

Virome and Human Health

Student: Kevin S Lam, Mphil candidate

Supervisor: Prof. Paul KS Chan, Prof. Siew C Ng

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香港中文大學醫學院

Faculty of Medicine

The Chinese University of Hong Kong



Outline

- The earliest gut virome
- Gut virome development
- Alterations in gut virome in gastrointestinal diseases
- Clinical significance
- Summary

ARTICLE

<https://doi.org/10.1038/s41586-019-1451-5>

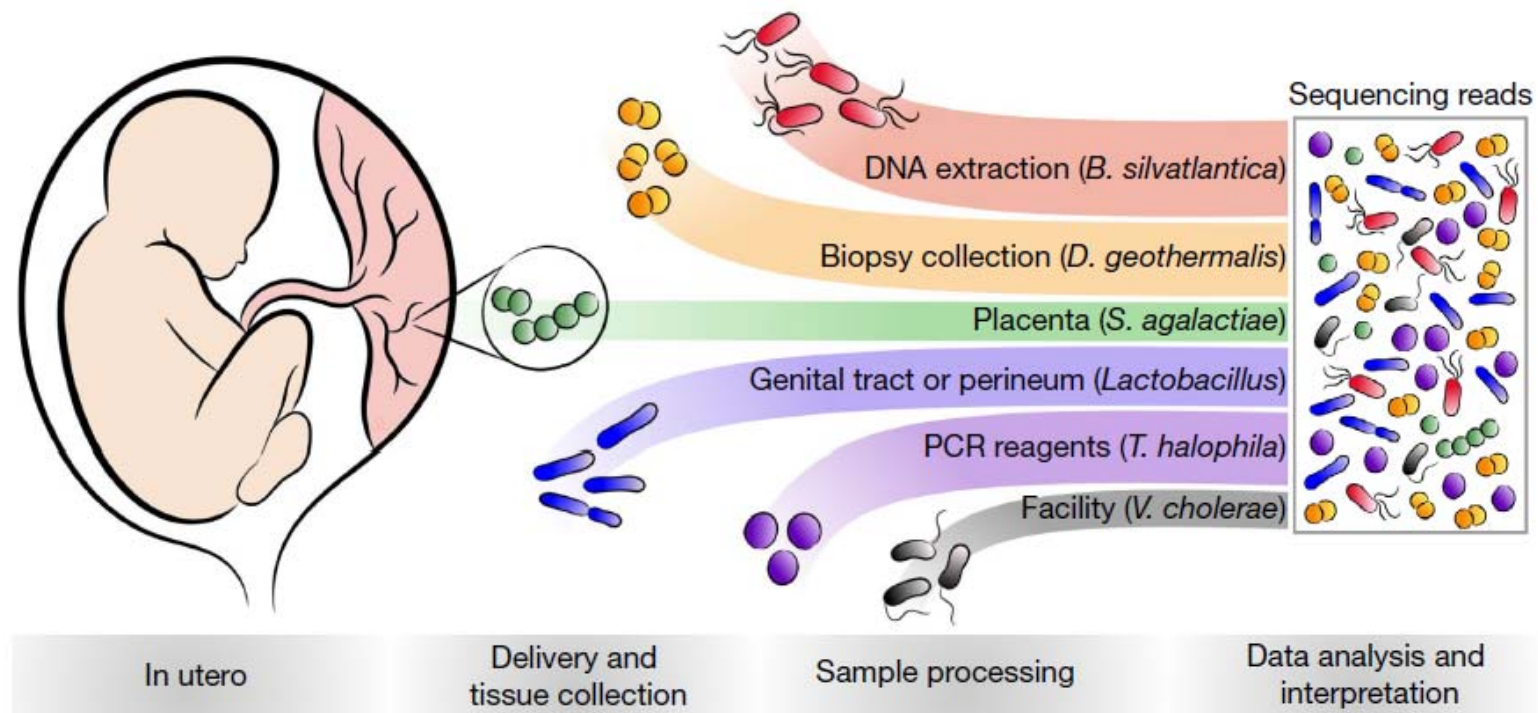
Human placenta has no microbiome but can contain potential pathogens

Marcus C. de Goffau^{1,2,8}, Susanne Lager^{3,4,5,8}, Ulla Sovio^{3,4}, Francesca Gaccioli^{3,4}, Emma Cook³, Sharon J. Peacock^{1,6,7}, Julian Parkhill^{1,2*}, D. Stephen Charnock-Jones^{3,4,9} & Gordon C. S. Smith^{3,4,9*}

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Acquisition of microbiota during labour and delivery



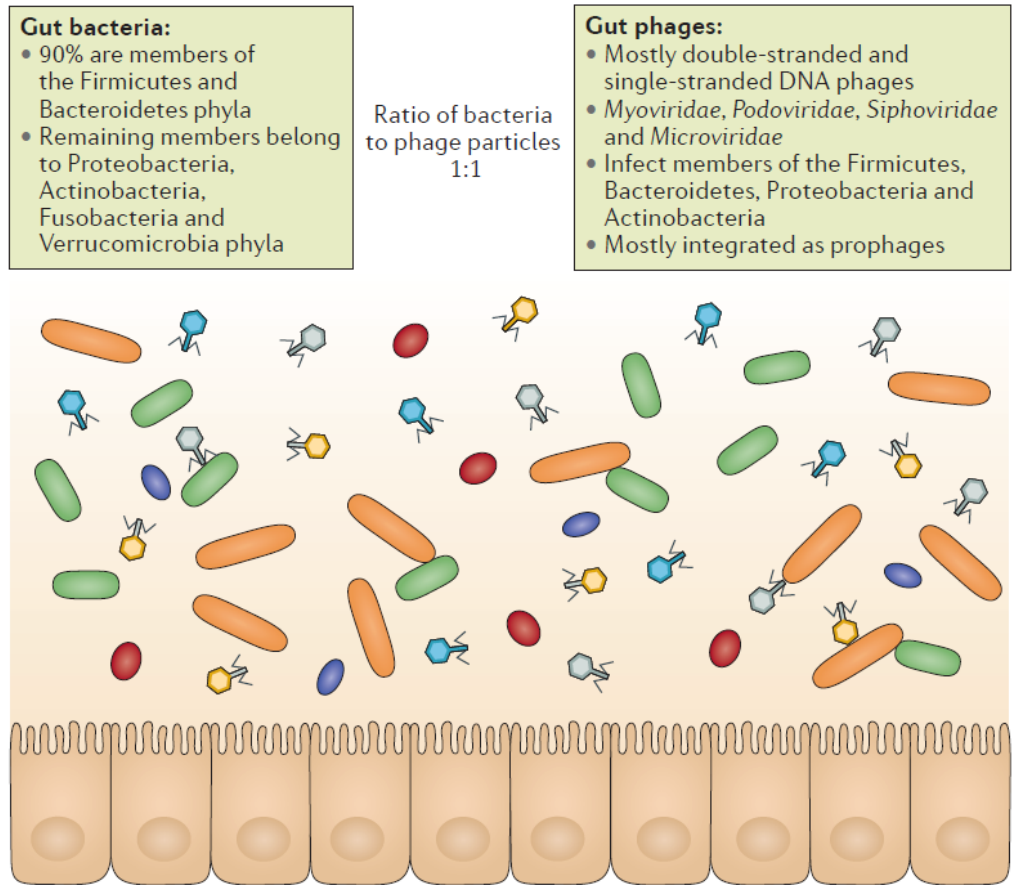
Meconium – Our First Stool

- Infant stool is sterile
- No microorganisms could be detected by direct epifluorescent microscopy examination

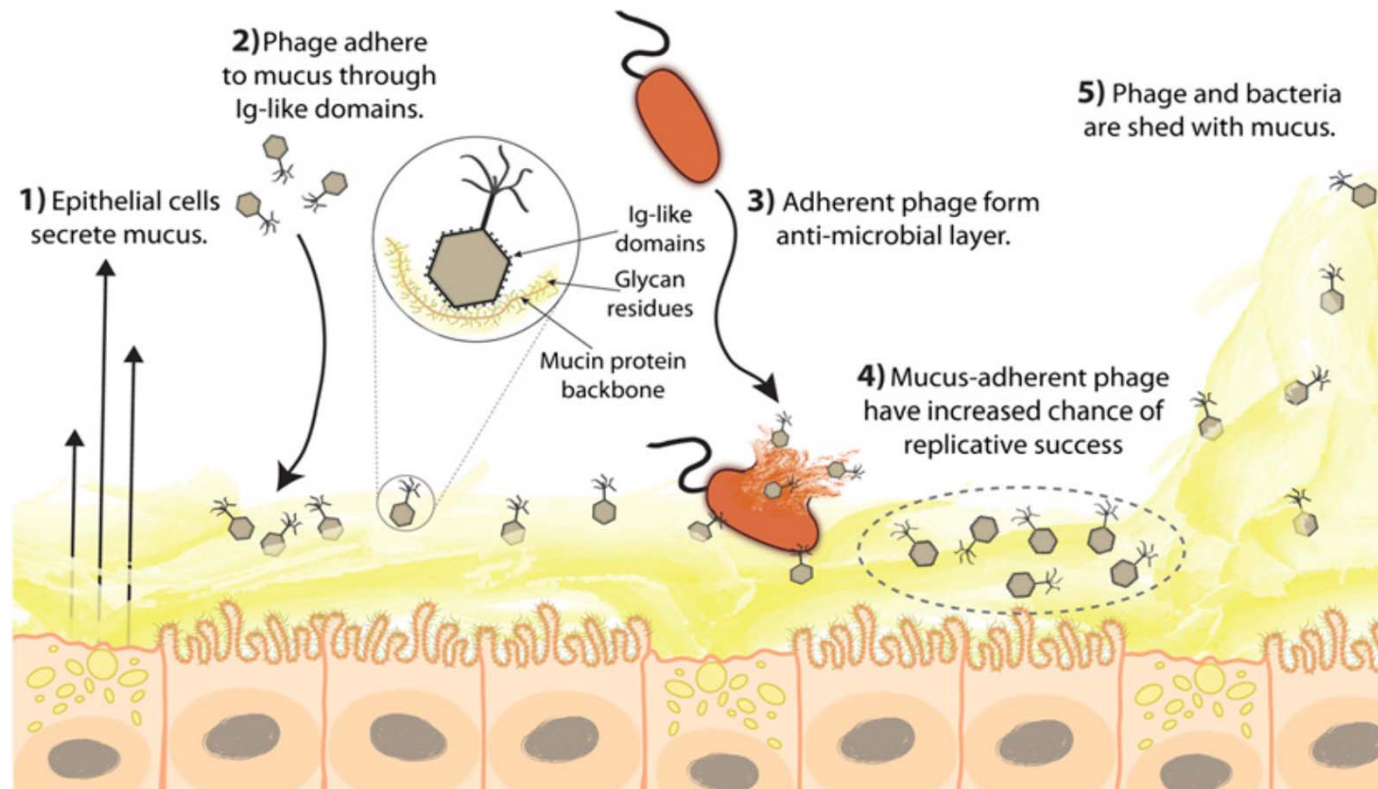


Gut Development and Maturation

- Phages rapidly appear after earlier bacterial colonisation
- Reports of 10^8 virus-like particles (VLP) per gram of faeces 1 week after birth
- Stabilised with aging
- Still less diverse than the healthy adult phageome



Phage – Host Interactions

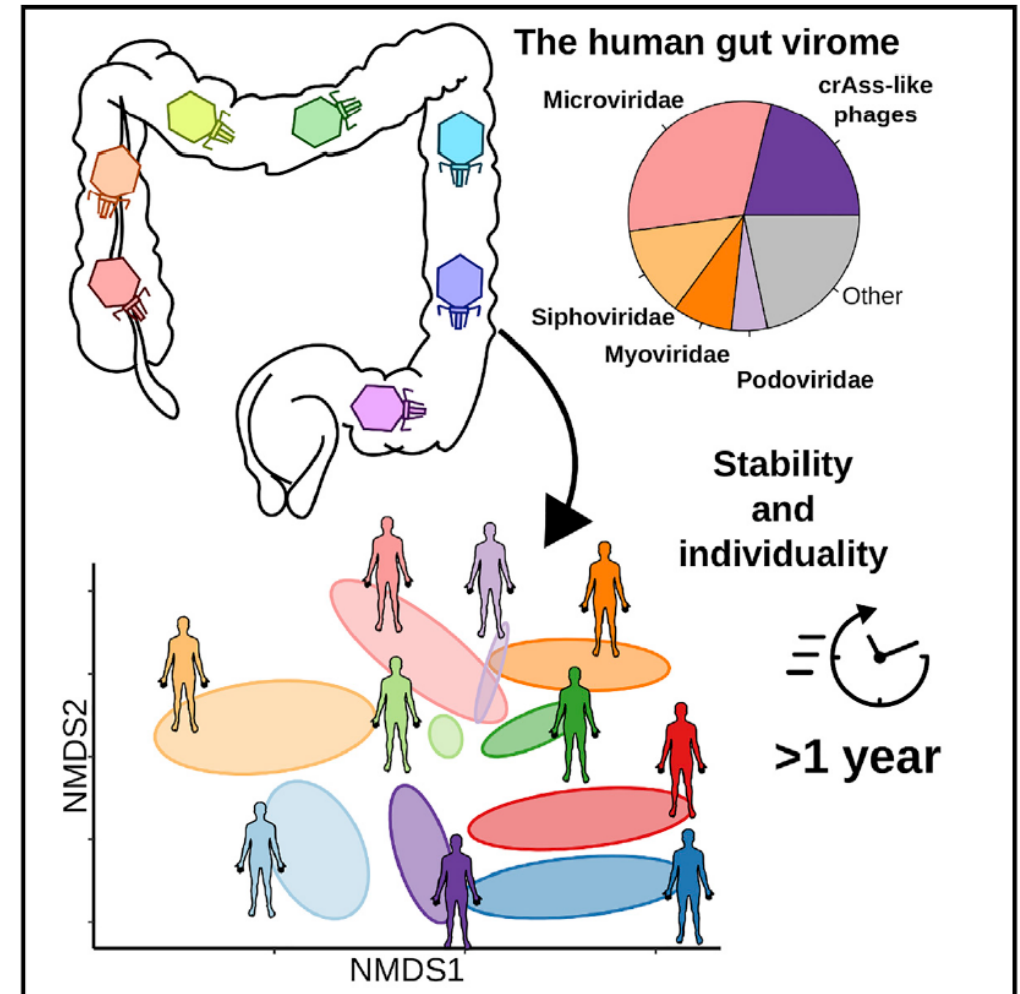


- Conferring protections in healthy individuals
- Protecting the underlying epithelium from bacterial infection.
- A non-host-derived immunity to the human gut.

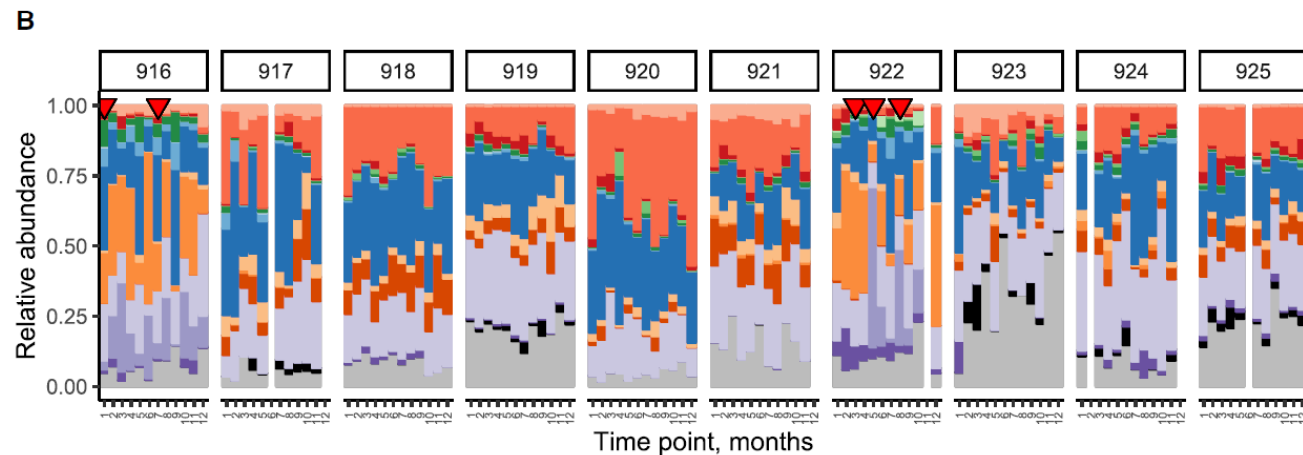
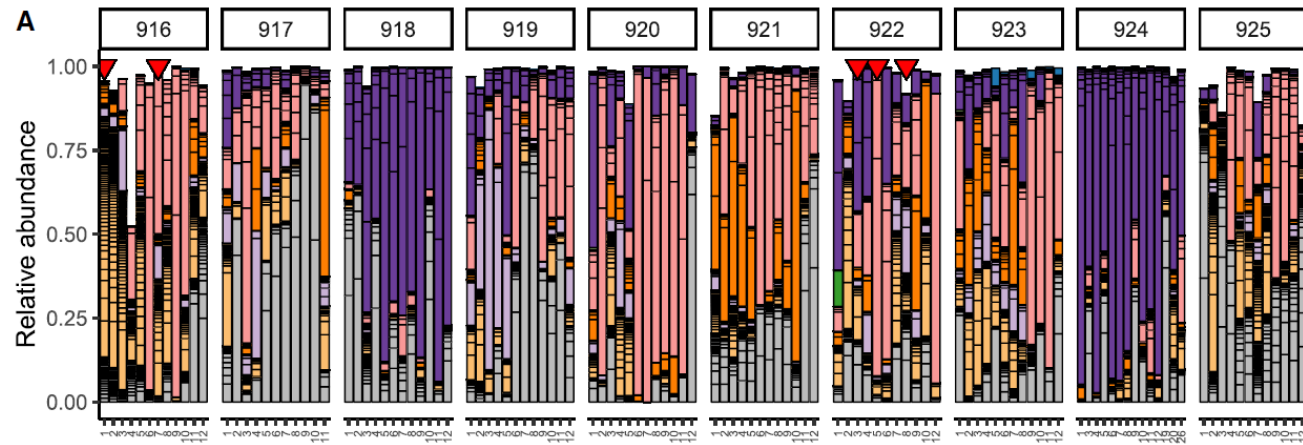
(Barr et al., 2013)

Human Gut Virome Is Highly Diverse, Stable, and Individual Specific

- The human gut virome is highly individual and stable for up to 1 year
- A stable and predominant fraction of viruses constitutes a persistent personal virome
- Persistent bacteriophages can be linked to highly predominant gut bacterial taxa
- Virulent crAss-like and Microviridae bacteriophages predominate and persist in the gut



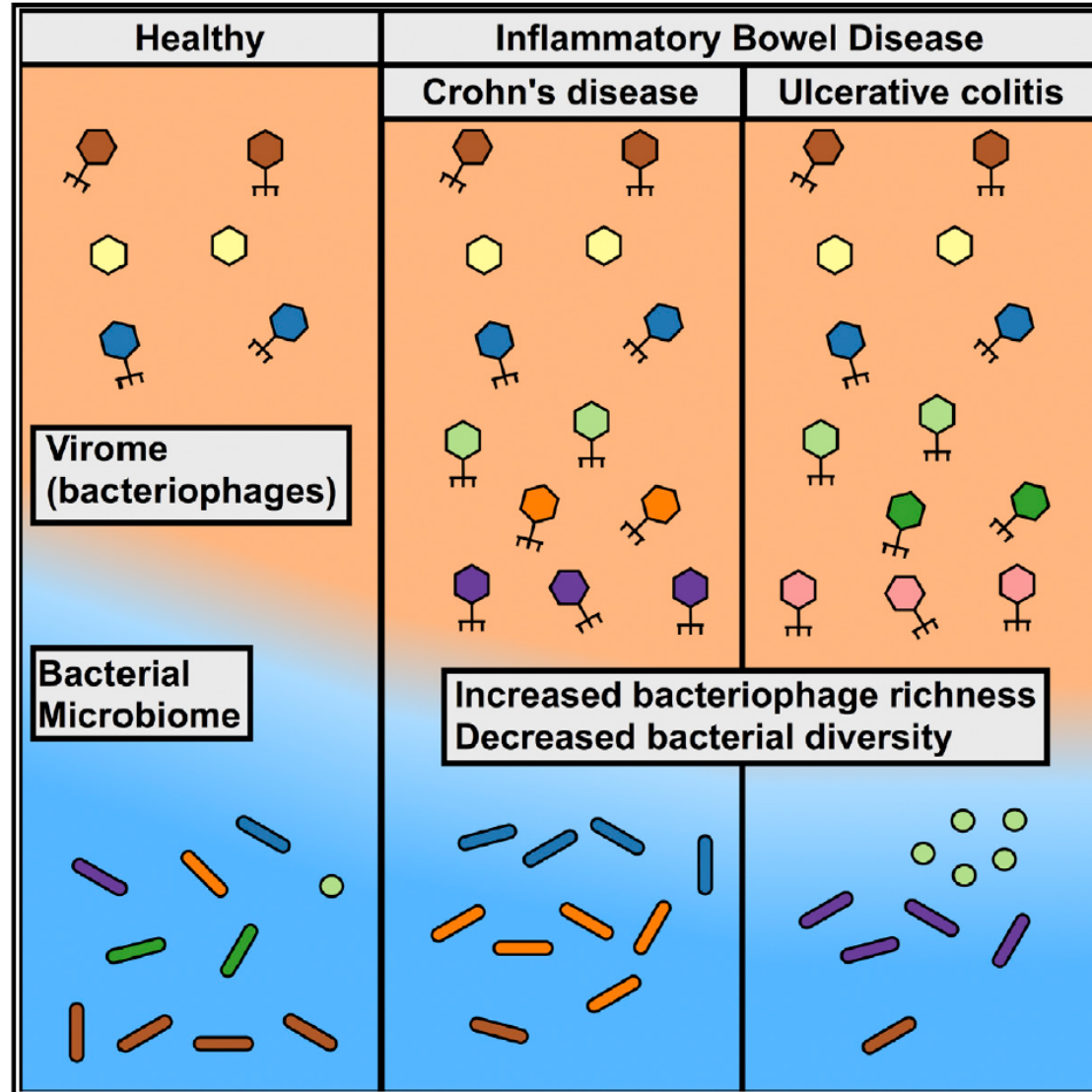
Human Gut Virome Is Highly Diverse, Stable, and Individual Specific



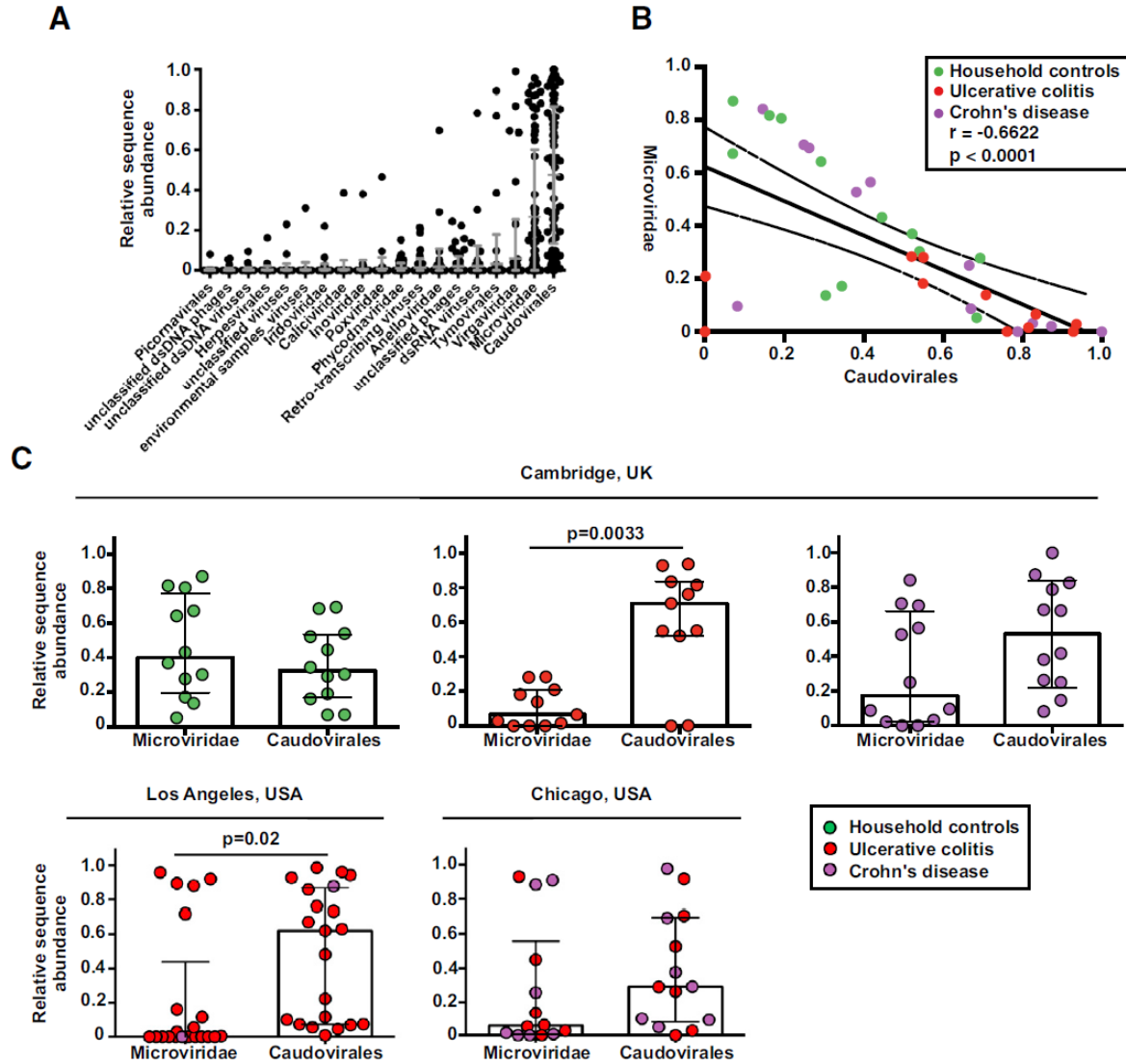
Alterations in Gut Virome are associated with GI diseases

- Inflammatory bowel diseases (Autoimmune disease)
- *Clostridium difficile* infection (Infectious disease)

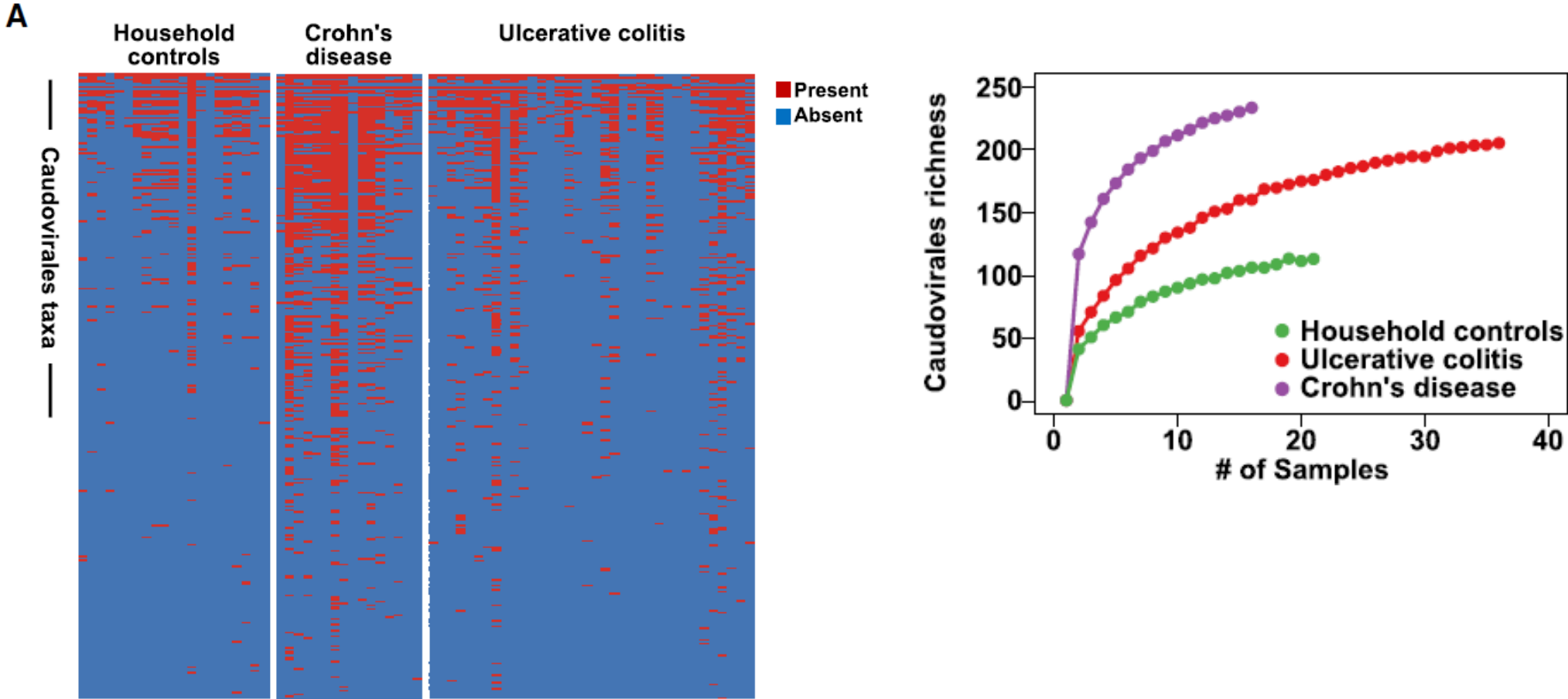
Alterations in Virome in IBD



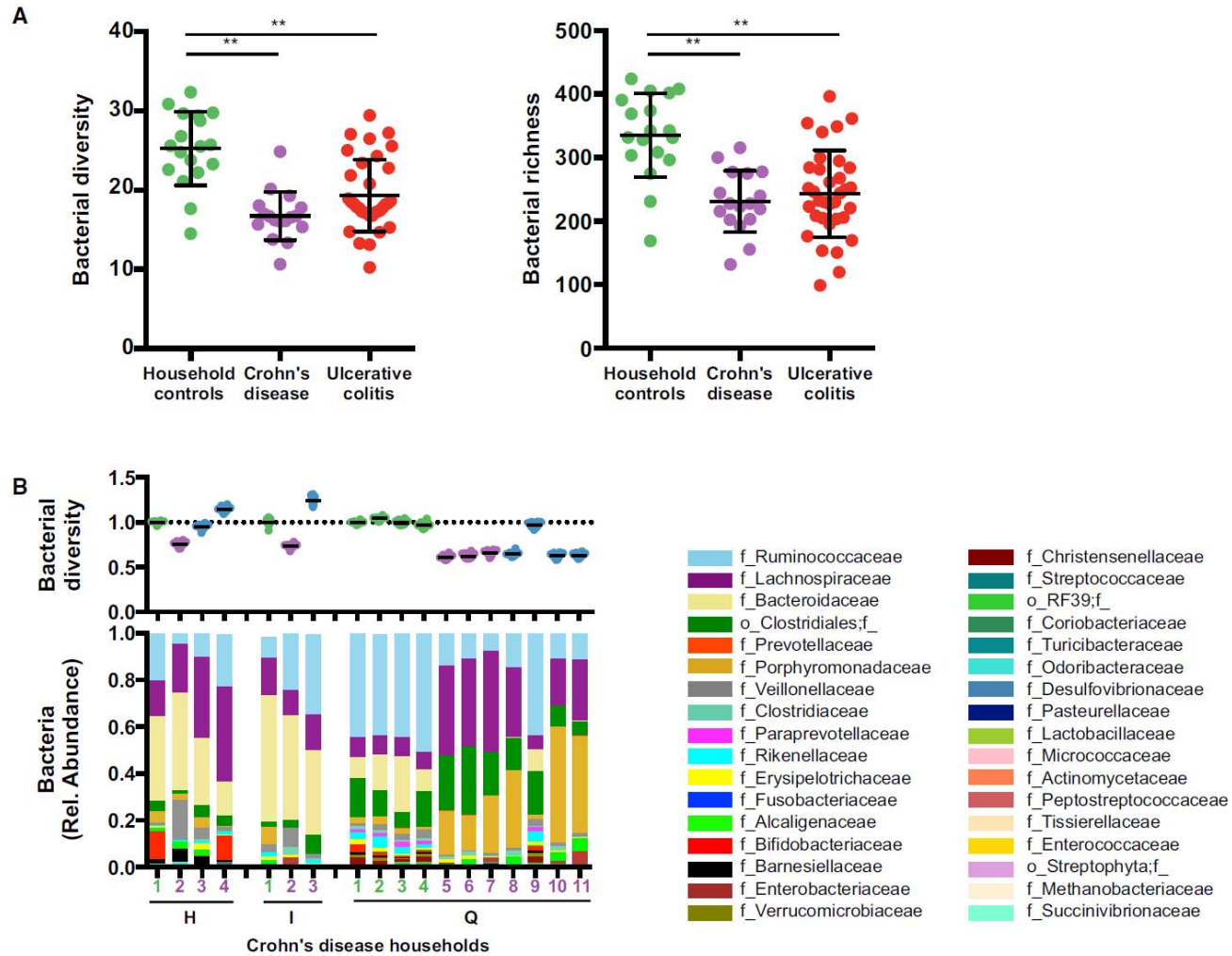
Alterations in Virome in IBD



Alterations in Virome in IBD



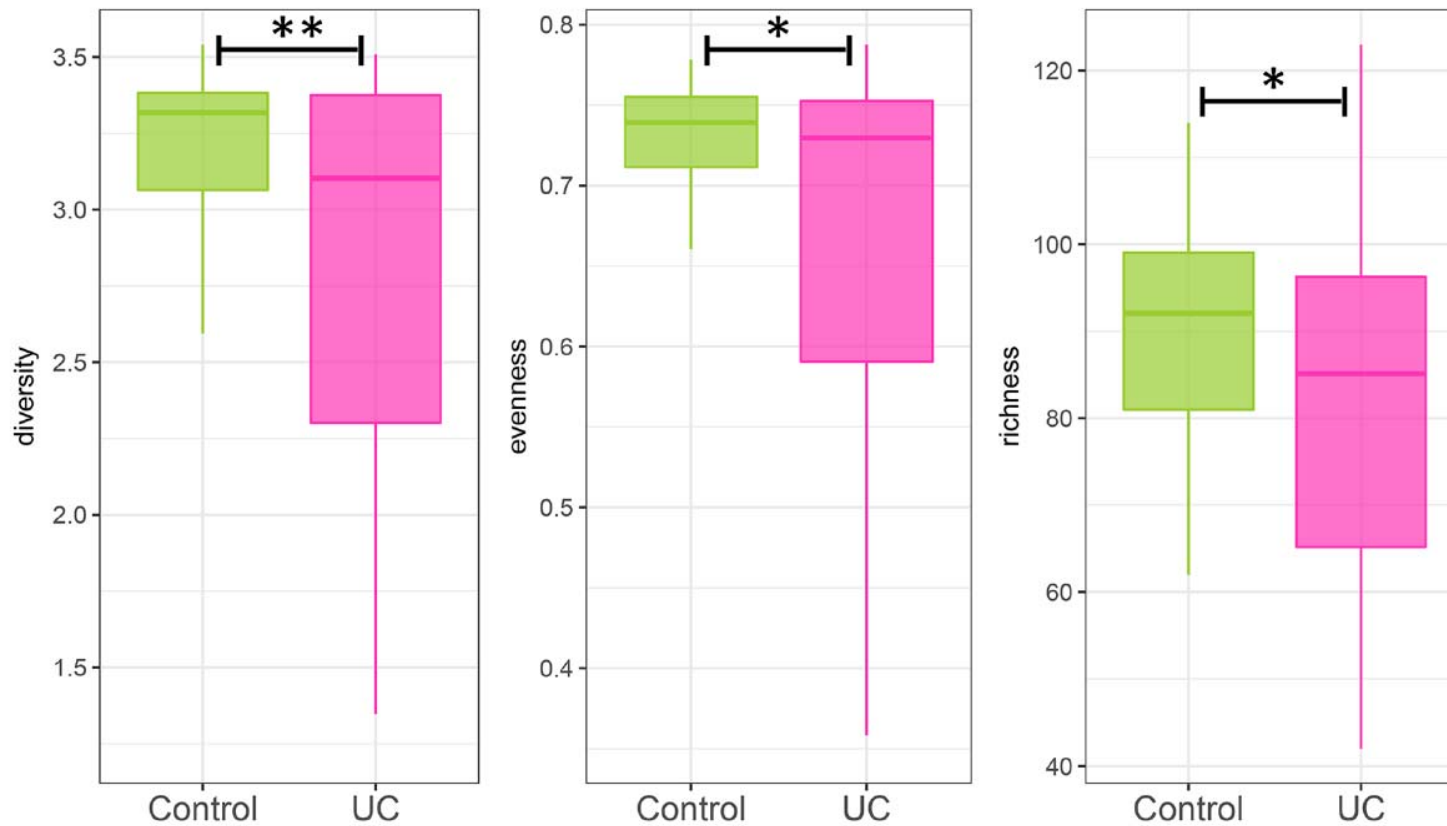
Collaterally alters bacteriome in IBD



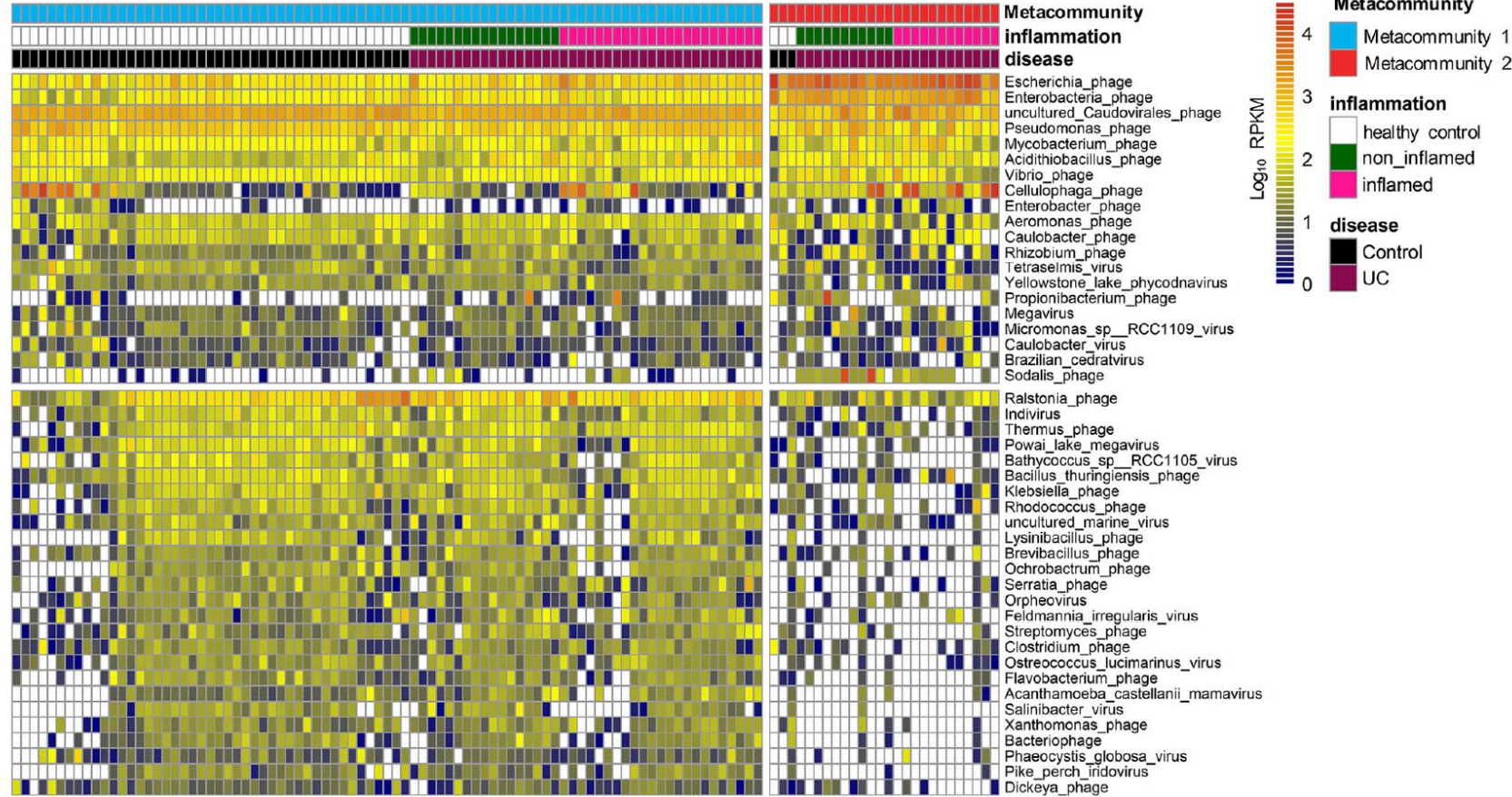
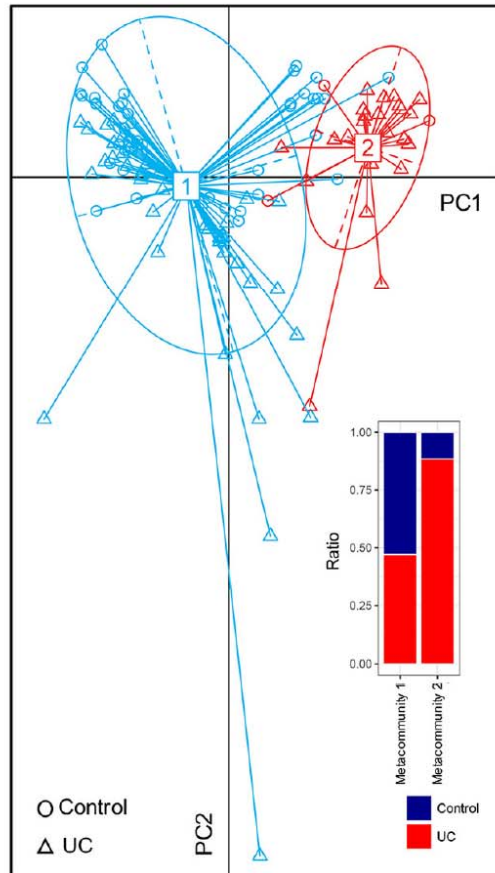
Alterations in Virome in IBD

- The enteric virome is abnormal in multiple inflammatory bowel disease patient cohorts
- The enteric virome richness increases in Crohn's disease and ulcerative colitis
- Virome changes in Crohn's disease and ulcerative colitis are disease specific

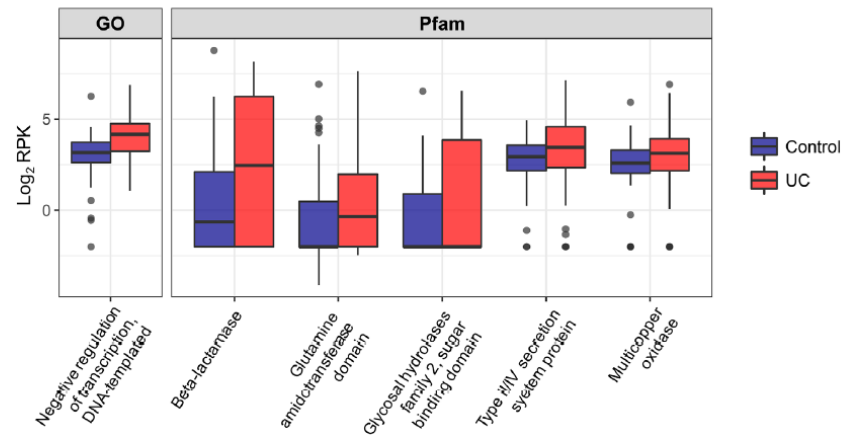
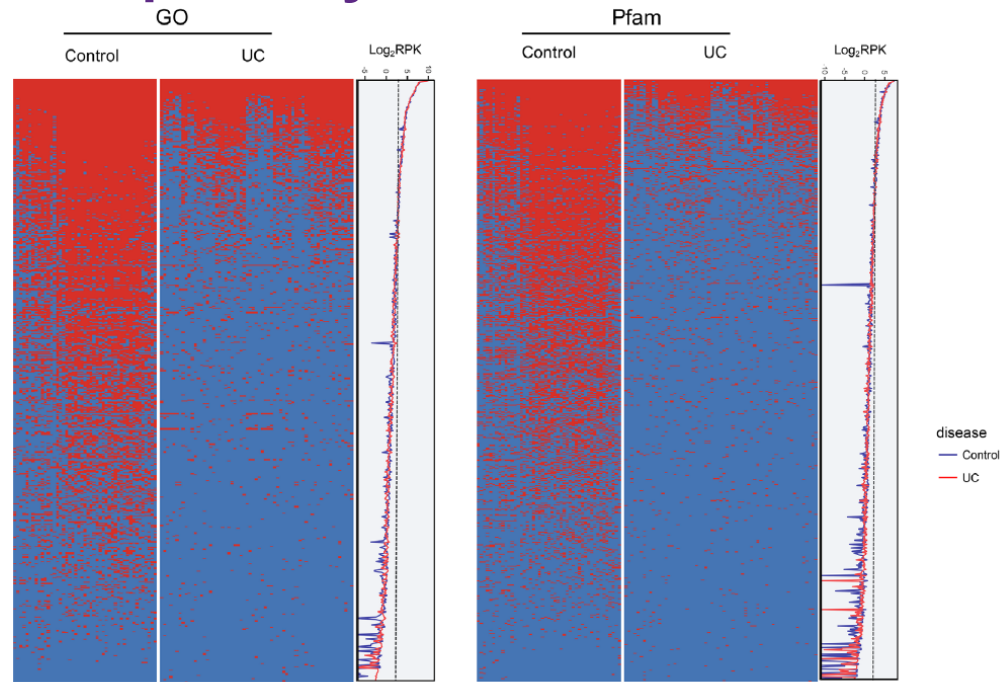
Similar Viral alterations appeared in UC mucosa



A distinguished metacommunity appeared in UC mucosa



Metabolic pathways were less abundant in UC



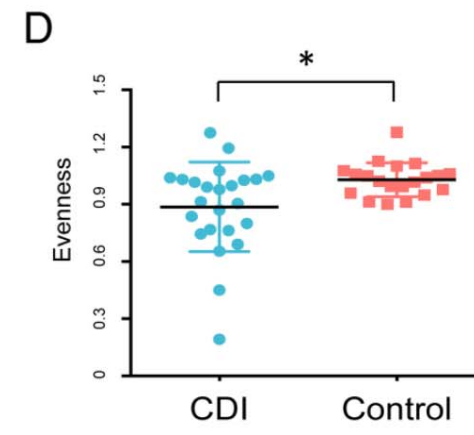
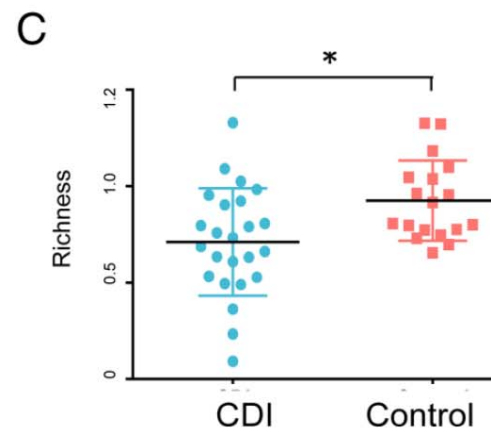
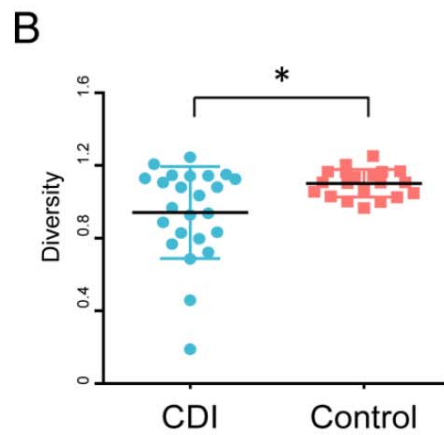
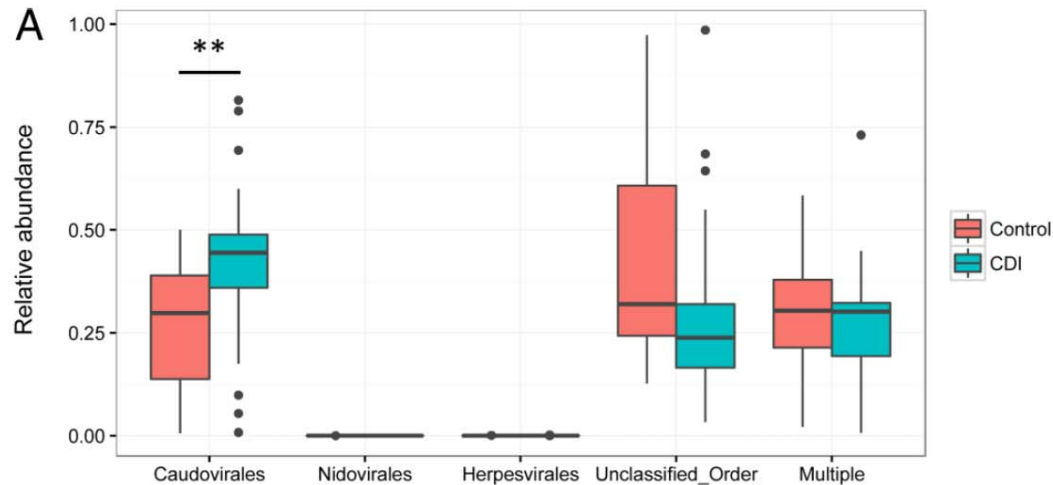
How might it impact on clinical practice in the foreseeable future?

- Alterations of mucosal virome in UC may contribute to disease pathogenesis.
- Therapeutic approaches involve targeting the over-presented Caudovirales bacteriophages, including Escherichia phage and Enterobacteria phage
- Reconstituting the gut microbial homeostasis between mucosa bacteria and viruses should be explored.

Similar viral alterations appear in *Clostridium difficile* infection (CDI)

- CDI was characterised by a high abundance of Caudovirales bacteriophages and a low Caudovirales diversity and evenness compared with healthy household controls.

Bacteriophage transfer during FMT in CDI is associated with treatment outcome

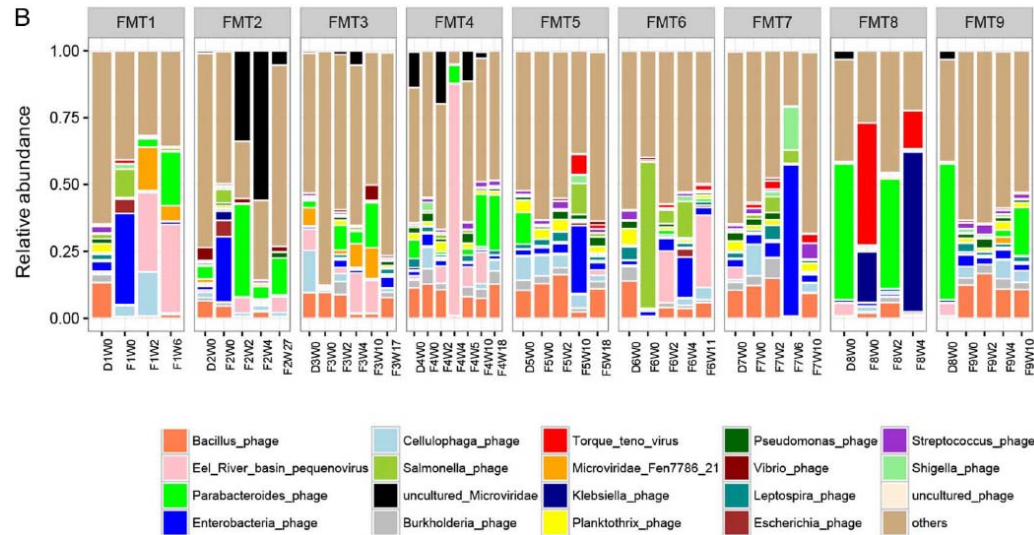
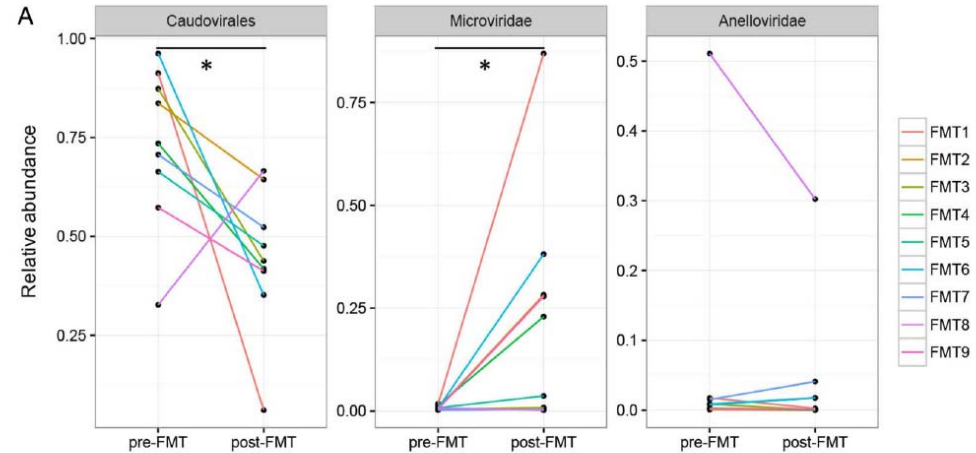


Bacteriophage transfer during FMT in CDI is associated with treatment outcome

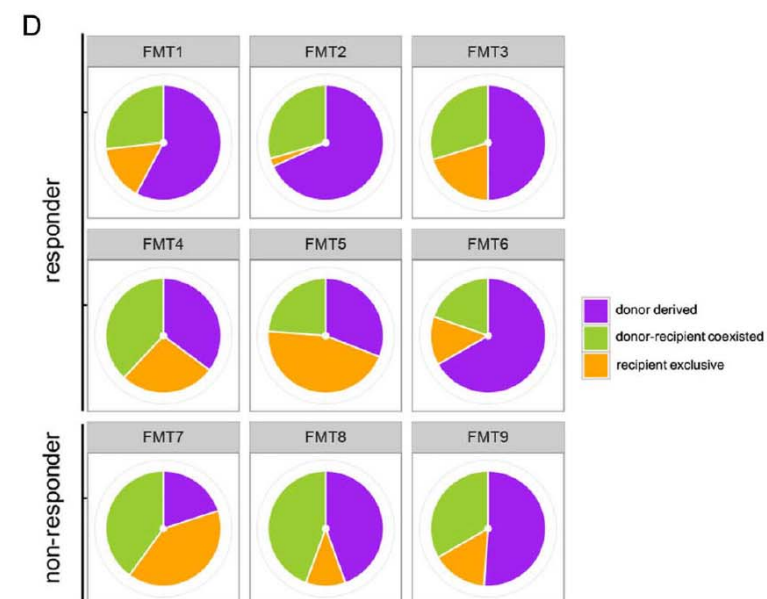
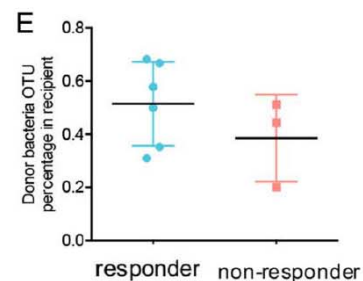
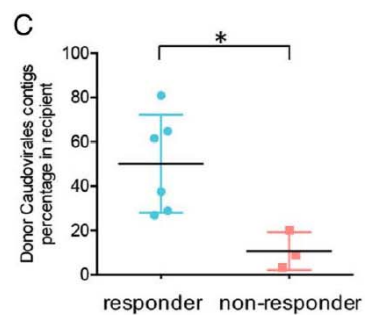
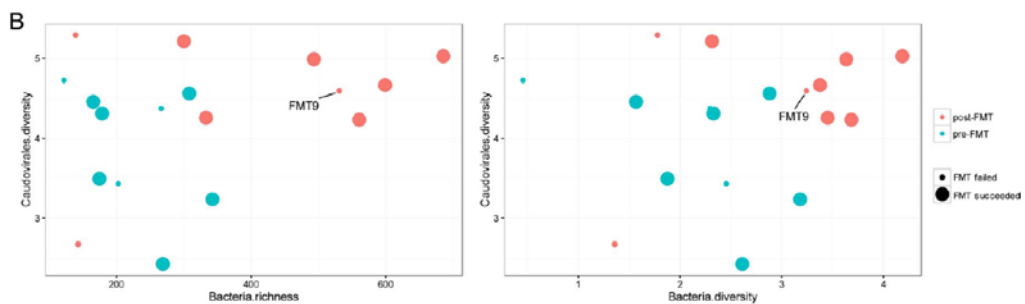
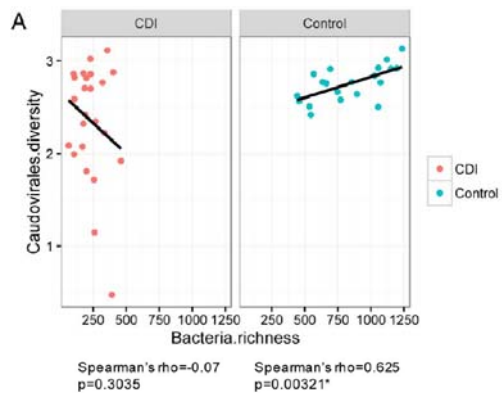
Table 1 Clinical characteristics and outcomes of subjects who received FMT or vancomycin for *Clostridium difficile* infections

Subject	Sex	Age	Smoking	Severe/moderate	Duration of follow-up (weeks)	Outcome (till last follow-up)
FMT1	M	80	Ex-smoker	Moderate	16	Cured
FMT2	M	52	No	Severe	27	Cured
FMT3	M	38	No	Moderate	17	Cured
FMT4	F	76	No	Moderate	18	Cured
FMT5	M	63	No	Severe	18	Cured
FMT6	M	88	No	Severe	23	Cured
FMT7	M	45	Ex-smoker	Severe	20	Recurrence at week 19
FMT8	F	89	No	Moderate	11	Recurrence at week 5
FMT9	F	38	No	Severe	28	Recurrence at week 28
STD1	M	88	Ex-smoker	Severe	20	Recurrence at week 12
STD2	M	93	No	Moderate	7	Recurrence at week 7
STD3	F	78	Smoker	Severe	14	Cured
STD4	F	83	No	Severe	17	Cured
STD5	F	99	No	Moderate	26	Cured

FMT, faecal microbiota transplantation; STD, standard therapy (vancomycin).



Bacteriophage transfer during FMT in CDI is associated with treatment outcome



What are the new findings?

- CDI was characterised by a higher abundance of Caudovirales but drops in its diversity, richness and evenness compared with healthy controls.
- FMT decreases Caudovirales richness in the responders.
- At the same time, FMT restores the diversity of Caudovirales in the recipients is beneficial to the treatment outcome.

Summary

- Human placenta and the earliest infant stool have no microbiome
- After give birth, phages rapidly emerge after bacterial colonisation
- In healthy individuals, viral diversity is overall higher than in diseased state
- Gut virome was found altered in different GI diseases, including IBD and CDI
- Particularly, Caudovirales is increased in IBD and CDI and its abundance is associated with FMT outcome in CDI
- FMT restores Caudovirales diversity that is favourable to treatment outcome



Thank you