

## Human Virome Program – A Common Fund Proposal

**Background:** The human virome is large and diverse with as many as  $10^{13}$  particles per human. Excluding the relatively small number of viruses that cause obvious clinical disease, eukaryotic and prokaryotic (bacteriophages) viruses are largely understudied and their interactions with the human body and long-term impacts on health and disease are unknown. While recent technological advances have improved the ability to discover and annotate viruses, challenges remain in detection sensitivity, contaminant removal, scalability, and sample adequacy, which have hindered progress in the field.

**Program Goal:** To extensively characterize the “healthy” human virome and define its role in human health and disease. Coordination between the initiatives will be crucial for the success of the program. The program will also work to coordinate with other federal agencies and ongoing microbiome efforts to increase program impact.

### Proposed Initiatives:

**1. Characterizing the human virome in longitudinal, diverse cohorts across the lifespan (U01s)**

This initiative aims to vastly expand the catalog of viruses and phages that comprise the “healthy” human virome across multiple body sites, in all phases of life, and across diverse populations.

**2. Develop tools, models, and methods to interrogate and annotate the human virome (R01s)**

This initiative aims to address remaining technological and methodological challenges that currently hinder robust interrogation into the constituents and functionality of the human virome.

**3. Elucidate the human host/virome interactome (R01s)**

This initiative aims to support functional, multi-omic studies to elucidate the interactions between the human host and the virome.

**4. Data analysis and coordinating center (U24)**

This initiative will support a data analysis and coordinating center (DACC) that will serve as an organizational and communication hub for the consortium.

**Deliverables:** The deliverables for phase 1 will include a catalog of human commensal viruses across a diverse cohort from multiple body sites, along with the development of tools, technologies, and methods to improve viral detection and annotation. There will be support of functional assays interrogating interactions between the human host and virome, but these efforts will ramp up in the second phase of the program.

### Budget Phase 1: \$228.25M over 5 years

	FY24	FY25	FY26	FY27	FY28	Total
<b>Initiative 1 – Virome in diverse cohorts (U01)</b>	\$10M	\$30M	\$30M	\$30M	\$20M	<b>\$120M</b>
<b>Initiative 2 – Tools, models, methods (R01)</b>	\$4M	\$8M	\$8M	\$8M	\$4M	<b>\$32M</b>
<b>Initiative 3 – Host/virome interactome (R01)</b>	\$7.5M	\$15M	\$15M	\$15M	\$7.5M	<b>\$60M</b>
<b>Initiative 4 – DACC (U24)</b>	\$3M	\$3M	\$3M	\$3M	\$3M	<b>\$15M</b>
<b>RMS</b>	\$250K	\$250K	\$250K	\$250K	\$250K	<b>\$1.25M</b>
<b>TOTAL</b>	<b>\$24.75M</b>	<b>\$56.25M</b>	<b>\$56.25M</b>	<b>\$56.25M</b>	<b>\$34.75M</b>	<b>\$228.25M</b>