# HMP2Data: Integrative Human Microbiome Data R Bioconductor package

https://github.com/katiasmirn/HMPDataWorkshop

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# Integrative Human Microbiome Project (iHMP) https://hmpdacc.org/ihmp/

### Pregnancy & Preterm Birth

The Vaginal Microbiome Consortium team at Virginia Commonwealth University is conducting the Multi-Omic Microbiome Study: Pregnancy Initiative (MOMS-PI) in

### Onset of Inflammatory Bowel Disease (IBD)

The Inflammatory Bowel Disease (IBD) Multi'omics Data (IBDMDB) research team, led by Ramnik Xavier and Curtis

### Onset of Type 2 Diabetes

Type 2 diabetes mellitus (T2D) is a significant health problem facing our nation. In a collaborative effort to systematically understand diabetes and its etiology, the

# Novel data: first results just out of press

MENU

nature
International journal of science

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Perspective | OPEN | Published: 29 May 2019

## The Integrative Human Microbiome Project

The Integrative HMP (iHMP) Research Network Consortium

*Nature* **569**, 641–648 (2019) | Download Citation

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0 Citations | 180 Altmetric | Article metrics

### Abstract

The NIH Human Microbiome Project (HMP) has been carried out over ten years and two phases to provide resources, methods, and discoveries that link interactions between humans and their microbiomes to health-related outcomes. The recently completed second phase, the Integrative Human Microbiome Project, comprised studies of dynamic changes in the microbiome and host under three conditions: pregnancy and preterm birth; inflammatory bowel diseases; and stressors that affect individuals with prediabetes. The associated

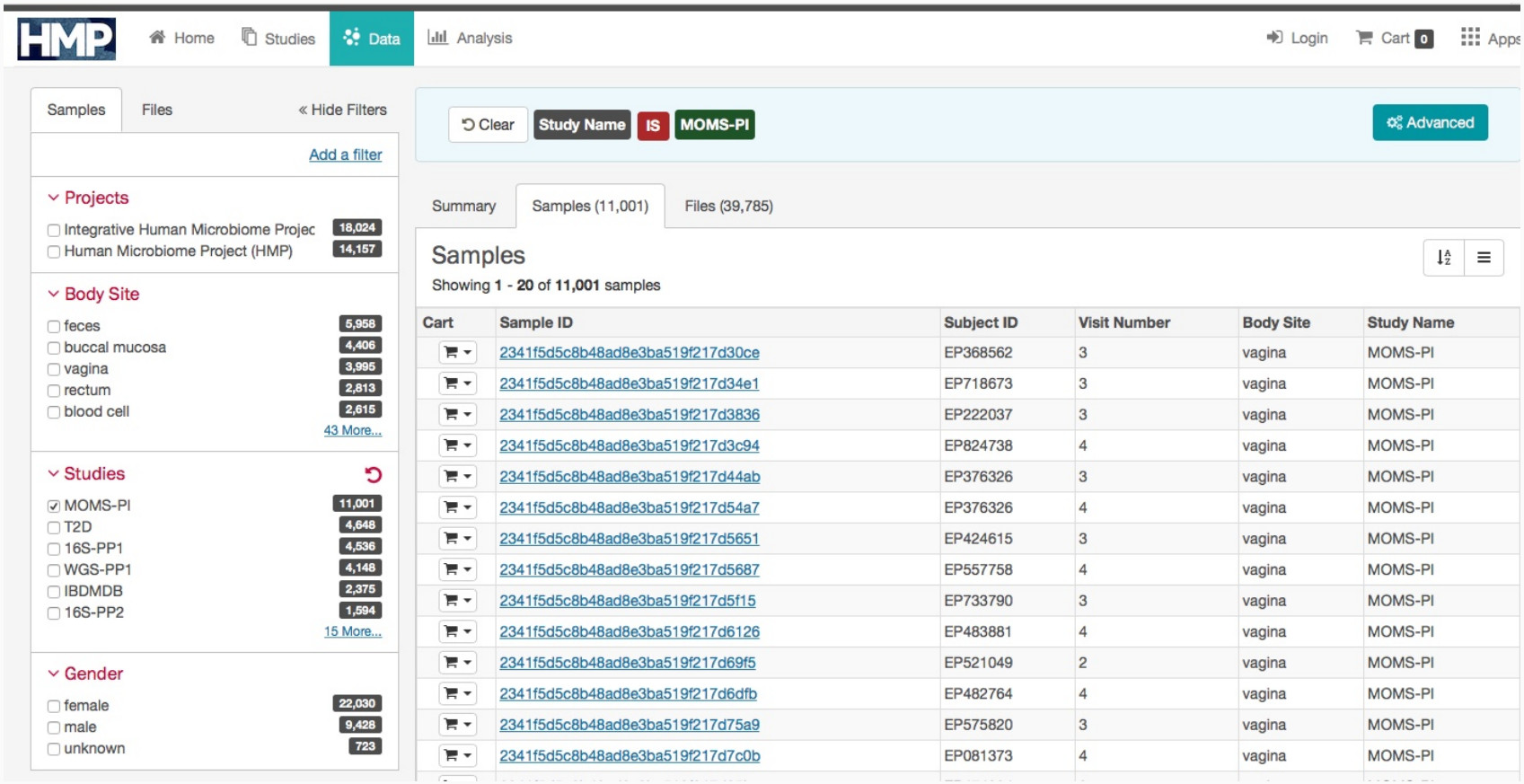
Associated Content

Special
Human Microbiome Project, part 2

*Nature* | Article | OPEN
Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases
Jason Lloyd-Price, Cesar Arze […] Curtis Huttenhower

*Nature Medicine* | Article
Racioethnic diversity in the dynamics of the vaginal microbiome during pregnancy
Myrna G. Serrano, Hardik I. Parikh […] Gregory A. Buck

# Human Microbiome Project Data Portal (https://portal.hmpdacc.org/)




| Cart | Sample ID | Subject ID | Visit Number | Body Site | Study Name |
|---|---|---|---|---|---|
| | 2341f5d5c8b48ad8e3ba519f217d30ce | EP368562 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d34e1 | EP718673 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d3836 | EP222037 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d3c94 | EP824738 | 4 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d44ab | EP376326 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d54a7 | EP376326 | 4 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d5651 | EP424615 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d5687 | EP557758 | 4 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d5f15 | EP733790 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d6126 | EP483881 | 4 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d69f5 | EP521049 | 2 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d6dfb | EP482764 | 4 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d75a9 | EP575820 | 3 | vagina | MOMS-PI |
| | 2341f5d5c8b48ad8e3ba519f217d7c0b | EP081373 | 4 | vagina | MOMS-PI |

# Open data, but...

- Need **Aspera client** (or similar) to download the data
  - not every lab/researcher has these expertise
- After download still need to:
  1. map taxonomy ids from the database
  2. merge with meta data – not available on the DAC portal
  3. construct phylogenetic tree
  4. merge -omics modalities

# HMP2Data package

- Motivated by `HMP16SData` (Bioconductor link)
- Currently under review by Bioconductor
- When accepted can be installed using

```
BiocManager::install("HMP2Data")
```

*Note: not available yet*

# Dependence packages

```
library(phyloseq)
library(SummarizedExperiment)
library(MultiAssayExperiment)
library(dplyr)
library(ggplot2)
library(UpSetR)
```

# Development version

Install from John Stansfield's GitHub

https://github.com/jstansfield0/HMP2Data

```
if(!require("HMP2Data")){
    BiocStyle::CRANpkg("devtools")
    devtools::install_github(
      "jstansfield0/HMP2Data")
}

library(HMP2Data)
```

# Multi-omics microbiome study pregnancy initiavite (MOMS-PI)


(http://vmc.vcu.edu/momspi)

# Analysis opportunities

- Early results: term and pre-term birth
- Only a subset of samples was used
- More available through DAC portal
- Novel longitudinal and multi-omics models not explored
- Many opportunities for statistical models development and data exploration!
- 16S and cytokines data

# Data structure

Available as:

- `Matrix` format for metadata, 16S, taxa table
- `Phyloseq`
- `SummarizedExperiment` for cytokines
- `MultiAssayExperiment`:
  - combine 16S and cytokines

# Data objects

## 16S data as Phyloseq object

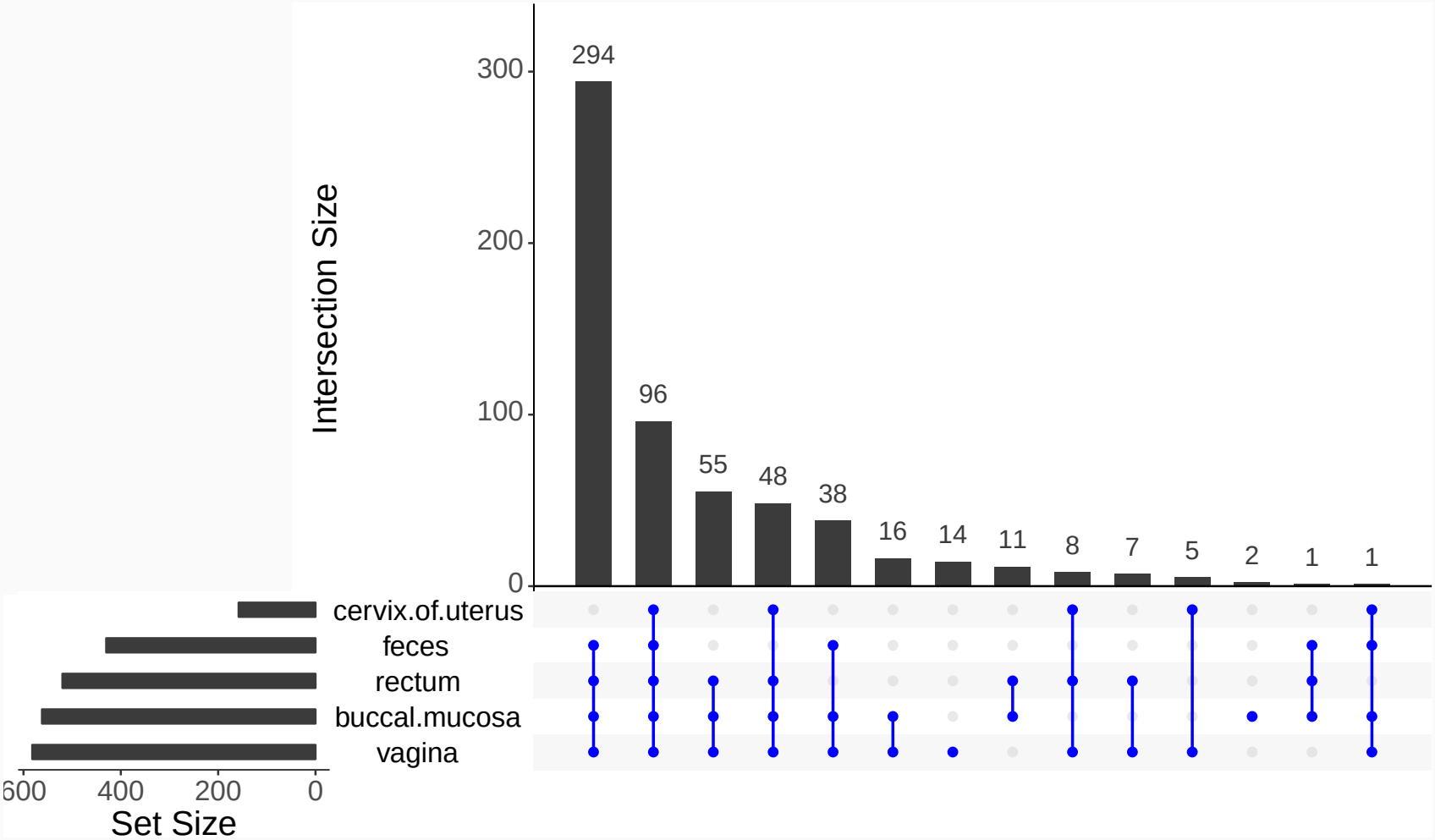
```
momspi16S_phyloseq <- momspi16S()
momspi16S_phyloseq
#> phyloseq-class experiment-level object
#> otu_table()   OTU Table:         [ 7665 taxa and 9107 samples ]
#> sample_data() Sample Data:       [ 9107 samples by 13 sample variables ]
#> tax_table()   Taxonomy Table:    [ 7665 taxa by 7 taxonomic ranks ]
```

## Cytokine data as SummarizedExperiment object

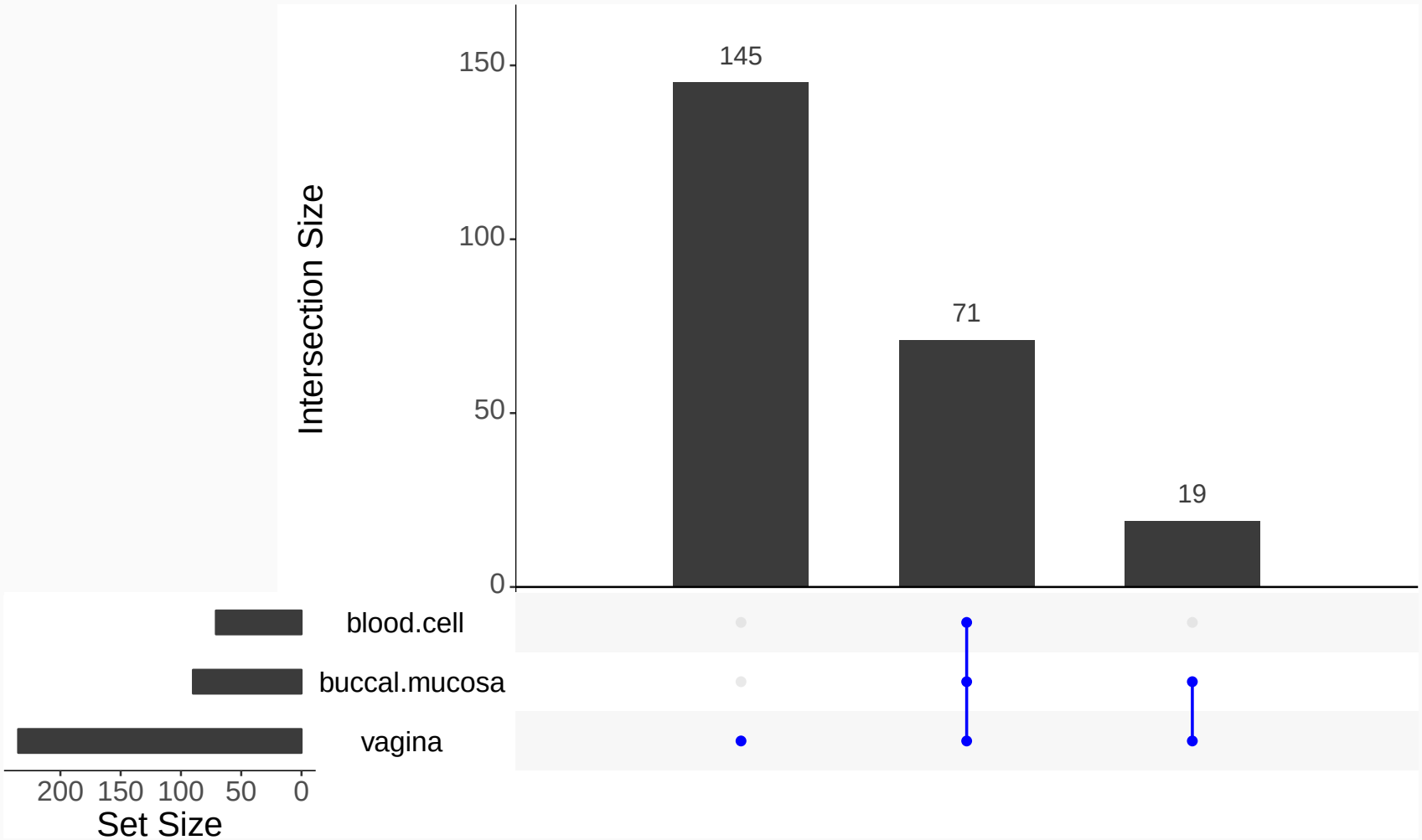
```
momspiCyto <- momspiCytokines()
momspiCyto
#> class: SummarizedExperiment
#> dim: 29 1396
#> metadata(0):
#> assays(1): ''
#> rownames(29): Eotaxin FGF ... FGF basic IL-17
#> rowData names(1): cytokine
#> colnames(1396): EP004835_K10_MVAX EP004835_K20_MVAX ...
#>   EP996091_K40_MVAX EP996091_K60_MVAX
#> colData names(13): file_id md5 ... study_full_name project_name
```

| | MOMS-PI 16S | | MOMS-PI Cytokines | | IBD 16S | | T2D 16S | |
|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % |
| **Body Site** | | | | | | | | |
| buccal mucosa | 3313 | 36.38 | 311 | 22.28 | 0 | 0 | 0 | 0 |
| cervix of uterus | 162 | 1.78 | 0 | 0 | 0 | 0 | 0 | 0 |
| feces | 765 | 8.4 | 0 | 0 | 178 | 100 | 1041 | 47.15 |
| rectum | 2679 | 29.42 | 0 | 0 | 0 | 0 | 0 | 0 |
| unknown | 146 | 1.6 | 0 | 0 | 0 | 0 | 0 | 0 |
| vagina | 2042 | 22.42 | 979 | 70.13 | 0 | 0 | 0 | 0 |
| blood cell | 0 | 0 | 106 | 7.59 | 0 | 0 | 0 | 0 |
| nasal cavity | 0 | 0 | 0 | 0 | 0 | 0 | 1167 | 52.85 |
| **Sex** | | | | | | | | |
| male | 0 | 0 | 0 | 0 | 84 | 47.19 | 1248 | 56.52 |
| female | 9107 | 100 | 1396 | 100 | 94 | 52.81 | 947 | 42.89 |
| unknown | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 0.59 |
| **Race** | | | | | | | | |
| african american | 0 | 0 | 0 | 0 | 5 | 2.81 | 117 | 5.3 |
| asian | 0 | 0 | 0 | 0 | 0 | 0 | 235 | 10.64 |
| caucasian | 0 | 0 | 0 | 0 | 164 | 92.13 | 1657 | 75.05 |
| ethnic other | 0 | 0 | 0 | 0 | 8 | 4.49 | 73 | 3.31 |
| hispanic or latino | 0 | 0 | 0 | 0 | 0 | 0 | 126 | 5.71 |
| american indian or alaska native | 0 | 0 | 0 | 0 | 1 | 0.56 | 0 | 0 |
| unknown | 9107 | 100 | 1396 | 100 | 0 | 0 | 0 | 0 |
| **total samples** | 9107 | 100 | 1396 | 100 | 178 | 100 | 2208 | 100 |

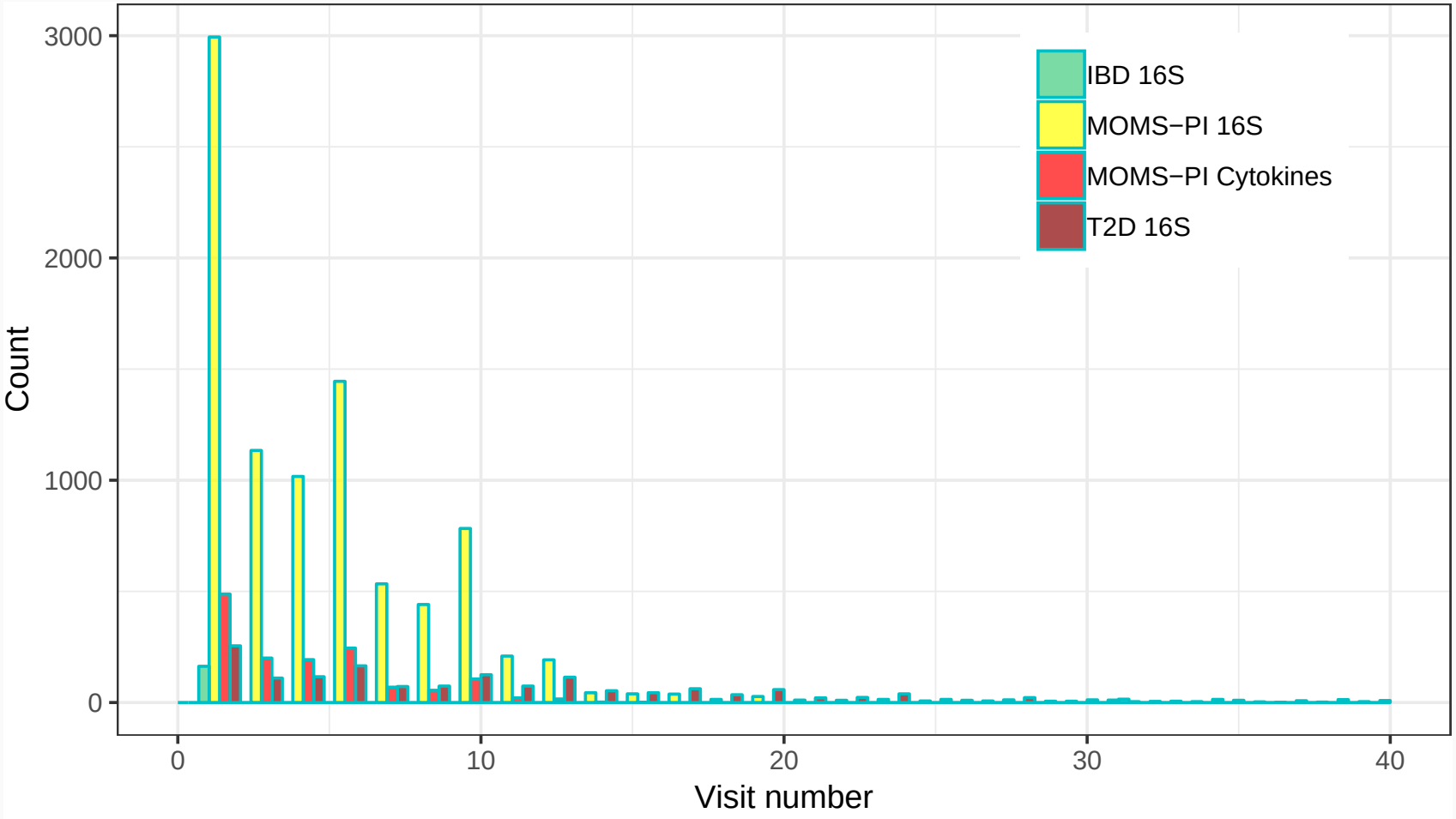
# MOMS-PI 16S common samples



# MOMS-PI Cytokines common samples



# Multiple visits



# Metadata (MOMS-PI) “dbGap“


**Multi-Omic Microbiome Study-Pregnancy Initiative (MOMS-PI)**

**dbGaP Study Accession:** phs001523.v1.p1

Request Access

**Authorized Access**

- **Data access provided by:** dbGaP Authorized Access
- **Release Date:** May 02, 2019
- **Embargo Release Date:** May 02, 2019
- Data Use Certification Requirements (DUC)
- **Use Restrictions**

| Consent group | Is IRB required? | Data Access Committee | Number of participants |
|---|---|---|---|
| Disease-Specific (Pregnancy Complications, IRB, PUB, MDS) | Yes | NICHD-DAC (HD-DAC@mail.nih.gov) | 597 |

- List of components downloadable from Authorized Access

**Publicly Available Data (Public ftp)**

Connect to the public download site. The site contains release notes and manifests. If available, the site also contains data dictionaries, variable summaries, documents, and truncated analyses.

*Note: not available yet*

# Metadata (IBD): available through the package

```
Table1Var <- c("subject_gender", "Age.at.diagnosis", "race", "visit_number",
               "site_name", "Education.Level", "Antibiotics", "BMI")

demo_data = sample_data(IBD)[ ,c("sample_id", "subject_id", Table1Var, "diagnosis")] %>%
            data.frame()

#all <- CreateTableOne(vars = Table1Var, data = demo_data)
#kableone(all)

stratified = tableone::CreateTableOne(
  vars = Table1Var,
  data = summarytools::unlabel(demo_data), strata = "diagnosis", includeNA = TRUE)
stratified <- print(stratified, printToggle = FALSE, showAllLevels = FALSE)
stratified[,!(colnames(stratified) %in% "test")]%>%
  knitr::kable(format = "html", caption = "Characteristics of the Study Cohort",
               col.names = c("CD", "nonIBD",
                             "UC", "p-value"))%>%
  kable_styling("striped", full_width = T)
```

| | CD | nonIBD | UC | p-value |
|---|---|---|---|---|
| n | 86 | 46 | 46 | |
| subject_gender = male (%) | 43 ( 50.0) | 24 ( 52.2) | 17 ( 37.0) | 0.264 |
| Age.at.diagnosis (mean (SD)) | 21.34 (11.31) | NaN (NA) | 25.65 (15.21) | 0.067 |
| race (%) | | | | 0.002 |
| American Indian or Alaska Native | 1 ( 1.2) | 0 ( 0.0) | 0 ( 0.0) | |
| Black or African American | 0 ( 0.0) | 0 ( 0.0) | 5 ( 10.9) | |
| More than one race | 0 ( 0.0) | 2 ( 4.3) | 2 ( 4.3) | |
| Other | 4 ( 4.7) | 0 ( 0.0) | 0 ( 0.0) | |
| White | 81 ( 94.2) | 44 ( 95.7) | 39 ( 84.8) | |
| visit_number (mean (SD)) | 5.33 (10.80) | 2.35 (6.39) | 1.67 (4.57) | 0.034 |
| site_name (%) | | | | <0.001 |
| Cedars-Sinai | 21 ( 24.4) | 2 ( 4.3) | 23 ( 50.0) | |
| Cincinnati | 28 ( 32.6) | 20 ( 43.5) | 11 ( 23.9) | |
| MGH | 24 ( 27.9) | 18 ( 39.1) | 6 ( 13.0) | |
| MGH Pediatrics | 13 ( 15.1) | 6 ( 13.0) | 6 ( 13.0) | |

# Current and future directions

- Revise the package to include MOMS-PI dbGap data
- Already implemented in `HMP16SData`
- Package vignettes:
  1. `HMP2Data` package introduction
  2. Analysis workflow for MOMS-PI, IBD and T2D studies
  3. Multi-omics analysis combining 16S and cytokines data
- June 25: Bioconductor 2019 workshop on `HMP16SData` and `HMP16SData` packages