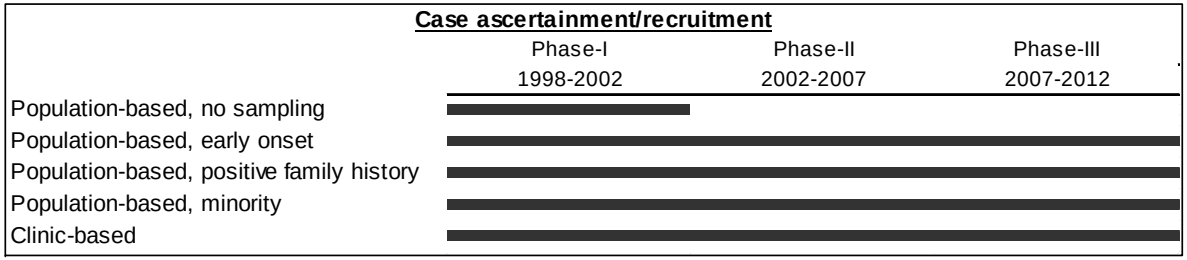
Overview of Colon CFR Resource

1997 - 2007 | **2007 - 2012**

PROGRESS TO DATE (Phases I & II) | **RESEARCH PLAN** | Supporting | **PROPOSED CORE ACTIVITIES**

Case ascertainment/recruitment



Enrollment	**Pop-based**	**Clinic-based**
Probands	7,252	1,117
Family members	15,920	5,2209
Controls (P-B & spouse)	5,091	--

Data Collection

Family history: 12,178	Epi/risk factors: 28,263
Follow-up: 15,711	Pathology records: 6,012
Blocks (PET): 7,589	Fresh frozen tissue: 272
Blood: 25,254	EBV lines: 4,100

Tumor Phenotyping

MSI	4,000	IHC	4,000
Methylation of *MLH1*	2,469		

Germline Testing for MMR (*MLH1, MSH2, MSH6*)

DNA sequence variance testing (via dHPLC)	1,747
Deletions & duplications (via MLPA)	1,747

Multidisciplinary Research-ongoing

- Germline MMR testing (*MLH1, MSH2, MSH6, PMS2*)
- Tumor methylation (*MLH1*)
- Mapping of new susceptibility genes
  - Genetic Linkage in CRC Families
  - Fine mapping/positional cloning
  - *TGFB*
- Etiologic pathways (candidate gene)
  - NSAIDs & COX/PG Metabolism
  - Folate, vitamin D, and Calcium
  - Metabolic Syndrome, Obesity, and IGF
- MYH association studies
- Research on Minority Populations
- Intervention study to promote colonoscopy screening
- Numerous studies under grant review
- Numerous studies initiated by outside investigators

Etiologic Research (incl. ***proposals under review***)

- MMR Gene Research
- Base excision repair
- Mapping new CRC genes, e.g.:
  - Syndrome X Families
  - ***LD Mapping in Hispanic Families***
  - ***Whole Genome Association study***
- Candidate gene studies, e.g.:
  - Alpha-1-antitrypsin
  - ***Lipid peroxidation***
  - ***HCAs, PAHs, and Nitrosamines***
- Genome-wide association studies
- Epigenetic epidemiology, e.g.:
  - ***CIMP***
  - BRAF
- Incorporating emerging technology (e.g., CGH)
- Incorporating methodological research

Clinical Research

- MSI & prognosis
- HNPCC & heterogeneity of cancer risks
- Pathology and clinical research
- Pharmacogenetics

Behavioral Research

- Screening & CRC risk factor knowledge gaps
- Education and counselilng (including newsletters)

Prevention & Screening

- NSAIDS
- Vitamin D with/without Calcium
- Other screening studies

Collaborations with Other Initiatives

- EDRN
- NHGRI Medical Sequencing Program
- The Cancer Genomic Atlas (TCGA)
- CAPP2

Phase III Recruitment Core

- Population-based cases <50 yrs or + family history
- Clinic-based cases
- Multiple-case Newfoundland families
- Minority recruitment
- CRC-affected first-degree relatives (FDR)
- FDR of mutation positive probands
- FDR of Lynch Syndrome & Amsterdam II probands.
- FDRs of Syndrome X probands

Retention & Follow-up Core (current & proposed)

Active Follow-up Data Collection

- Family cancer history
- Personal health history and CRC screening
- Epidemiology/risk factors data collection
- Quality of Life (QOL)

Passive Follow-up Data Collection

- Vital status and address updates
- Newsletters, other participant information

Biospecimen Core (current & proposed, ***proposed)***

- Biospecimen (blood/buccal, tissue) collection
- DNA extraction (from blood/buccal & tissue)
- Tracking and reporting
- Quality Assurance and Quality Control
- ***Central repository and dispatch***
- ***EBV transformation &/or WGA***
- ***Tissue Micro Arrays (TMA)***
- ***Virtual tissue repository***

Mol. Char. Core (current & proposed, ***proposed***)

- IHC testing
- MMR testing (***DNA sequencing***, MLPA)
- ***MYH mutation testing***
- ***BRAF mutation testing***
- MLH1 methylation
- ***New gene testing***

Clinical Outcomes Core (***proposed)***

- ***Baseline diagnosis & treatment data collection***
- ***Treatment & outcomes data collection***
- ***Recurrences & new primaries***

Bioinformatics & Biostatistics Core

Administration Core