Oct 08, 2024

Sinai SCENT TMC - Human Colonoscopy Tissue Collection

DOI
dx.doi.org/10.17504/protocols.io.rm7vzjz4xlx1/v1

Ksenija Sabic[1], Colleen Chasteau[1], Judy Cho[1]

[1]Icahn School of Medicine at Mount Sinai

Cellular Senescence Net…

Sojin Kim
Icahn School of Medicine at Mount Sinai

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DOI: dx.doi.org/10.17504/protocols.io.rm7vzjz4xlx1/v1

Protocol Citation: Ksenija Sabic, Colleen Chasteau, Judy Cho 2024. Sinai SCENT TMC - Human Colonoscopy Tissue Collection. **protocols.io** https://dx.doi.org/10.17504/protocols.io.rm7vzjz4xlx1/v1

Protocol status: Working
We use this protocol and it's working

Created: October 08, 2024

Last Modified: October 08, 2024

Protocol Integer ID: 109398

Abstract

For this study we will utilize the world-renowned Inflammatory Bowel Disease program at MSSM, started by Dr. Burrill B. Crohn in the Division of Gastroenterology. Eminent physicians, surgeons, radiologists, hepatologists, and pathologists have provided a rich body of knowledge in the diagnosis and management of inflammatory bowel disease, peptic ulcer disease, esophageal disorders, gastrointestinal cancer, and liver, biliary, pancreatic diseases, and Crohn's Disease. Mount Sinai has been on the forefront of research, identification, and treatment of gastrointestinal illness since the division's early days. An outpatient clinic was founded and devoted solely to GI diseases in 1913. Today, Mount Sinai gastroenterologists care for more patients with inflammatory bowel disease (IBD) than any medical center in the country. Gastroenterologists from throughout the New York tristate area send their most challenging cases to our IBD physicians. This study will be one of many, on-going collaborations with faculty and staff from several groups involved with IBD research and clinical care throughout the Mount Sinai Medical Centers. In addition, the Mount Sinai Health System now has affiliated sites that are directly involved in the care of IBD patients seen at Mount Sinai Health System affiliated clinics and offices. These include the endoscopy centers at Beth Israel, Mount Sinai West, Mount Sinai St. Luke's, and Carnegie Hill Endoscopy. Participants will be patients recruited from one of the largest gastroenterological outpatient clinic in the city.

RECRUITMENT LOCATIONS

1 1. Mount Sinai School of Medicine and Medical Centers including affiliated sites within the Mount Sinai Health System such as Mount Sinai Queens, Mount Sinai Brooklyn, Beth Israel, Mount Sinai West, and Mount Sinai St. Luke's. Endoscopy Center of New York, 201 East 93rd Street
2. Gastroenterology, Endoscopy and other IBD Clinics
3. The Recanati/Miller Transplantation Institute at Mount Sinai
4. We will request clinical data relevant to the subjects diagnosis from The Mount Sinai Data Warehouse (MSDW). We will also request MRNs for eligible patients identified through the Mount Sinai Data Warehouse. These patients will be contacted and invited to join the study.

STUDY POPULATION

2 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Inclusion for subjects:

I. Patients (Affected)

1. Subjects must have a confirmed diagnosis of Crohn's disease or Ulcerative Colitis.
2. Subject must be greater than 3 years of age at the time of recruitment
3. Subjects may be newly starting on biologic therapy (infliximab, adalimumab, certolizumab, golimumab, ustekinumab, natalizumab, and/or vedolizumab).

II. Controls (Unaffected)

1. Subjects must have no personal history of Crohn's disease or Ulcerative Colitis.
2. Subjects must be greater than 17 years of age at the time of recruitment.
3. Subjects must have a diagnosis of Primary Sclerosing Cholangitis (Only for the IBD-PSC sub study)
4. Subjects must not be actively undergoing any chemotherapy or radiation, including cancer treatment (ONLY for the IBD-Senescence sub-study)
5. Subjects must not have coagulopathy disorders such as end stage renal disease.

The treating physician will determine patient eligibility for inclusion in this study. Eligibility will be determined based on these doctors' knowledge of and interactions with their patient, populations, and during the patient's regular standard of care outpatient clinic visits. Eligibility will also be determined by the research study coordinator based on comparison of the inclusion and exclusion criteria to the patient's medical record.

3 EXCLUSION CRITERIA

Exclusion for subjects:

I. Patients (Affected)

1. Subjects do not have a confirmed diagnosis of Crohn's disease or Ulcerative Colitis.
2. Subject is less than 3 years of age at the time of recruitment.

II. Controls (Unaffected)

1. Subjects have a personal history of Crohn's disease or Ulcerative Colitis.
2. Subject is less than 17 years of age at the time of recruitment.

STANDARD OPERATING PROCEDURES FOR SAMPLE AND DATA COLLECTION AND PROCESSING

4 Following sample collection, a unique identifier will be assigned to each subject. The GRID (global research identifier) will be used to label all biospecimen and data collected.

5 Blood Collection: Blood will be drawn by experienced clinical staff or certified phlebotomist. Blood draws will not exceed 50 ml for pediatric subjects or 100 ml for adults. The physician's discretion and assessment of the patient's health at the time of blood draw will determine the exact amount of blood to be collected. DNA and plasma will be isolated.

6 Saliva Collection: If subject prefers, or the phlebotomist is not available we will collect saliva instead of blood. A 2 ml saliva kit will be used.

7 Medical Record Information: Subjects will be asked questions that address medical and environmental factors potentially related to disease expression, course, and complications. These questions include details about age at onset, family history of defined disease criteria, cigarette smoking history, disease site designation, HLA-type (potential disease modifier), inflammatory pattern, presence of pANCA, ASCA, or other serological markers, and response to specific medical interventions. Information from any disease-related indices such as the Harvey Bradshaw Index or Mayo Score may be collected. In addition medical records will be reviewed for details related to disease location, including colonoscopy, radiology and pathology reports, types of surgery, extraintestinal manifestations, laboratory results, and other information related to the patients' symptoms, diagnoses and treatment for IBD. Patient medical data can be followed prospectively through the electronic health record system to identify new events including but not limited to new medications, change in laboratory findings, new imaging/endoscopy/pathology findings, change in disease phenotype, new medical problems, surgeries, hospitalizations, and complications.

8 Biopsy, Colonic resection tissue, Lavage or Mucosal Brush cytology: Intestinal biopsies are collected at several sites within the length of the intestine, as standard of care: terminal ileum, cecum, colon and rectum. Also, as standard of care, samples are collected at affected and unaffected sites. It is standard in IBD patients to biopsy grossly normal tissue for histological analysis as the presence of microscopic inflammation may predict future disease course. The

patient can expect to have a maximum of 15 diagnostic/standard of care biopsies. For this study we will request 4 additional biopsies for each area that is sampled as standard of care. For non-IBD patients undergoing a routine screening colonoscopy, we will request 2 additional biopsies for each area that is sampled as standard of care/routine screening. We will only receive research biopsies if biopsies are being retrieved for screening. Biopsies or surgical tissue will be used for RNA isolation, cytokine analysis, mass cytometry or spatial transcriptomic analysis.

9 Pathology Specimen: Patients consenting to the study who have archived paraffin-embedded tissues from intestinal or colonic biopsies or resections, explanted liver tissue, liver resection or biopsies and bile duct resection or biopsies can have old and future H&E slides reviewed and sections from those samples cut if sufficient excess sample is available. If additional sections are available they may be used for additional analyses including immunohistochemistry, mass cytometry, and DNA/RNA extraction. Paneth cell morphology will be evaluated for a subset of subjects. If a patient joins this study and underwent any procedure at Mount Sinai where tissue was collected, analyzed and stored with the Pathology Department we will request some of that tissue.

10 Isolation of peripheral blood mononuclear cells (PBMC) for CyTOF analysis and immune phenotyping by fluorescence-activated cell sorting (FACS) or RNA analysis. PBMC are a type of cell lines generated from blood cells. This will be conducted on sub-set of patients starting treatment with biologic therapy and a sub-set of CD patients with and without perianal disease. Briefly, PBMC will be isolated per density gradient. $5X10^6$ PBMC will be used per condition (baseline, cultured and stimulated, cultured and unstimulated) for CyTOF analyses. The following are some of the markers that will be assayed:

1. Phenotypic markers: CD19 (B cells), CD4 and CD8 subsets of T cells, CD16 (monocytes, NK cells), CD56 (NK cells) CD66 (neutrophils, basophils), CD14 (monocytes, neutrophils, dendritic cells), BDCA1 (CD1a dendritic cells), CD123 (plasmacytoid dendritic cells, basophils), BDCA3 (CD141 cross presenting dendritic cells)
2. Immunological memory markers: CD45 (hematopoietic cells), CD45 RA (naïve vs. memory), CD27 and CCR7 (central memory vs. effector memory vs. transitional memory)
3. Cellular activation markers: HLA-DR, CD38
4. Cytokine production: TNF-a, IFN-g, IL-6, IL-17A, IL-10

11 Everyday Discrimination Scale: Participants will be asked to complete a 9-item questionnaire that measures the association between experienced discrimination and health outcomes. All participants will be asked to complete this form, they have the option to refuse if they wish to.

FUTURE USE OF STORED SPECIMENS AND DATA

12 All biospecimen and data will be de-identified immediately following collection. Each subject will be assigned a unique GRID (global research identifier). Drs. Cho and Peter, and only

IRB-approved research study personnel will have access to the key linking the GRID to the subject's protected health information (PHI). PHI will never be stored with the de-identified samples or collected data/phenotype.

The biospecimen will be kept secure in a freezer in Dr. Cho's lab at the Mount Sinai School of Medicine. The unique GRID will be the only label for any DNA, RNA and serum extracted from the biospecimen. Specimen and extracted materials will be banked for future use, indefinitely. Only Drs. Cho and Peter will have the authority to share the de-identified specimen/materials with other researchers. Biospecimen information will be entered and tracked using FreezerPro or other Laboratory Information System (LIMS), commercial software that is internally supported by the Mount Sinai Department of Pathology and Sinai Information Technology.

Samples will be maintained indefinitely or until the subject provides a written request to withdraw authorization for sample storage. At the discretion of the PI or MSSM IRB, a sample may be removed and destroyed, without the subject's consent.

De-identified materials will be shared with members of the NIDDK IBD Genetics Consortium and other researchers studying IBD. Wide sharing of materials is not planned; however under the requirements for NIH/NIDDK funded research sharing of de-identified data is necessary, via dbGaP or other NIH-approved sharing mechanisms. The link identifying the data with the PHI will not be shared with anyone outside of MSSM.

In compliance with the consenting process, subjects will be asked if their stored specimens can be used in future research studies, how they would like their specimens store-deidentified or anonymized, if they give us permission to keep the specimens indefinitely and use them for studies not related to IBD, and if they give us permission to share portions of the collected specimens with other researchers.