.edu">Francesca.madiai@osumc.edu</a></td>
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<tr>
<td>University Title:</td>
<td>Research Associate</td>
</tr>
<tr>
<td>OSU ID Number:</td>
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<td>Phone:</td>
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**APPENDIX M2**
Waiver of Consent Documentation

Complete this form to request a waiver of consent documentation for the proposed research. DHHS regulations permit waivers of documentation of the consent process if the research meets certain conditions. DHHS and FDA regulations differ regarding when an IRB may waive the requirement to document the informed consent process.

Do not complete this form to request a waiver or alteration of the consent process, use Appendix M1.

Additional guidance can be found at 45 CFR 46.117 and 21 CFR 56.109.

---

**PI Name:** Sudha Agarwal / David Flanigan / Kevin Hackshaw

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<tr>
<td>1.</td>
<td>Is the research subject to FDA regulations (e.g., involves use of a food, drug, biologic, device)?</td>
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<td>[ ] Yes</td>
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**If Yes, only section (2) may be used to request waiver of consent documentation.**

**If No, either section (2) or (3) may be used to request waiver of consent documentation.**

*Documentation of consent cannot be waived under the conditions of the last section below if the research involves a product regulated by FDA or the results of the research may be submitted to FDA as part of a marketing application.*

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<td>2.</td>
<td>Both answers below (2a and 2b) must be No for a waiver of consent documentation:</td>
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<td></td>
<td>a. Does the research present greater than minimal risk?</td>
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<td>[ ] Yes</td>
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<td></td>
<td>b. Does the research involve procedures for which written consent is normally required outside the research context?</td>
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<td>[ ] Yes</td>
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**If No, explain how the research meets both (2a and 2b) of the conditions above.**

2a. The research requires 1 CC of blood samples drawn at the time of blood collection for normal treatment of patients. The blood draw from healthy controls, in few cases may impose a minimal risk of a small hematoma at the site of venipuncture.

2b. Research protocol seeks to obtain cartilage and bone specimens that are discarded during the surgical procedures. Thus, it does not require any procedure specifically for this study.

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<td>3.</td>
<td>Both answers below (3a and 3b) must be Yes for a waiver of consent documentation:</td>
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<tr>
<td></td>
<td>a. Would the only record linking the participant and the research be the consent document?</td>
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<td>X Yes</td>
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<td></td>
<td>b. Would the principal risk to the participant be potential harm resulting from a breach in confidentiality?</td>
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<td>X Yes</td>
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*Note: The participant should be asked whether he/she wants documentation linking the participant with the research; the participant’s wishes will govern.*

**If Yes, explain how the research meets both (3a and 3b) of the conditions above.**

3a. All patient identities will be removed and a new number given to all of the specimens before the lab analysis. Therefore, if we take consent from the patients, it will be the only identity that would link specimens to the patient.

3b. The bone and cartilage samples will be obtained from the tissue that is already discarded during the surgery. This discarded tissue will not have patient identifiers. If we ask for consent form, the patient identity will be disclosed. This may lead to potential chances of a breach of confidentiality of patients. Additionally, Drs. Flanigan and Hackshaw will be obtaining the consent for tissue / blood specimens procurement, and numbering them prior to sending them to the lab.
They will take verbal consent of the patients for the blood and tissue specimen for use in the study. Script of the consent is attached with form M2.
APPENDIX N
Waiver of HIPAA Research Authorization

<table>
<thead>
<tr>
<th>PROJECT TITLE</th>
<th>PI NAME</th>
<th>OSU PROTOCOL NUMBER</th>
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<tbody>
<tr>
<td>Investigations on BCRF as a biomarker for joint disease progression</td>
<td>Sudha Agarwal, Co-Pis Kevin Hackshaw, David Flanigan</td>
<td>2010-H0110</td>
</tr>
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</table>

Complete this form to request a waiver/alteration of HIPAA authorization to access, use, or disclose Protected Health Information (PHI) for the proposed research. The Privacy Rule permits waivers (or alterations) of authorization if the research meets certain conditions.

**PHI** is health information containing one or more 18 identifiers, see HIPAA Definitions and Identifiers.

For more information, see 45 CFR Parts 160 and 164 or “Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule.”

1. Indicate the type of waiver/alteration requested:
   - [X] Partial Waiver (recruitment purposes only)
   - [ ] Full Waiver (entire research study)
   - [ ] Alteration (written documentation)

2. List the source(s) of the PHI (e.g., OSUMC Information Warehouse, eResults, physician’s office records, clinical database, etc.). Be as specific as possible.

   *Only PHI to be used from the physician’s records is patient’s approximate age, sex and the type of disease being treated, i.e., osteoarthritis, osteoporosis, or rheumatic disease. Dr. Flanigan / Hackshaw will be obtaining the specimens from patients being treated in the clinic and number the specimens with approximate age, sex and disease from their records. Subsequently, the specimens will be sent to the lab for analysis. OSUMC Information warehouse, eResults, clinical data base will NOT BE USED for this study.*

3. Provide information below about the PHI involved in the research (e.g., medical record number, health history, diagnosis, test results, etc.). Be as specific as possible.
   a. Describe the PHI accessed for the research.

   In this pilot study, the physicians will provide approximate age, sex and diagnosis of the patient, when they give the specimens for lab analysis. Drs. Flanigan and Hackshaw will give the tubes with specimen number, disease, approximate age and sex (new identifiers to the specimen), prior to lab analysis. No other patient health information will be accessed from medical records.
   b. Describe information that will be recorded and provide a copy of the data collection form(s) to be used.

   The only information recorded from the patient will be the disease and approximate age of the patient. No other identifiers will be used. Please see the attached Sample Form.

4. Explain why access to and/or use of the PHI is essential to conduct the research.

   Access to and/or use of PHI is not required for this study. The only information needed is the approximate age and sex of the patient and the disease being treated. No other PHI is essential for this study.

5. Explain how the PHI described above represents the minimum necessary information to accomplish the objectives of the research.

   The approximate age of the patient, sex and the disease being treated is the minimal necessary information for the study to assess whether BCRF can be used as a biomarker for disease activity. This minimal information would suffice to accomplish the goals of the study.

6. Explain how the access, use, or disclosure of PHI presents no more than a minimal risk to the privacy of the individual.
The specimens will be identified with a new identification number, age and disease of the patient and all other identifiers will be removed prior to specimen being sent for analysis in the lab. Thus, there is no possibility of the disclosure of the privacy of the patient. However, if we do have a consent form or any other form with patient identity, this may impose a risk of the disclosure of patient identity.

7. Describe your plan to protect the identifiers (or links to identifiable data) associated with the PHI from improper use and disclosure, including where PHI will be stored, what security measures will be applied, and who will have access to the information. Describe the safeguards for electronic and/or hard copy records.

The physicians, Drs. Flanigan or Hackshaw will have the patient identifiers with their clinical records. They will provide samples with an identification number, approximate age, sex and disease on the tube, prior to sending the specimens to the laboratory. No other identifiers will be used on the specimens. Once the tubes are numbered with required data, any other PHI will not be required or accessed. The PHI will be stored at the medical center according to the routine procedure. The only person who will have the information is the physicians taking care of the patient. No other individual will be accessing the patient health information. Patient information will not be used in e-records, hard copies, publications, or presentations for research reporting or data collection.

8. Will identifiers (or links to identifiable data) be destroyed?

☐ Yes – Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. Include when and how identifiers will be destroyed.

☐ No – Provide the legal, health, or research justification for retaining the identifiers. Legal justification should include a brief description/citation of the legal requirement.

X N/A – Will not record identifiers or create links or codes to connect the data.

9. Explain why a waiver or alteration (instead of written authorization) is needed to conduct the research.

The patient identifiers are not essential for this study. We will be examining the presence of BCRF in the bone and/or cartilage fragments and levels of BCRF in the blood. The only information required is patient’s age, sex and disease to correlate the levels of BCRF to the disease activity. If we obtain a written consent from patients, this consent form will then be connected to the specimen identity and have a greater chance of loss of protection of privacy of the patient. Drs. Hackshaw or Flanigan will ask verbal consent of the patient to use their discarded tissue specimens or one extra cc of blood, after explaining the basis for this research as described in the script for verbal approval. They will then give a number to the specimen and thus there is much secure way of protecting patients identity and PHI.
Appendix N – WAIVER OF HIPAA RESEARCH AUTHORIZATION

Investigator Assurance

I assure that the Protected Health Information obtained as part of this research will not be reused or disclosed to any other person or entity other than those listed (except as required by law for authorized oversight of the research project) without additional approval and that I will seek IRB/Privacy Board approval for other research involving the use or disclosure of this PHI. As necessary, I must document and account for all disclosures or releases of identifiable information granted under this waiver. My signature below indicates my agreement to collect only the minimum necessary Protected Health Information to meet the research objectives and to limit access to this information as described above. I acknowledge that it is my responsibility as the Principal Investigator that all Co-Investigators, research staff, employees, and students assisting in the research are trained on privacy and confidentiality and will be informed of their obligations in complying with the above.

[Signature]
[Name]

Date

All persons who will access medical information must sign and date below:

I assure that the Protected Health Information obtained as part of this research will not be reused or disclosed to any other person or entity other than those listed (except as required by law for authorized oversight of the research project) without additional approval and that I will seek IRB/Privacy Board approval for other research involving the use or disclosure of this PHI. My signature below indicates my agreement to collect only the minimum necessary Protected Health Information to meet the research objectives and to limit access to this information as described above.

[Signature]
[Name]

Date

[Signature]
Date

[Signature]
Date

[Signature]
Date

[Signature]
Date

IRB or Privacy Board Approval

[Signature]
[Name]

Date

Form Date: 09/25/09
Version 2.2
Investigator Assurance

I assure that the Protected Health Information obtained as part of this research will not be reused or disclosed to any other person or entity other than those listed (except as required by law for authorized oversight of the research project) without additional approval and that I will seek IRB/Privacy Board approval for other research involving the use or disclosure of this PHI. As necessary, I must document and account for all disclosures or releases of identifiable information granted under this waiver. My signature below indicates my agreement to collect only the minimum necessary Protected Health Information to meet the research objectives and to limit access to this information as described above. I acknowledge that it is my responsibility as the Principal Investigator that all Co-Investigators, research staff, employees, and students assisting in the research are trained on privacy and confidentiality and will be informed of their obligations in complying with the above.

[Signature]
Date: 3/16/10

Printed name of Principal Investigator (or Advisor)

All persons who will access medical information must sign and date below:

I assure that the Protected Health Information obtained as part of this research will not be reused or disclosed to any other person or entity other than those listed (except as required by law for authorized oversight of the research project) without additional approval and that I will seek IRB/Privacy Board approval for other research involving the use or disclosure of this PHI. My signature below indicates my agreement to collect only the minimum necessary Protected Health Information to meet the research objectives and to limit access to this information as described above.

[Signature]  [Signature]  [Signature]  [Signature]  [Signature]
Date: 3/15/2010  Date  Date  Date  Date  Date

IRB or Privacy Board Approval

[Signature]
Date: 4/29/10

Signature of IRB or Privacy Board Chair
Information that will be provided verbally or in written form to the subjects that are recruited in the study

Study title: **BCRF: as a biomarker for joint disease progression**

In this study we are asking your willingness to participate. Please consider the information carefully. If you decide to participate, feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.

- Your participation is voluntary. You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.

- You may or may not benefit as a result of participating in this study. You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate. If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

- **1. Why is this study being done?** We have discovered that BRF is not produced in the body during arthritis in animal models. This protein is very important in bone function and healthy bone formation. Therefore, to find out if BRF is lower in patients with arthritis, we are recruiting participants for this study.

- **2. How many people will take part in this study?** We anticipate recruiting 80 people for the study.

- **3. What will happen if I take part in this study?** You will be asked to (i) give 1 CC of blood while your blood is being drawn for clinical tests, and (ii) the tissue that would be discarded during surgery will be saved and used for this study.

- **4. How long will I be in the study?** You are not being recruited for any time period in the study. We are only asking permission to (i) use the diseased tissue that is discarded during joint surgery, (ii) obtain 1 extra cc of blood, while the blood is being drawn for your clinical tests, necessary for your treatment.

- **5. Your participation is voluntary.** You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

- **6. Will my study-related information be kept confidential?** Efforts will be made to keep your study-related information confidential. However, there may be
circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

7. What are the costs of taking part in this study? None.

8. Will I be paid for taking part in this study? No.

9. What happens if I am injured because I took part in this study? There are no extra procedures being performed just for this study. We are asking for: (i) One cc (half a teaspoon) of blood when you give blood for the diagnosis and treatment of your disease. (ii) A small piece of diseased or injured tissue that is discarded during surgery.

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center. The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

10. What are my rights if I take part in this study? If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study. You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable to carry out studies after a verbal consent of the subject. According to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

11. Who can answer my questions about the study? For questions, concerns, or complaints about the study you may contact Dr. Flanigan or Dr. Hackshaw.