



IBD Plexus Summary for CDA Applicants

September 2021



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1. Overview

The Crohn's & Colitis Foundation (Foundation) is excited to make IBD Plexus data and biosamples available to Career Development Award Investigators.

IBD Plexus® was founded by the Foundation to advance science, accelerate progress towards precision medicine and improve the care of patients living with IBD. The first-of-its kind, national-scale, cloud-based platform integrates clinical, patient-reported, genetic and other molecular data from diverse research study cohorts, real world clinical care settings and patients' experiences. IBD Plexus provides researchers with access to analysis-ready datasets to more rapidly perform activities that promise to speed treatment development, optimize existing therapies through development of biomarkers and diagnostics, and improve health outcomes. IBD Plexus unites clinicians, scientists, educators, industry partners, and patients to answer questions that are critically important to advance the field of IBD research.

The multi-component IBD Plexus includes a biobank, pediatric and adult patient clinical data, patient-reported data, biosamples, central reference labs to generate genetic and 'omics data (genetic, transcriptomic, microbiomic, etc.), as well an analytical platform to house, organize, aggregate, and provide data for research.

The novel technological platform supports the mining of data for insights into IBD causes, mechanisms, biomarkers and potential new treatments. The "exchange" model functions under the guiding principle that researchers who take advantage of the resources will also contribute back the raw data (not the analyses) they derive from patient biosamples. As more stakeholders, including patients, clinicians, and researchers, contribute data, the IBD Plexus platform will evolve into an even more powerful database for future scientific research benefitting the entire IBD community.

2. IBD Plexus Cohorts

IBD Plexus centralizes and links data across diverse IBD research cohorts to facilitate sharing across the research community. The cohorts are all independent programs that have unique goals but the Foundation encourages clinicians and patients to participate in multiple cohorts, when applicable. IBD Plexus links the data and biosamples across these cohorts to create a robust individual patient dataset, enabling Plexus to achieve a comprehensive collection of holistic information to facilitate research and advance the scientific understanding of IBD.

This RFP provides the opportunity to gain access to biosamples and / or data from these study cohorts. Please click on the cohort hyperlink to learn more.

- **RISK** – A pediatric research study of newly diagnosed Crohn's disease patients, designed to identify risk factors associated with developing penetrating and/or stricturing complications within 3 to 5 years of diagnosis (*Data sets and biosamples available – Table 1*)
- **SPARC IBD** – A translational research study that enrolls adult patients with Crohn's disease and ulcerative colitis and follows them longitudinally to support

the advancement of precision medicine (*Data sets and biosamples available – Table 1*)

- **IBD Qorus** – A longitudinally-followed adult quality of care program designed to drive progress towards improved care and health outcomes for patients living with IBD (*Data sets available – Table 1*)
- **IBD Partners** – An internet-based registry, open directly to patients, designed to better understand the patient view of the course of IBD and how patient experiences and unique IBD journeys impact disease course (*Data sets available – Table 1*)
- **SHP647 program** – Discontinued SHP647 program clinical trial data and biosamples will be made available to the scientific community through IBD Plexus. More details to come.

Patient-level data and biosamples collected from various cohorts include:

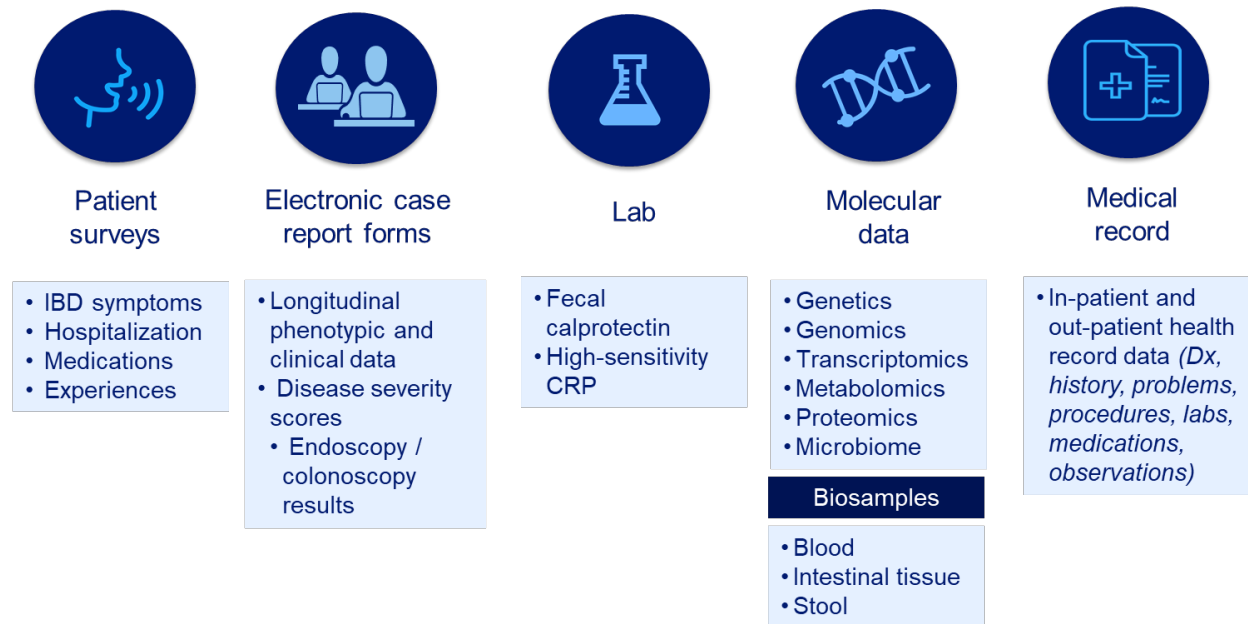


Table 1: Cohorts Data and Biosamples Collection Details

Cohort	Clinical Data	Patient Reported Data	Molecular Data	DNA	RNA	Plasma	PMBCs	Stool	Tissue Biopsies
SPARC IBD	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙
RISK	⊙	⊙	⊙	⊙	⊙	⊙		⊙	⊙
IBD Qorus	⊙	⊙							
IBD Partners		⊙							

Note: More details to come for the SHP647 program data and biosamples.

Further details about the data collected in these cohorts can be found in the IBD Plexus Patient Data Specification document. This document is located in proposalCENTRAL within the Download Templates & Instructions section.

Table 2: Select clinical and demographic characteristics of IBD Plexus patients

Characteristics	RISK	SPARC IBD	IBD Qorus	IBD Partners
Gender				
Female	42%	55%	56%	72%
Male	58%	45%	44%	28%
Age at enrollment				
<21	100%	24%	24%	4%
21 - 40	n/a	37%	35%	45%
41 - 60	n/a	30%	30%	38%
>60	n/a	9%	11%	13%
Diagnosis at enrollment				
Crohn's Disease	63%	66%	57%	62%
Ulcerative Colitis	8%	32%	40%	35%
IBD-U	10%	2%	3%	2%
Not IBD	20%	n/a	n/a	n/a
Medications (at any encounter)				
5-ASAs	43%	25%	26%	48%
Antibiotics	35%	9%	6%	12%
Biologics	44%	71%	75%	44%
Immunomodulators	51%	32%	37%	33%
Steroid therapies	61%	16%	12%	30%
Biologics breakdown				
Adalimumab	13%	27%	12%	20%
Certolizumab	1%	3%	2%	5%
Golimumab	n/a	0.8%	1%	0.6%
Infliximab	40%	35%	48%	21%
Natalizumab	0.2%	0.1%	0.5%	0.9%
Ustekinumab	n/a	16%	8%	2%
Vedolizumab	n/a	19%	28%	5%

Table 3: SPARC IBD Plexus Molecular Data

Service	SPARC IBD		
	Samples	Patients	
Global screening array (genotyping)	2,950 blood DNA	Collection Time Period: Anytime CD: 1,949 UC: 948 IBD-U: 53	
Whole exome sequencing (genomics)	2,949 blood DNA	Collection Time Period: Anytime CD: 1,947 UC: 949 IBD-U: 53	
Total RNAseq @ 50M reads (transcriptomics)	1,780 enrollment tissue 207 follow-up tissue	Collection Time Period: Enrollment CD: 369, 35, 211 UC: 204, 110 IBD-U: 14	Collection Time Period: Follow-up CD: 48, 22 UC: 23, 17
FFPE digitization	1,342 enrollment tissue	Collection Time Period: Enrollment CD: 396 UC: 204 IBD-U: 14	Collection Time Period: Follow-up CD: 48 UC: 23
WGS - bacteria and fungi (metagenomics)	1,433 enrollment stool 367 follow-up stool	Collection Time Period: Enrollment CD: 913 UC: 192 IBD-U: 26	Collection Time Period: Follow-up CD: 150 UC: 103 IBD-U: 5
WGS viruses (metagenomics)	247 enrollment stool	Collection Time Period: Enrollment CD: 100 UC: 148	

Table 4: RISK Plexus Molecular Data

Service	RISK	
	Samples	Patients
ImmunoChip (genotyping)	1,456 blood DNA	1,456
Global screening array (genotyping)	1,000 blood DNA	982
Protein expression (proteomics) 13 Olink Panels, 1196 proteins	250 plasma	250
RNAseq @ 10 M reads (transcriptomics)	778 (baseline tissue) 10 (longitudinal tissue)	565 10 (longitudinal)
RNAseq @ 30 M reads (transcriptomics)	850 baseline tissue 44 longitudinal tissue	567 29 (longitudinal)
RNAseq from FFPE slides	188 baseline FFPE slides 281 longitudinal FFPE slides 24 unknown timepoint FFPE slides	183 (baseline) 169 (longitudinal) 24 (unknown timepoint)
16S (rDNA sequencing)	888 tissue and stool	625
WGS - bacteria and fungi (metagenomics)	295 baseline stool	295
WGS viruses (metagenomics)	100 baseline stool	100
Methylation (epigenetics)	402 baseline and follow-up blood DNA	238

Table 5: IBD Plexus RISK Biosamples

RISK Biosamples			
Source	Sample Type	Time Point	Samples available details
Peripheral Blood	DNA	Enrollment, 1 year, 2 years and 3 years	DNA extracted
Peripheral Blood	Tempus™ RNA	Enrollment, 1 year, 2 years and 3 years	RNA extracted
Peripheral Blood	Plasma	Enrollment, 1 year, 2 years and 3 years	Stored -80C
Stool	Unprocessed	Enrollment	Aliquots stored -80C
Intestinal Tissue	RNAlater	Scope	RNA/DNA extracted

Periodicity of RISK Biosample Collection

Baseline blood and stool samples were collected at / or around the time of enrollment. Follow-up blood samples were collected at year 1 and years 2 and 3. Mucosal biopsies are collected during routine colonoscopy as part of patient’s clinical care.

Peripheral Blood

Collected at the time of baseline, year 1, year 2, and year 3. Blood samples were used to isolate plasma, DNA and RNA, and thus whole blood samples or PBMCs are not available.

Stool

Fresh fecal samples were collected within 2 weeks of enrollment and flash frozen.

Intestinal tissue biopsies

Pinch biopsies were collected from Crohn’s disease patients during routine scheduled colonoscopies. 4 ileal and 4 rectal biopsy samples were collected in triplicate and stored in RNAlater.

Table 6: IBD Plexus SPARC IBD Biosamples

Periodicity of SPARC IBD Biosample Collection

SPARC Biosamples			
Source	Sample Type	Time Point	Samples available details
Peripheral Blood	DNA	Baseline	DNA extracted
Peripheral Blood	Paxgene RNA	Baseline, Scope and 3 months after scope if change in therapies	Stored -80C
Peripheral Blood	PBMC's	Baseline, Scope and 3 months after scope if change in therapies	Aliquots of 5 million cells
Peripheral Blood	Plasma	Baseline, Scope and 3 months after scope if change in therapies	Stored -80C
Stool	Nucleic Acid Archiving	Baseline, Scope and 3 months after scope if change in therapies	Stool in ethanol stored frozen
Stool	Unprocessed	Baseline, Scope, and 3 months after scope if change in therapies	faecal calprotectin generated + 6 aliquots unprocessed stored -80C
Intestinal Tissue (CD or UC or IBDU)	RNAlater	Scope	Stored -80C
Intestinal Tissue (CD or UC or IBDU)	Formalin	Scope	Paraffin embedded block
Intestinal Tissue (CD or UC or IBDU)	Flash Freeze (LN2)	Scope	Stored -80C

Biosamples are collected around the time of consent (blood and stool) and when the patient undergoes a sigmoidoscopy or colonoscopy as part of his or her clinical care. Blood and stool samples are also obtained approximately 3 months after a change in therapy that follows a colonoscopy or sigmoidoscopy if the patient has a follow-up office visit during that time.

Peripheral Blood

Collected at the time of enrollment, and used to isolate plasma, RNA and DNA. Additional samples are collected at the time of colonoscopy and 3 months after a colonoscopy if change in therapy where plasma, RNA, and PBMCs are isolated. These samples can be used for a variety of purposes including genotyping, transcriptomics, proteomics and metabolomics.

Stool

For baseline stool sample collection participants are provided with a stool kit at their first visit with instructions to collect the stool sample immediately after their visit. Participants

collect the sample at home and ship cool whip container of preservative-free stool and an aliquot of stool stored in 95% alcohol to preserve the sample for metabolomics. For the collection of stool at the time of colonoscopy, participants receive the stool kit 2 weeks prior the colonoscopy with instructions to collect samples preceding their bowel preparation. Preservative-free samples are sub-aliquoted upon arrival to the biobank and stored at -80°C. Stool samples are suitable for microbiomics, proteomics and metabolomics studies as well as for measurement of routine inflammatory markers such as fecal calprotectin.

Intestinal tissue biopsy

For patients with Crohn's disease undergoing colonoscopy up to 5 pinch biopsies are obtained using forceps from the ileum or the most proximal extent of the exam and the rectum (at 20 cm from the anal verge). If both the rectum and the ileum (or cecum) appear normal on insertion of the colonoscope, an additional 5 pinch biopsies are obtained from an area with macroscopically active disease, if present.

For those with ulcerative colitis or IBDU, up to 5 pinch biopsies are obtained from the cecum (or most proximal extent of the exam) and the rectum (at 20 cm). When there is not pancolitis, if feasible and safe, biopsies from the normal area just adjacent to the transition area from abnormal to normal appearing mucosa are obtained. If the only evidence of inflamed tissue on colonoscopy is located distal to 20 cm, the biopsies from the rectum are obtained more distally in the area of active inflammation.

For each anatomical region, biopsies are collected in RNAlater, snapped frozen at sites equipped with LN2, and collected in formalin and embedded into paraffin blocks at the biobank within 24hrs of collection.

3. Data and Biosamples Use

Investigators accessing IBD Plexus data and biosample need to abide by data use and material transfer agreement terms. Please reference IBD Plexus Data Use Agreement and Material Transfer Agreement for more details. Please note, in particular, Section 5 of both appendices (Intellectual Property Rights; New Resources), which explains terms relevant to the role of IBD Plexus as a data exchange platform.