IBD Plexus
Summary for CDA Applicants

September 2021
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>
<thead>
<tr>
<th>Patient surveys</th>
<th>Electronic case report forms</th>
<th>Lab</th>
<th>Molecular data</th>
<th>Medical record</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD symptoms</td>
<td>Longitudinal phenotypic and clinical data</td>
<td>Fecal calprotectin</td>
<td>Genetics</td>
<td>In-patient and out-patient health record data (<em>Dx, history, problems, procedures, labs, medications, observations)</em></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>Disease severity scores</td>
<td>High-sensitivity CRP</td>
<td>Genomics</td>
<td>Blood</td>
</tr>
<tr>
<td>Medications</td>
<td>Endoscopy / colonoscopy results</td>
<td>Transcriptomics</td>
<td>Metabolics</td>
<td>Intestinal tissue</td>
</tr>
<tr>
<td>Experiences</td>
<td></td>
<td>Metabolics</td>
<td>Proteomics</td>
<td>Stool</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Cohorts Data and Biosamples Collection Details
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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RISK</th>
<th>SPARC IBD</th>
<th>IBD Qorus</th>
<th>IBD Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>42%</td>
<td>55%</td>
<td>56%</td>
<td>72%</td>
</tr>
<tr>
<td>Male</td>
<td>58%</td>
<td>45%</td>
<td>44%</td>
<td>28%</td>
</tr>
<tr>
<td><strong>Age at enrollment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;21</td>
<td>100%</td>
<td>24%</td>
<td>24%</td>
<td>4%</td>
</tr>
<tr>
<td>21 - 40</td>
<td>n/a</td>
<td>37%</td>
<td>35%</td>
<td>46%</td>
</tr>
<tr>
<td>41 - 60</td>
<td>n/a</td>
<td>30%</td>
<td>30%</td>
<td>38%</td>
</tr>
<tr>
<td>&gt;60</td>
<td>n/a</td>
<td>9%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Diagnosis at enrollment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>63%</td>
<td>66%</td>
<td>57%</td>
<td>62%</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>8%</td>
<td>32%</td>
<td>40%</td>
<td>36%</td>
</tr>
<tr>
<td>IBD-U</td>
<td>10%</td>
<td>2%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Not IBD</td>
<td>20%</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Medications (at any encounter)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-ASAs</td>
<td>43%</td>
<td>25%</td>
<td>28%</td>
<td>48%</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>36%</td>
<td>9%</td>
<td>6%</td>
<td>12%</td>
</tr>
<tr>
<td>Biologics</td>
<td>44%</td>
<td>71%</td>
<td>75%</td>
<td>44%</td>
</tr>
<tr>
<td>Immunomodulators</td>
<td>51%</td>
<td>32%</td>
<td>37%</td>
<td>33%</td>
</tr>
<tr>
<td>Steroid therapies</td>
<td>61%</td>
<td>16%</td>
<td>12%</td>
<td>30%</td>
</tr>
<tr>
<td><strong>Biologics breakdown</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>13%</td>
<td>27%</td>
<td>12%</td>
<td>20%</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>1%</td>
<td>3%</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Golimumab</td>
<td>n/a</td>
<td>0.8%</td>
<td>1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>40%</td>
<td>36%</td>
<td>48%</td>
<td>21%</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>n/a</td>
<td>16%</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>n/a</td>
<td>19%</td>
<td>26%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Table 3: SPARC IBD Plexus Molecular Data
## Table 4: RISK Plexus Molecular Data

<table>
<thead>
<tr>
<th>Service</th>
<th>Samples</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global screening array</strong> (genotyping)</td>
<td>2,950 blood DNA</td>
<td>Collection Time Period: Anytime</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 1,949</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 948</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD-U: 53</td>
</tr>
<tr>
<td><strong>Whole exome sequencing</strong> (genomics)</td>
<td>2,949 blood DNA</td>
<td>Collection Time Period: Anytime</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 1,947</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 949</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD-U: 53</td>
</tr>
<tr>
<td><strong>Total RNAseq @ 50M reads</strong> (transcriptomics)</td>
<td>1,780 enrollment tissue, 207 follow-up tissue</td>
<td>Collection Time Period: Enrolment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 365, 35, 211</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 204, 110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD-U: 14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collection Time Period: Follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 48, 22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 23</td>
</tr>
<tr>
<td><strong>FFPE digitization</strong></td>
<td>1,342 enrollment tissue</td>
<td>Collection Time Period: Follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 23</td>
</tr>
<tr>
<td><strong>WGS - bacteria and fungi</strong> (metagenomics)</td>
<td>1,433 enrollment stool, 367 follow-up stool</td>
<td>Collection Time Period: Enrolment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 913</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 192</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD-U: 26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collection Time Period: Follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 103</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD-U: 5</td>
</tr>
<tr>
<td><strong>WGS viruses</strong> (metagenomics)</td>
<td>247 enrollment stool</td>
<td>Collection Time Period: Enrollment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UC: 148</td>
</tr>
</tbody>
</table>

## Table 5: IBD Plexus RISK Biosamples

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

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### Table 6: IBD Plexus SPARC IBD Biosamples

<table>
<thead>
<tr>
<th>Source</th>
<th>Sample Type</th>
<th>Time Point</th>
<th>Samples available details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Blood</td>
<td>DNA</td>
<td>Enrollment, 1 year, 2 years and 3 years</td>
<td>DNA extracted</td>
</tr>
<tr>
<td>Peripheral Blood</td>
<td>Tempus™ RNA</td>
<td>Enrollment, 1 year, 2 years and 3 years</td>
<td>RNA extracted</td>
</tr>
<tr>
<td>Peripheral Blood</td>
<td>Plasma</td>
<td>Enrollment, 1 year, 2 years and 3 years</td>
<td>Stored -80°C</td>
</tr>
<tr>
<td>Stool</td>
<td>Unprocessed</td>
<td>Enrollment</td>
<td>Aliquots stored -80°C</td>
</tr>
<tr>
<td>Intestinal Tissue</td>
<td>RNAlater</td>
<td>Scope</td>
<td>RNA/DNA extracted</td>
</tr>
</tbody>
</table>
Periodicity of SPARC IBD Biosample Collection

### SPARC Biosamples

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

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.

\textit{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.

\section*{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.