IBD

PI: Ilke Nalbantoglu
IRB ID #: 201307092

Project Details

I. Demographics

I.1 Project Title:
INFLAMMATORY/INFECTIOUS DISEASES OF THE GASTROINTESTINAL TRACT

I.2 Short Title (required):
IBD

I.3 Project is primarily:
Biomedical

I.4 Do you want the IRB to give this project
Regular (expedited or full board) review

I.7 Enter the estimated date you will be ready to begin recruiting participants or collecting data for this project.
08/01/2013

I.8 Provide a short summary of the purpose and procedures of the study proposed in this IRB application.

- DO NOT include information on studies not proposed in this application. (If your source of support proposal describes multiple aims, refer to the information button for an example on how to complete this question.)
- Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.
- DO NOT cut and paste technical abstracts from source of support applications that may not be understood by a general audience.

Inflammatory dieases of GI tract are heterogenous group of diseases, that manifest both in upper and lower gastrointestinal as well as systemic involvement. The patients present with diarrhea, heartburn,liver and other systemic diseases. The etiology of these group of diseases are poorly understood and the looks under the microscope can be very similar to other processes. Since some of these are relapsing remitting diseases, pathology is very important in clinical follow-up and patient management in terms of diagnosis, disease activity, detection of dysplasias and secondary infections. Pathological exam is also important in diagnosing the mimickers of disease such as long standing infections and/or medication efects. The diagnosis is usually made by clinico-pathological correlation.
The purpose of this pathology project is to study inflammatory/infectious diseases of the gastrointestinal tract in full spectrum, including the looks under the microscope, along with clinical findings. This big project includes a group of small individual projets to address each question in the field similar but not limited to what is described below.
An insight to definition of the injury patterns, inflammatory cell components(lymphocytes, red blood cells etc), diagnosis, differential diagnosis,etiology(cause)and, correlation with clinical features (right vs left sided disease, endoscopic features etc) is intended. The histologic, immunohistochemical, and molecular studies on previously obtained paraffin embedded tissue samples will be performed based on the specific questions such as "What are the inflammatory cell components in primary sclerosing cholangitis associated colitis patients and does it have any clinical significance?", "What are the histologic features of atypical lymphocytic colitis vs infectious colitis?", " Are there any specific immunohistochemical and/or molecular markers of dysplasia in inflammatory bowel disease?".

I.9 Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")

The study aim of this project (these projects) is to define the looks under microscope, the immunohistochemical, histochemical, and molecular (if needed) features of inflammatory diseases of the gastrointestinal tract and seek clinico-pathological correlation. We believe since these are a group of heterogenous group of diseases, they will help overlapping histologic, immunohistochemical etc features such as the injury pattern or the distribution in B and T cells. It is also hypothesized that diseases with similar looks under the microscope will have completely different cell distributions and clinical features. We would like to study and define the similarities and differences in the spectrum to aid better diagnose and understand the disease. This information may even be used to guide therapy in the future. However, this study does intend to work on the disease primarily from a pathology perspective with some clinical correlation mainly focusing on histology and other ancillary tests (as described above) that can be performed on paraffin embedded tissue.

I.10 Background and significance and/or Preliminary studies related to this project.
*(**do not** indicate "see protocol")*
There are a number of studies in the literature trying to address questions regarding disease etiology, connections, clinical outcome and pathology. Most studies point out that inflammatory diseases are a spectrum but not all the histologic features, the components of inflammation, etc are well described and understood. A few preliminary studies that is worth mentioning are the ones that are related to the definition of inflammatory cell components in inflammatory bowel diseases as well as microscopic colitis, the investigators found that IgG4 positive plasma cells are increased in a subset of patients with Primary sclerosing cholangitis associated colitis. However no studies done to look at patients who don't have colitis but PSC and see of the yhave similar features. Investigators also reported

rarae cases of collagenous colitis late in the disease course of ulcerative colitis, again there are no descriptive studies to higlight the histologic features and imuunohistchemical properties to these overlap cases. Another notable one is the "serrated lesion" in inflammatory bowel disease. Noone really knows about the clinical significance of this entity. We do have a number of cases and plan to give a detailed description in respect to proliferative zones and endoscopic correlation.

I.11 Literature cited / references (if attaching a grant or protocol enter N/A).

1. Metachronous occurrence of collagenous colitis and ulcerative colitis, F M Giardiello, F W Jackson, A J Lazenby, Gut, 1991,32,447-449
2. Mucosal IgG4 Cell Infiltration in Ulcerative Colitis Is Linked to Disease Activity and Primary Sclerosing Cholangitis Amit Raina, MD, CNSC, Dhiraj Yadav, MD, MPH, Miguel Regueiro, MD, Alyssa M. Krasinskas, MD,Melissa I. Saul, MS, Dee Ann M. Sapienza, David G. Binion, MD Douglas J. Hartman, MD,Inflamm Bowel Dis 2013;19:1232–1237
3. Hyperplastic/Serrated Polyposis in Inflammatory Bowel Disease A Case Series of a Previously Undescribed Entity.,Amitabh Srivastava, MD,Mark Redston, MD,w Francis A. Farraye, MD, MSc,z Rhonda K. Yantiss, MD,and Robert D. Odze, MD, FRCP, Am J Surg Pathol 2008;32:296–303

I.12 Select up to three key words below that best describe this research study:
- Internal Medicine
  - Gastroenterology
- Pathology

II. Research Team

II.0 Principal Investigator

Name	E-mail	Title	School
Ilke Nalbantoglu	inalbantoglu@path.wustl.edu	Asst Prof of Pathology & Immunol	School

II.1 The Principal Investigator of this study is:
Faculty

II.3 Do you want to add a team member who is a WUSTL faculty, student or staff member?
Yes

II.4 Do you want to add a team member who is **not** a WUSTL faculty, student or staff member?
No

II.5 Team Members

WUSTL Team Members

Role	Name	E-mail	Title	School	Department	Contact	WUST COI
PI	Ilke Nalbantoglu, MD	inalbantoglu@path.wustl.edu	Asst Prof of Pathology & Immunol	School Of Medicine	Anatomic & Molecular Pathology	Yes	
	John Chrisinger, BA, MD	jchrisinger@wupath.wustl.edu			Pathology & Immunology Lab	No	
	George Christophi, MD, PHD	gchristo@dom.wustl.edu			Barnes Hospital	No	
	Themistocles Dassopoulos, MD	themos@dom.wustl.edu			Im - Gastroenterology	No	
	Carmen Perrino, MD	cperrino@path.wustl.edu			Immunobiology	No	
	Yaman Tarabishy, MD	ytarabishy@path.wustl.edu			Immunobiology	No	
	Rao Watson, MD	rwatson@path.wustl.edu			Barnes Hospital	No	

Name	Financial Interests
Ilke Nalbantoglu, MD	none
John Chrisinger, BA, MD	none
George Christophi, MD, PHD	none
Themistocles Dassopoulos, MD	none
Carmen Perrino, MD	none
Yaman Tarabishy, MD	none
Rao Watson, MD	none

Non-WUSTL Team Members

Name	Institution	Location	FWA	Role	DHHS	Contact	WUSTL COI	Consent Process
Nothing found to display								

Name	Financial Interests

Nothing found to display

III. Source(s) of Support

III.1 Source(s) of Support

	Type	Source	Grant Title	Name of PI on Grant	Status	Status Description
	Departmental					

* new source name

IV. Waiver of Consent

IV.1 Are you requesting a waiver of informed consent (participants will not be given any oral or written information about the study prior to their participation)?
Yes, for all subjects

IV.3 Will you provide any information about the study after their participation?
No

IV.5 Indicate type of study (check all that apply)
- Retrospective review of medical record data with ALL data existing as of application date
  Estimated maximum number of charts/records: 800
- Analysis of archived specimens with ALL specimens existing as of application date
  Estimated maximum number of specimens: 800

IV.6 For the set of data you wish to review, list the earliest (beginning) date the data you wish to review were created:
01/01/2000

IV.7 List the latest (ending) date the data you wish to review were created:
08/01/2013

IV.8 Indicate sources of your data or specimens (check all that apply)
- WUSM/BJH/SLCH records/specimens - BJC Clinical Desktop

IV.9 List ALL

- data points
- identifiers or links to identifiers

you plan to obtain/use for purposes of this study. *(The information accessed should be the minimum data necessary for performing the desired analysis.)*
Two sets of general data will be needed for the purposes of these studies: General patient info: Patient age, gender, the onset of disease, clinical symptoms such as bloody/non-bloody diarrhea, constipation, primary sclerosing cholangitis, bacterial cultures etc, medication history, response to treatment, serum markers
Disease related: Endoscopic appearance, disease distribution, radiologic exams (if present) related to disease, pathology diagnosis

IV.10 A minimal risk study is a study in which 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.

Explain why this study involves no more than minimal risk to participants or to their privacy.
These studies will be performed on previously obtained pathology specimens for routine patient care. No additional tissue sampling or patient interaction, intervention is neccessary. Minimal clinical information and personal identifiers will be obtained related to the study. No patient names, social security numbers will be recorded. Even though this may still involve minimal risk, the patients will be stripped from any identifiers once the data is collected. The code will only be with the PI.

IV.11 Explain why this consent waiver will not adversely affect the participant's rights and welfare.
These are retrospective studies based on previously collected specimens for routine patient care. We intend to correlate and better understand the features and their clinical correlates. This will not interfere with patient management and care. The cases will be de-identified after data collection and the code will only be accessible to PI, which will be stored in a password protected computer in a locked office. The use of data sticks will not be allowed during this project.

IV.12 Explain why it is impracticable (not possible) to conduct this research without a waiver of consent.
It is impracticable to obtain consent from patients from a 13 year spectrum for this retrospective project. Most of these patients seeked care for only a short period of time at our hospital and are inaccessible. Some, unfortunately expired. It is also impractical since the study groups will be more flexible in terms of classifying disease and it is hard to know

which patients will be enrolled in the project.

IV.13 Will you be accessing any medical records or medical information, or do any of the data you plan to access meet the federal regulatory definition of **protected health information (PHI)**?
Yes

IV.14 Explain why it is impracticable (not possible) to conduct this research without access to and use of protected health information.
The only PHI that we will be collecting from patients is age and gender. Those are important clinical parameters for certain inflammatory diseases(such as primary sclerosing cholangitis is seen in young males, ulcerative colitis is seen both males and females with bimodal age distribution)therefore needed for this study.

IV.15 Describe your plan to protect any participant and/or specimen identifiers from improper use and disclosure. (Identifiers include but are not limited to names, addresses, dates directly related to the participant (such as birth date, date of admission/discharge, date of clinic visit/procedure/diagnosis), social security number, medical record number, pathology accession number, or other account numbers, etc.)
Once the data is collected, the cases will be stripped from any identifiers, and coded as "patient 1", "patient 1, Crohn's", "patient 1, microscopic colitis" etc. The codes will be stored in a password protected computer in a locked office which is located in a hallway with badge access. Only PI will have access to this information. The use of pen drives(data sticks) is not allowed in this project, any communication will be made within network email system, emails will be encrypted.

IV.16 Describe EITHER

- your plan to destroy participant identifiers at the earliest opportunity consistent with the conduct of the research, OR
- explain the health or research justification for retaining participant identifiers.

Once the data is collected, experiments are conducted, and the scientific papers are written, the data will be destroyed in PI's computer.

V. Other Institutional Reviews/Requirements

V.1 Do you or a family member have within the past twelve months or anticipate having within the next twelve months any financial interests in the company/organization providing support for this research or from a company/organization that owns or licenses the drug, device, or intellectual property being utilized in this research?

Name	Financial Interests
Ilke Nalbantoglu, MD	none
John Chrisinger, BA, MD	none
George Christophi, MD, PHD	none
Themistocles Dassopoulos, MD	none
Carmen Perrino, MD	none
Yaman Tarabishy, MD	none
Rao Watson, MD	none

V.4 Do any of the objectives of this study involve the diagnosis, prevention, screening, evaluation, treatment or support of cancer patients?
No

V.5 Are more than 30% of the patients involved in this study likely to have an active cancer diagnosis?
No

V.7 Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or radiopharmaceutical therapy)?
No

V.10 Does your study involve the administration of radiopharmaceuticals (radioactive drugs) for research purposes?
No

V.12 Will any participant be asked to undergo any of the following:

- a standard radiology procedure involving ionizing radiation (includes X-rays, fluoroscopy, DEXA, CT)

  OR

- a standard nuclear medicine examination with FDA-approved radioactive drugs (including bone scans, radionuclide ventriculogram (RVG or MUGA), myocardial perfusion imaging, FDG-PET)

- DO NOT include MRI or ultrasound

No

V.17 Will the study involve any of the following activity at WUSM or any BJC hospitals, *even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or*

no funding)?

- Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or
- Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)

No

V.18 Does this project involve administration of recombinant DNA (gene therapy) or microorganisms?
No

V.19 Does this study involve the use of human embryonic stem cells or human induced pluripotent stem cells?
No

V.20 Does this study involve research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero?
No

V.21 Will you be utilizing participants, data or tissue from the Memory & Aging Project (MAP) or Alzheimer's Disease Research Center (ADRC)?
No

V.22 Is the PI of this study a BJH Registered nurse or a staff member of Patient Care Services (Pharmacy, PT/OT/, Respiratory, Rehabilitation, and Social work)?
No

V.23 Will any portion of this project be conducted in any Center for Applied Research Sciences Units, Clinical Research Unit (CRU), Clinical Trials Unit (CTU) and/or the Pediatric Research Unit (PCRU)?
No

V.24 Will this research be performed in the Neonatal Intensive Care Unit (NICU)?
No

V.25 Is this research being conducted in the Emergency Department?
No

V.26 Are you recruiting or screening patients in the Emergency Department?
No

VI. Participants

VI.38 Does this project involve prisoners as participants?
No

VII.C. Genetic Research

VII.C.1 Does this project involve any research on genes or genetic testing/research?
No

VIII. Risks

VIII.1 What are the risks to participants including
- emotional or psychological
- financial
- legal or social
- physical?

There is no risk to the participants that will be enrolled in this study (studies). The projects will be dome on already obtained, and archieved material, after the diagnosis is given and the patient management is done. There is no financial, physical, legal, social, emotional or psycological risk to the participants. Thsi study aims to better understand and characterize this group of diseases. The only minimal risk is regarding the PHI, but extreme measures will be taken for protection of the limited information collected.

VIII.2 What have you done to minimize the risks?

- If applicable to this study ALSO include:
  - How you (members of your research team at WUSTL) will monitor the safety of individual participants.
  - Include a description of the availability of medical or psychological resources that participants might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)

These studies are completely retrospective and does not require any further patient contact, interaction and/or intervention.

IX. Benefits

IX.1 What are the direct benefits to the participant (do not include compensation)?
There are no direct benefits to the participant.

IX.2 What are the potential benefits to society in terms of knowledge to be gained as a result of this project?
There are several benefits to the society. With better understanding of these diseases, we can further classify them and have an insight into their cause and mechanism. This will also help pathologists to diagnose/classify these diseases better. The inital information can be used as a stepping board to improve care of these patients who are chronically ill and perhaps can open the door for therapeutic changes.

X. Privacy & Confidentiality

X.1 Describe your plans to protect the privacy interests of the participants during the conduct of the study including:

- How will you provide a private setting during the recruitment process
- How will you provide a private setting for the consent process including an opportunity for the participant to ask questions privately
- Describe how interventions occur in a private setting and/or how information will be collected using methods that protect the participant's privacy.
- Discuss why the information collected during the study is necessary to the conduct of the study and does not unnecessarily invade the rights of participants to privacy of their personal information.

The cases will be selected from pathology database using several keywords. Once the cases are selected and relevant clinical information is collected, the cases will be stripped form amy PHI and will be coded. The key to the codes will be stored in a password protected computer in PI's office. No patient interaction is necessary during these project. The patient's PHI will be strictly protected following the below described guidelines.

X.2 Are you collecting or using the Social Security Number of any participants for any purpose?
No

X.4 How will information/data be collected and stored for this study (check all that apply):

- Biologic samples (blood draws, cheek swabs, saliva samples, tissue samples, etc.) - Once the cases are selected, the slides will be reviewed and paraffin blocks will be selected in case an ancillary test(histochemistry, immunohistochemisty) is to be performed. The slides and the blocks are already being stored in the department of pathology following CAP (collage of American Pathology) and CLIA guidelines. The paraffin embedded tissue posses minimum to no risk for transmitting any diseases and no fresh tissue will be used in this study. The slides that need to be generated will also be stripped from patient identifiers.
- Electronic records (computer files, electronic databases, etc.) - The database of pathology will be seacrhed using words " Crohn's diease", "ulcerative colitis", "indeterminate colitis", "infectious colitis", "lymphocytic colitis", "collagemous colitis", "Quiescen colitis", "Low grade adenoma-like dysplasia" etc. The cases will be selected and grouped. The relevant clinical data such as age, gender, disease distribution, medication history, endoscopic impression etc will be collected. The cases then will be stripped from any potential identifiers and will be coded. The key to the codes will be stored in the PIs office in a password protected computer, in a locked office. The use of jump drives is not allowed during these projects, the communication will be made through our secure network, emails will be encrypted and any file that contains data will have a password. The only people who will have access to information will be the members of the research team.

X.5 Do the confidentiality protections indicated above allow only members of the research team to access identified data/specimens?
Yes

XI. Data Analysis

XI.1 Provide a summary of the analysis methods you will use, including, if applicable, the data points or outcomes you will analyze.
The appropriate statistical analysis will be performed on the obtained data.

XI.2 Provide the rationale or power analysis to support the number of participants proposed to complete this study.
Since this projects involves a group of smaller projects, each project requires a series of cases, including controls and comparison groups. It is also known that these are chronic diseases and ir would be helpful/informative to follow the disease pattern and lesions in time. Therefore, we elected to include samples from a long period of time, which increases our case volume and the power of statistical analysis.

XII. Future Research

XII.1 Do you wish to keep any information about participants involved with this research project so that other researchers outside the current study team may contact them for future research?
No

XII.3 Does this project involve storing any data for future research?
No

XII.4 Does this project involve storing any tissues or specimens for future research?
No