



Gut virome orchestrates nitrogen partitioning between the host and microbiome

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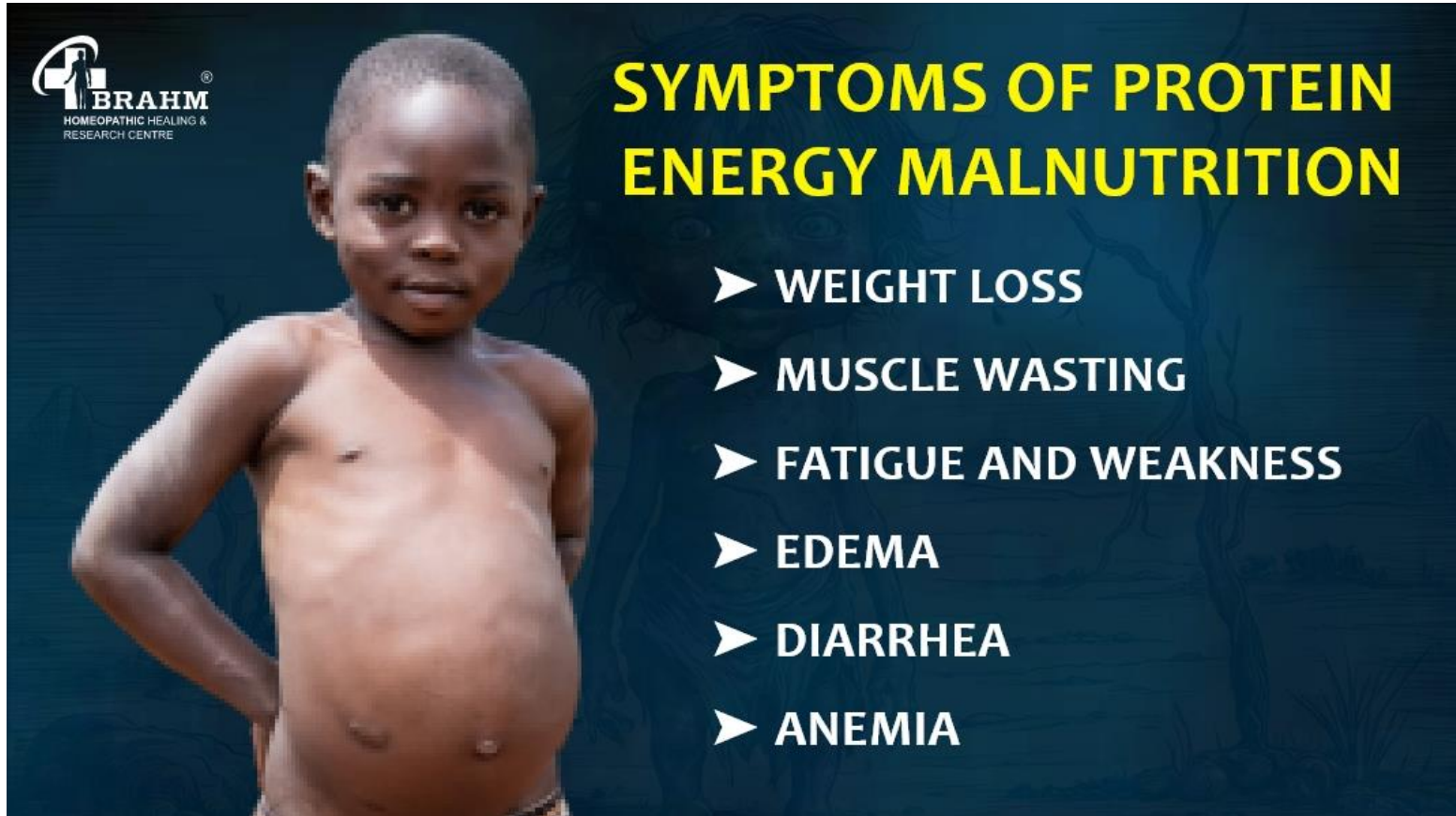
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Low-Protein Malnutrition and Impaired Growth



- PEM is associated with childhood stunting and impaired development.
- PEM-associated diets are high in carbohydrates and low in protein.

Gut Microbiota in Nutrient Metabolism: Upstream Drivers Remain Unclear

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Gut microbiome development and childhood undernutrition

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ORIGINAL ARTICLE



A Microbiota-Directed Food Intervention for Undernourished Children

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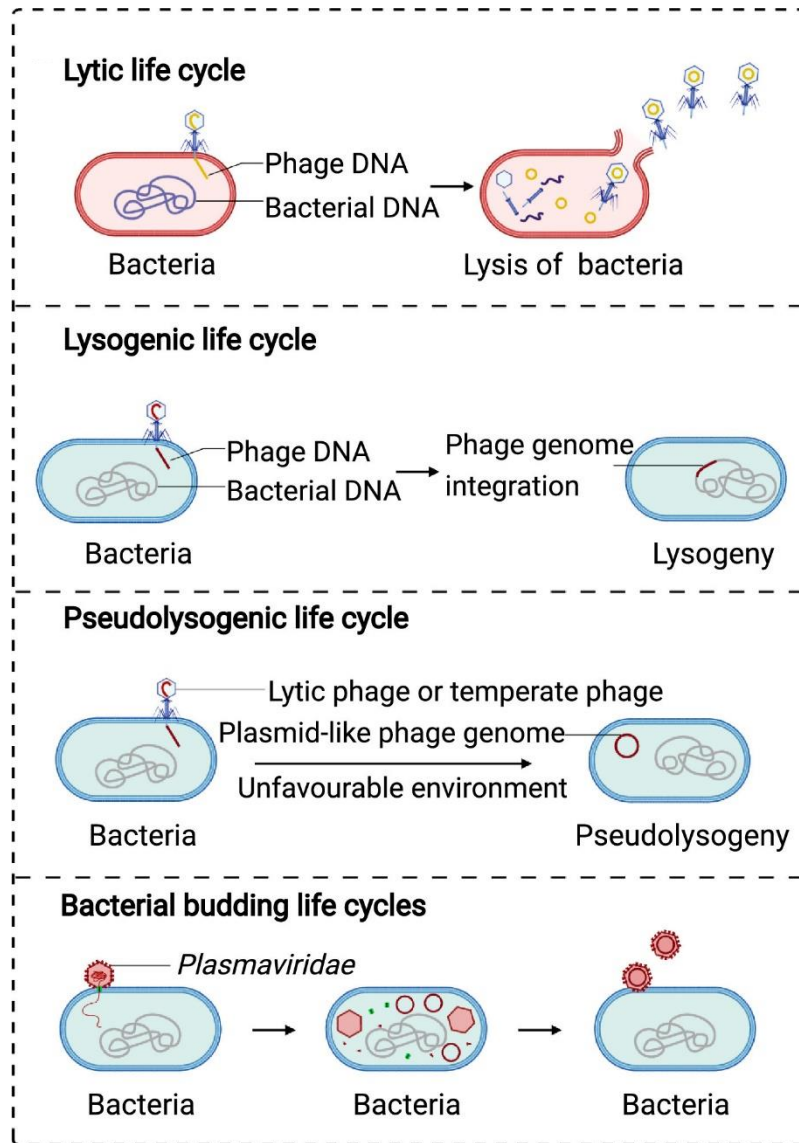
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- Host–microbiota interactions support nutrient metabolism and host nutrition.
- Malnutrition is associated with gut microbiota dysbiosis.
- Dysbiosis may impair nutrient utilization and host growth.
- Microbiota-based strategies can improve protein utilization.



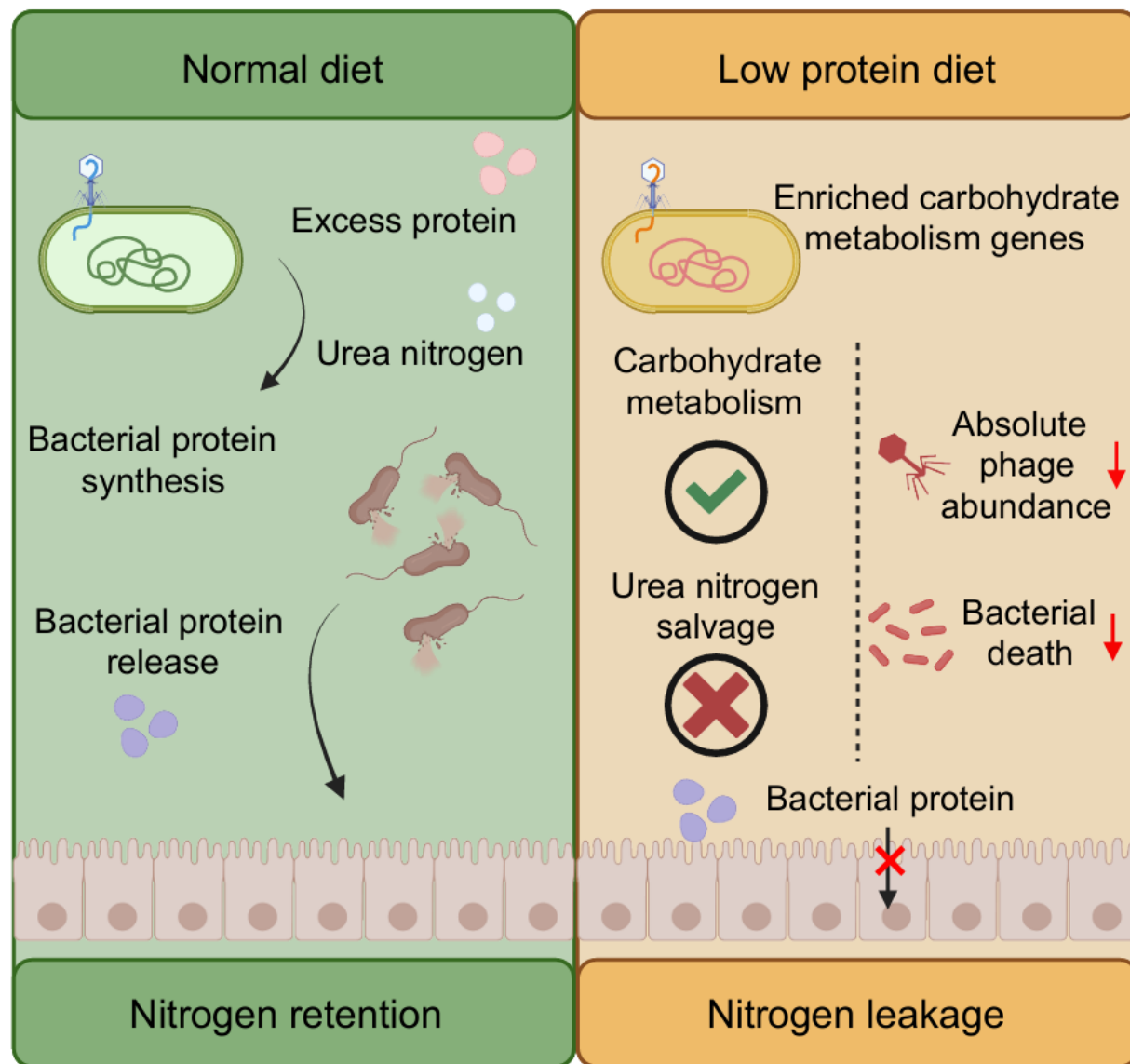
Gut Phages May Link Diet to Bacterial Metabolism



- Phages regulate bacteria mainly through two mechanisms:
- **Bacterial lysis:** Lysis of dominant bacteria alters nutrient flow within the microbial community.
- **Auxiliary metabolic genes (AMGs):** Phage-encoded AMGs can modulate host bacterial metabolism.
- **Scientific question:** Can dietary factors regulate phage–bacteria interactions and thereby influence bacterial metabolism and host nutrient utilization?

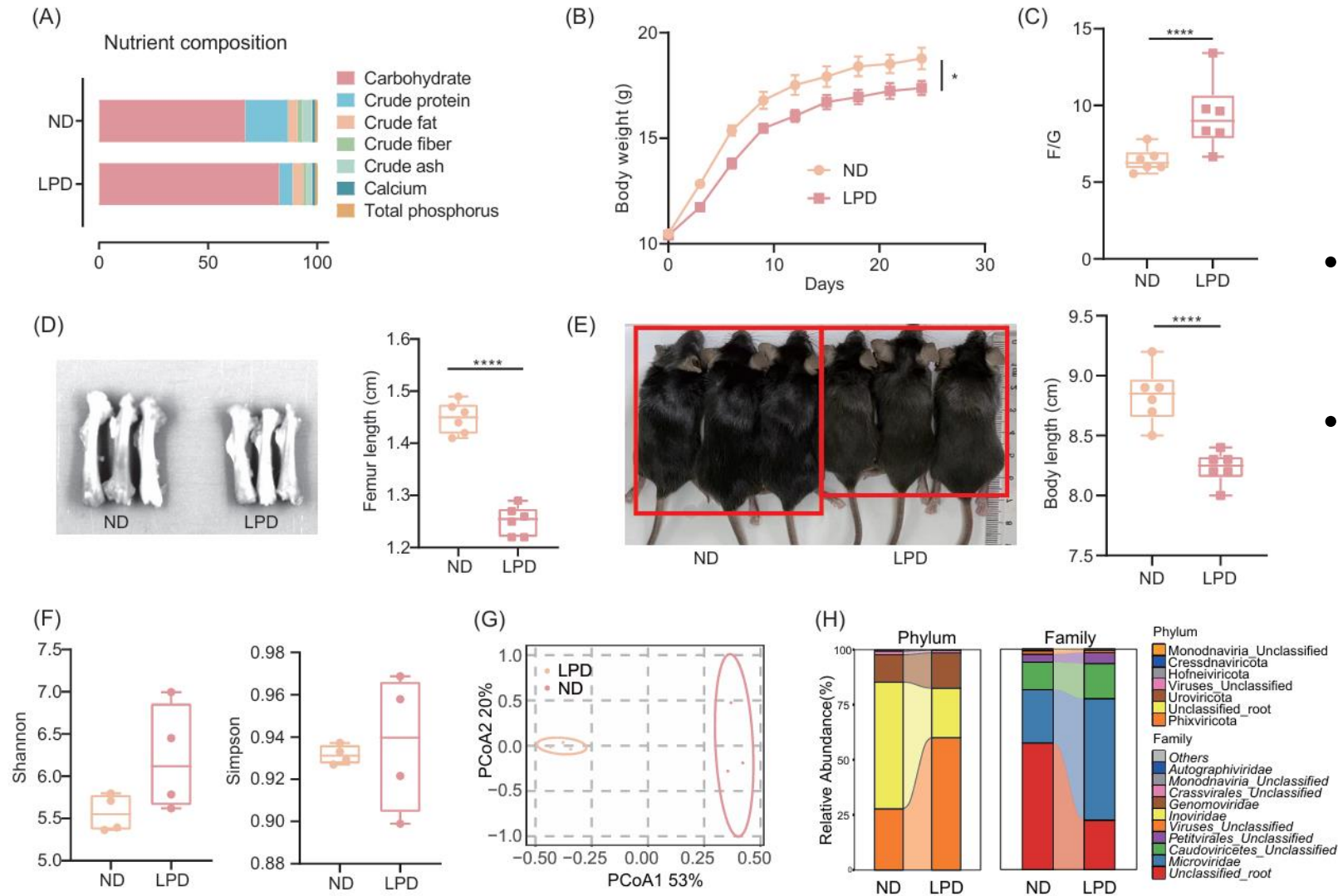


Highlight



- **Adequate protein intake** promotes lytic phage-mediated bacterial lysis, releasing microbial nitrogen available to the host.
- **Protein restriction** favors lysogenic maintenance, reducing bacterial lysis and nitrogen release.
- **Protein restriction** enriches carbohydrate metabolism-related AMGs, alters bacterial metabolism, and impairs urea nitrogen recycling.

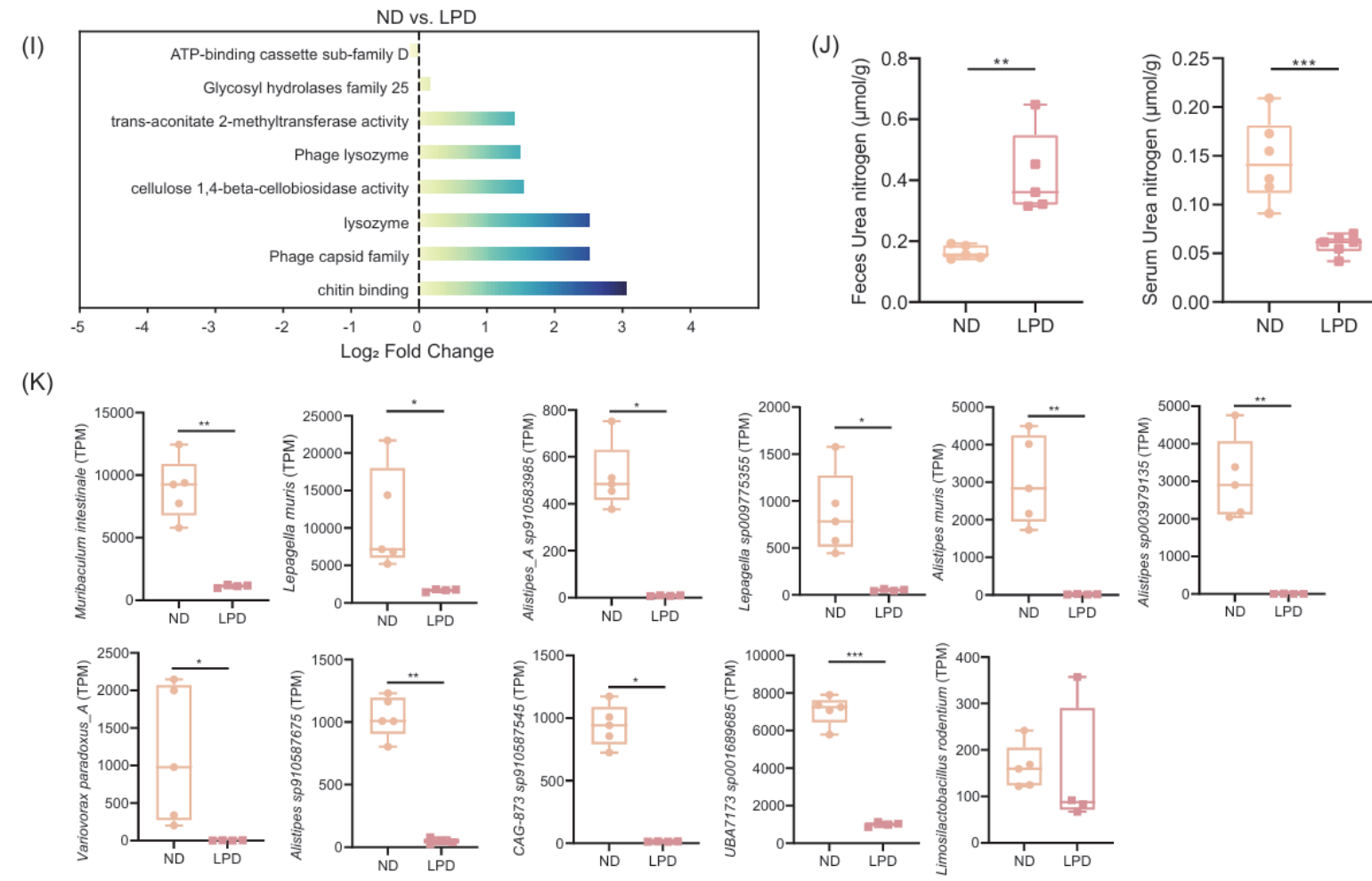
LPD Alters the Gut Virome and Impairs Nitrogen Recycling



- LPD impairs growth and increases feed conversion ratio.
- LPD alters gut virome composition and function, with increased Microviridae.

Fig.1. LPD impairs growth and alters the gut virome.

LPD Alters the Gut Virome and Impairs Urea Nitrogen Recycling



- Carbohydrate metabolism-related AMGs are enriched in the LPD virome, suggesting viral involvement in gut carbohydrate metabolism.
- LPD increases fecal urea nitrogen and decreases serum urea nitrogen, accompanied by reduced urea-degrading bacteria.

LPD-Derived Virome Transplantation Impairs Recipient Growth

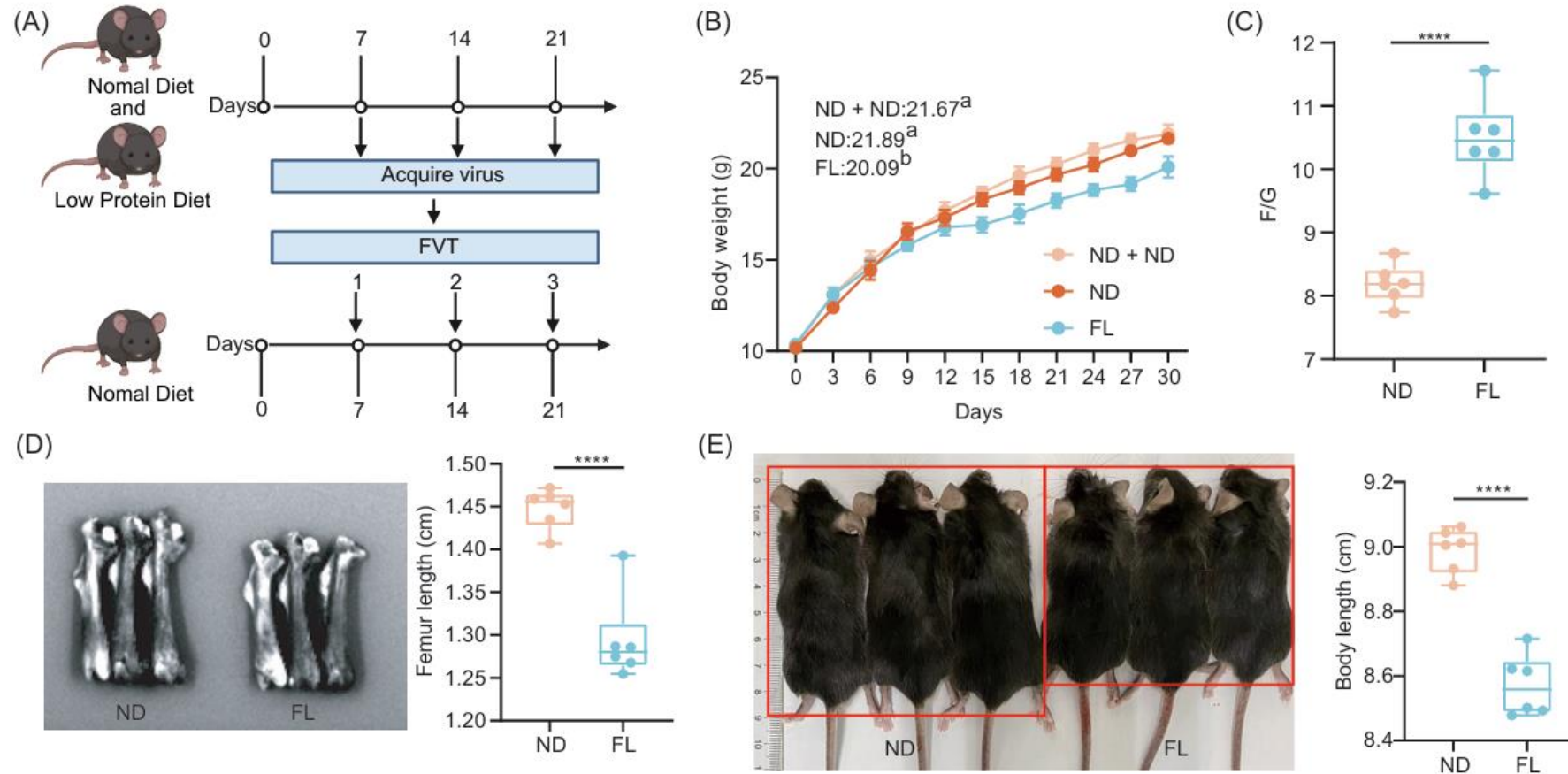
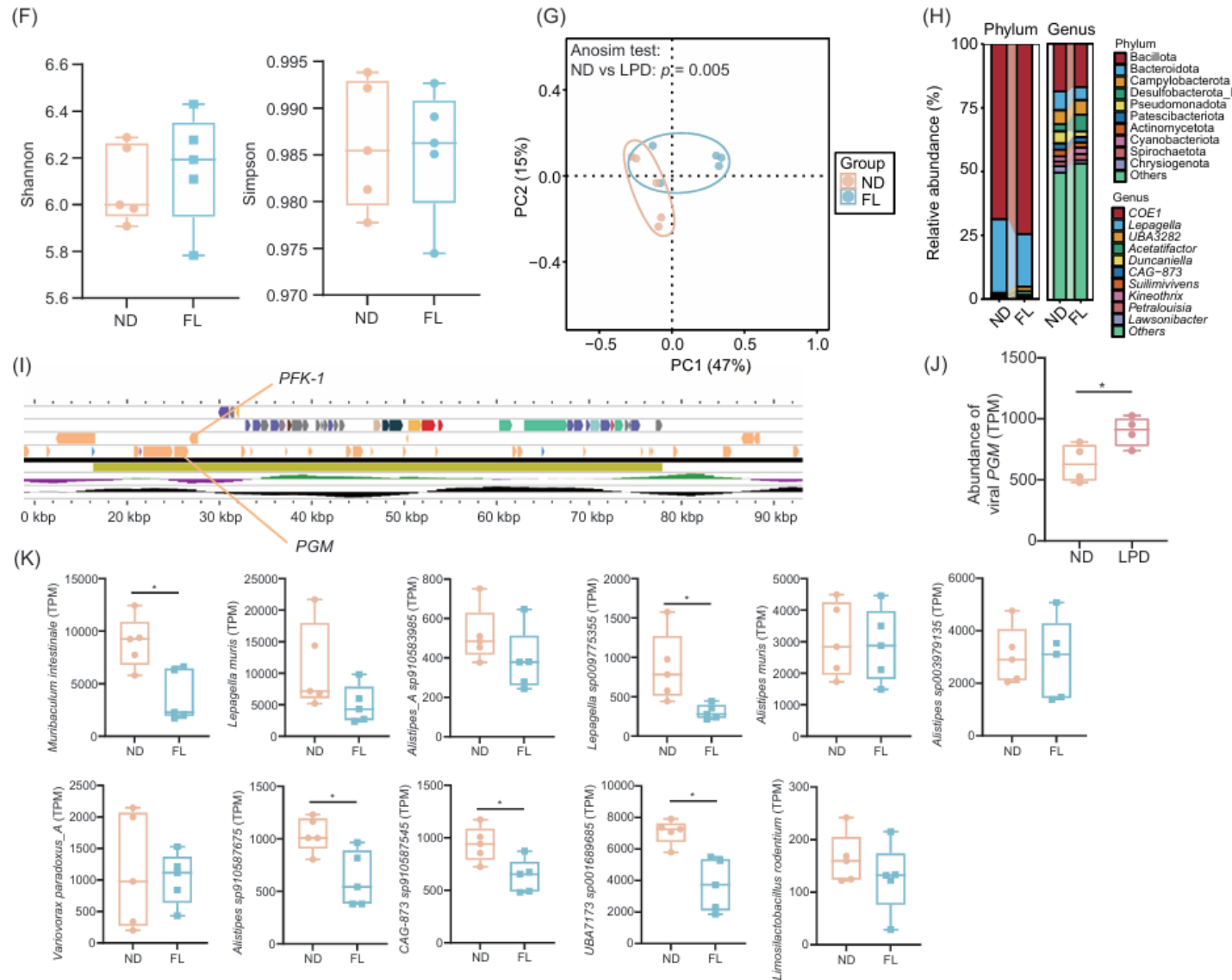


Fig.2. LPD-derived virome transplantation impairs recipient growth.

- LPD-derived virome transplantation partially recapitulates growth impairment in ND mice, reducing body weight, body length, and femur length.

LPD-Derived Virome Transplantation Impairs Urea Nitrogen Recycling



- LPD-derived virome transplantation alters the recipient gut microbiota, enriching carbohydrate-utilizing taxa such as *Acetatifactor*.
- *Acetatifactor*-associated prophages carry carbohydrate metabolism-related AMGs, including *pgm* and *pfkA*, alongside reduced urea-degrading bacteria.

Fig.2. LPD-derived virome transplantation impairs urea nitrogen recycling.

ND-Derived Virome Transplantation Improves LPD Mouse Growth

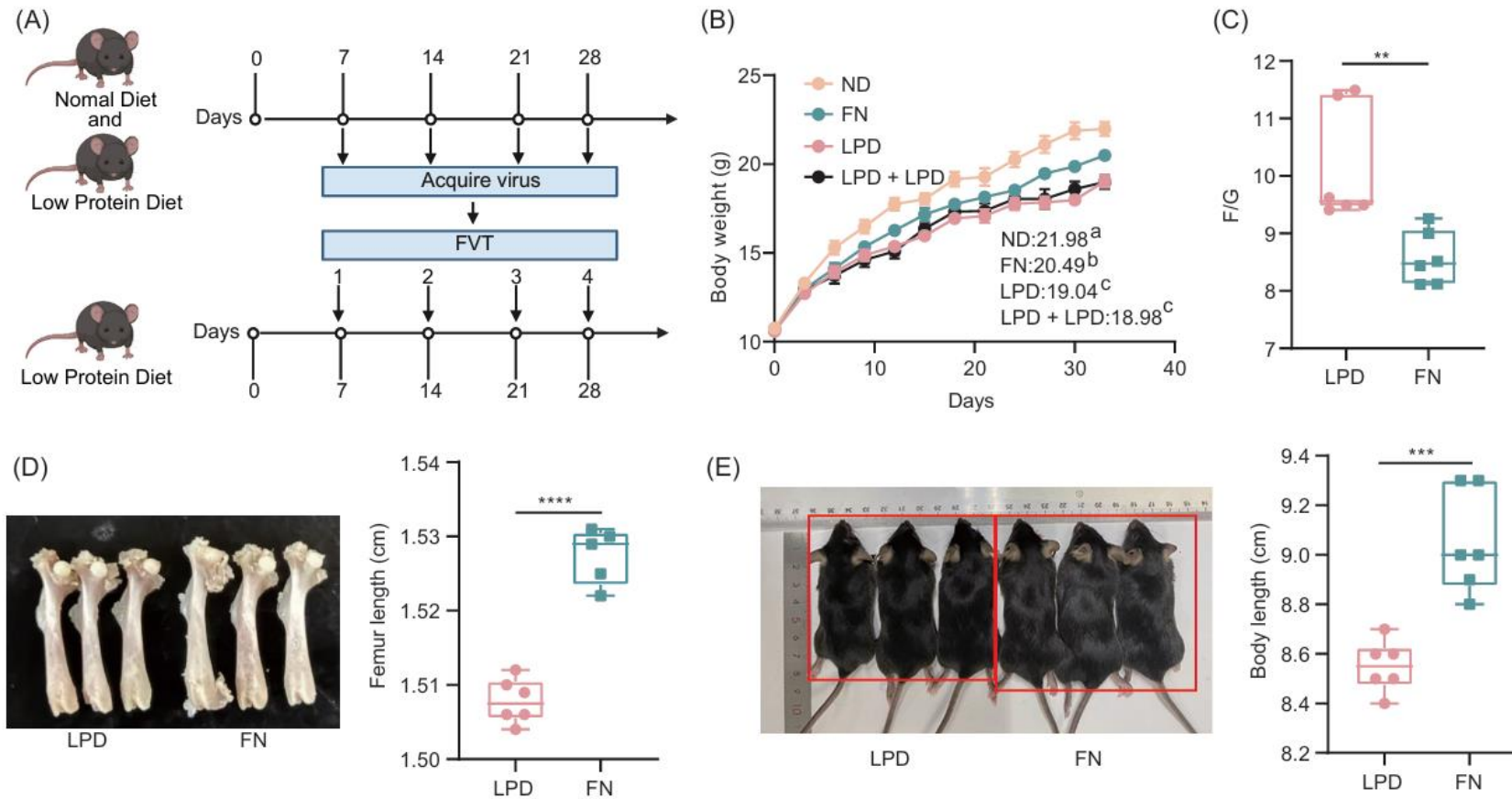


Fig.3. ND-derived virome transplantation improves LPD mouse growth.

- ND-derived virome transplantation improves growth impairment in LPD mice.

Virome Transplantation Fails to Restore Microbial Urea Nitrogen Recycling

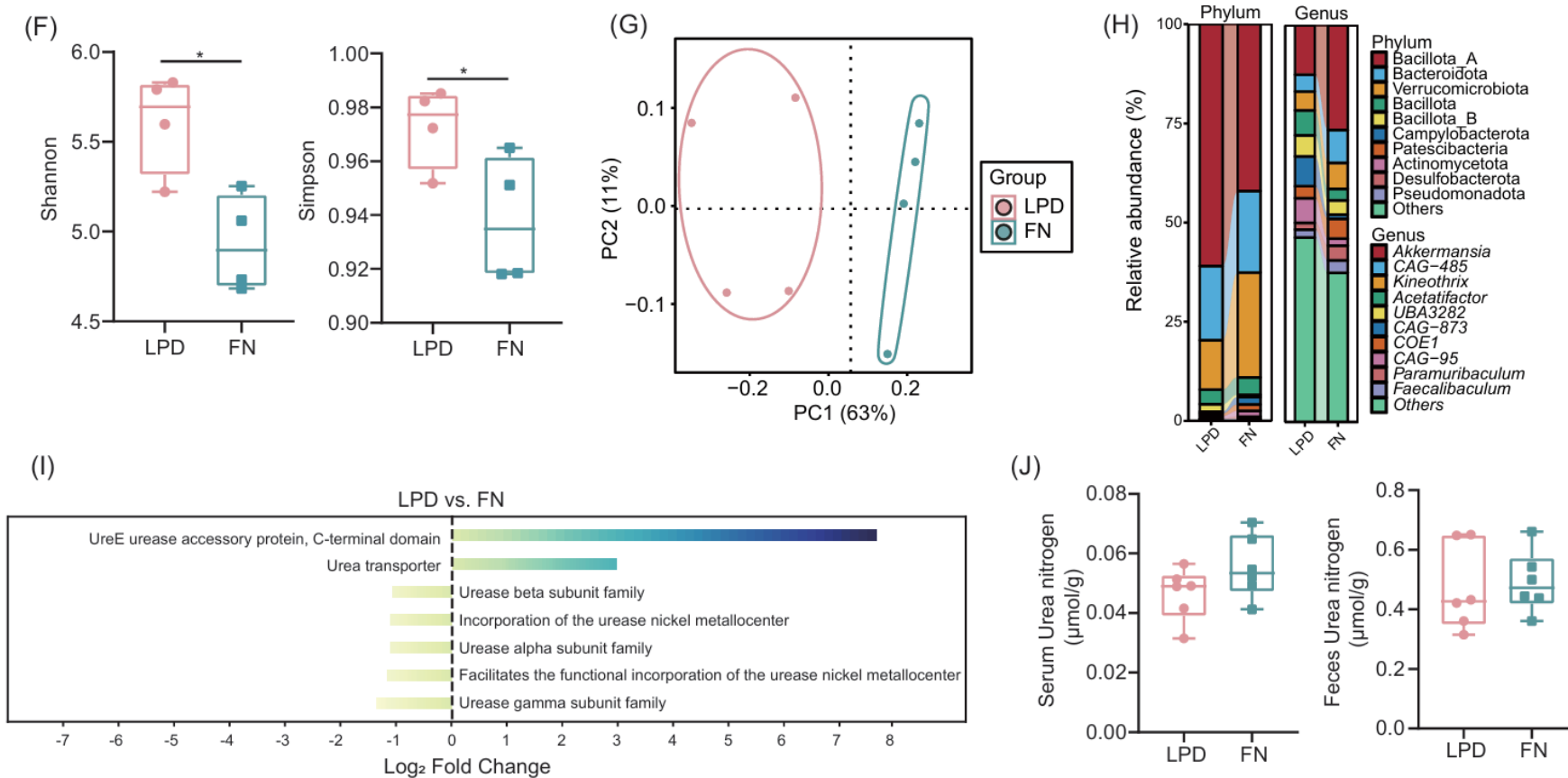


Fig.3. Virome transplantation fails to restore microbial urea nitrogen recycling in LPD mice.

- FN did not restore gut microbiota diversity or composition to ND levels.
- FN did not restore microbial urea nitrogen recycling.
- Serum urea nitrogen increased without a significant decrease in fecal urea nitrogen.



Greater Lytic Pressure on Gut Bacteria in ND Mice

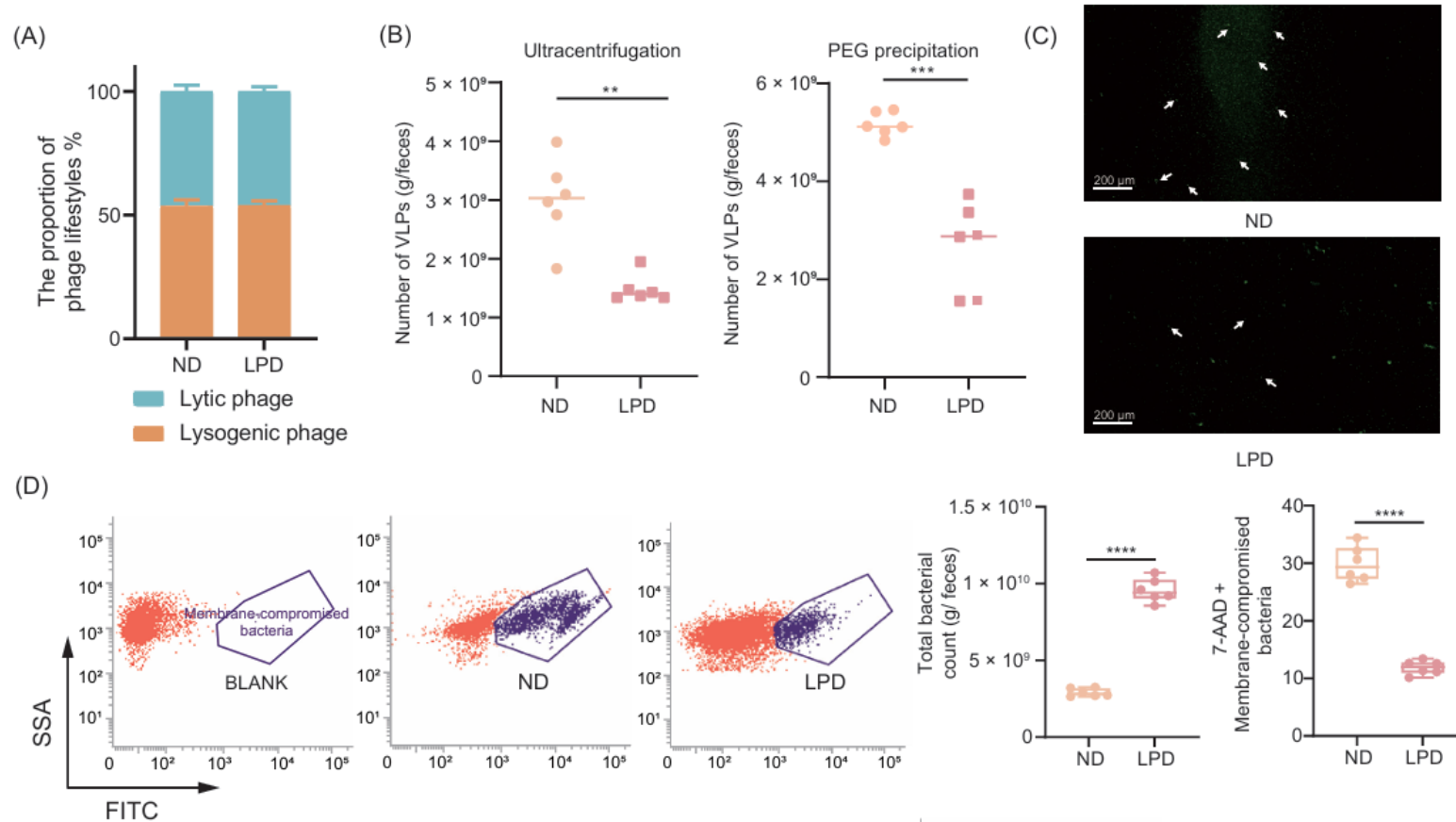
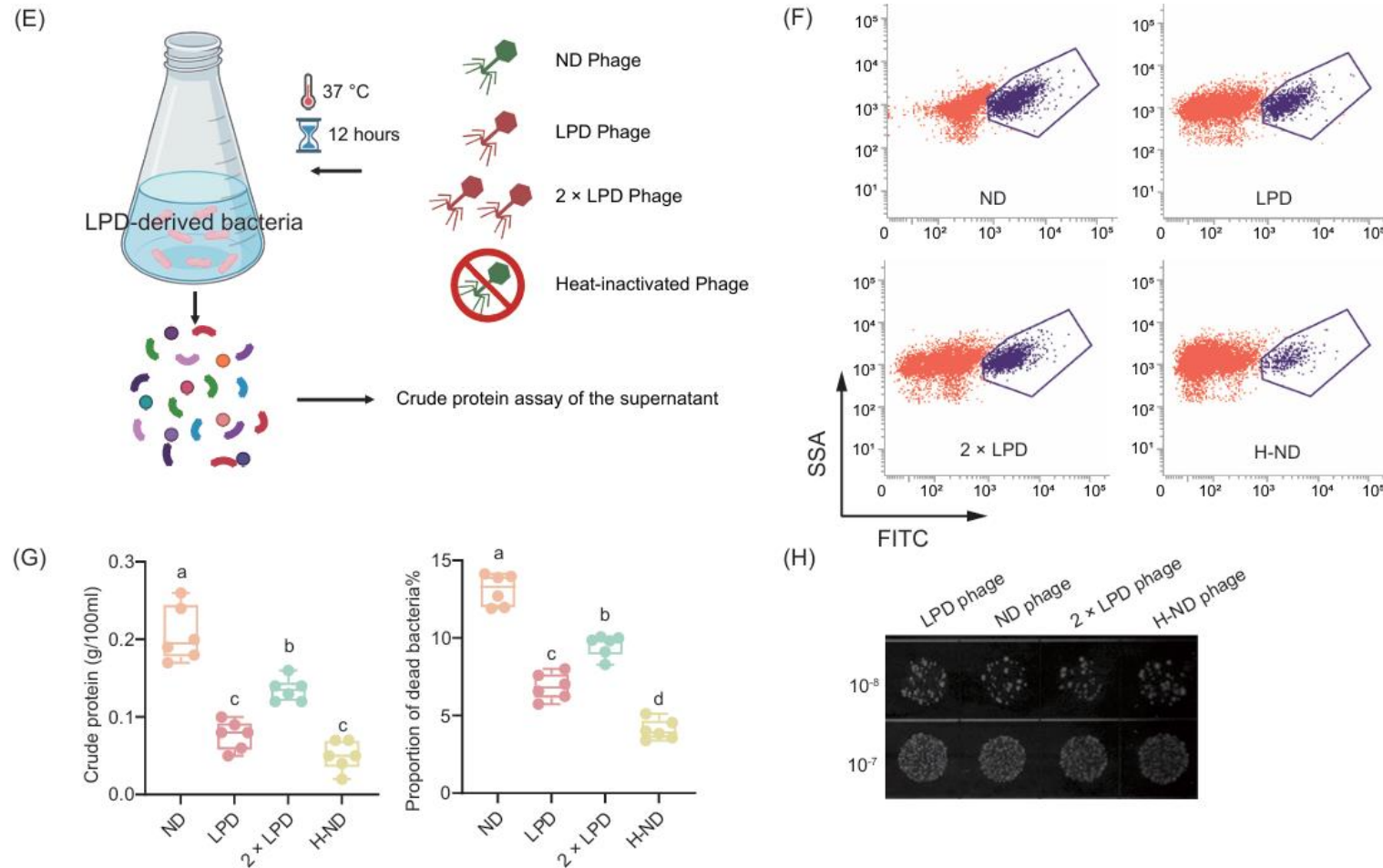


Fig.4. Higher viral abundance in ND feces imposes stronger lytic pressure on LPD bacteria.

- ND had ~2-fold higher viral particle abundance than LPD.
- LPD had fewer membrane-compromised bacteria, consistent with lower free phage abundance and higher bacterial load.

Higher Phage Lytic Pressure Promotes Bacterial Protein Release



- **ND-derived phages showed stronger lytic activity** against LPD-associated bacteria, increasing membrane damage.
- **ND-derived phages promoted greater bacterial protein release**, with 2×LPD showing an intermediate effect.

Fig.4. Higher phage lytic pressure promotes bacterial protein release.



Mouse Growth Correlates with Phage Lytic Activity

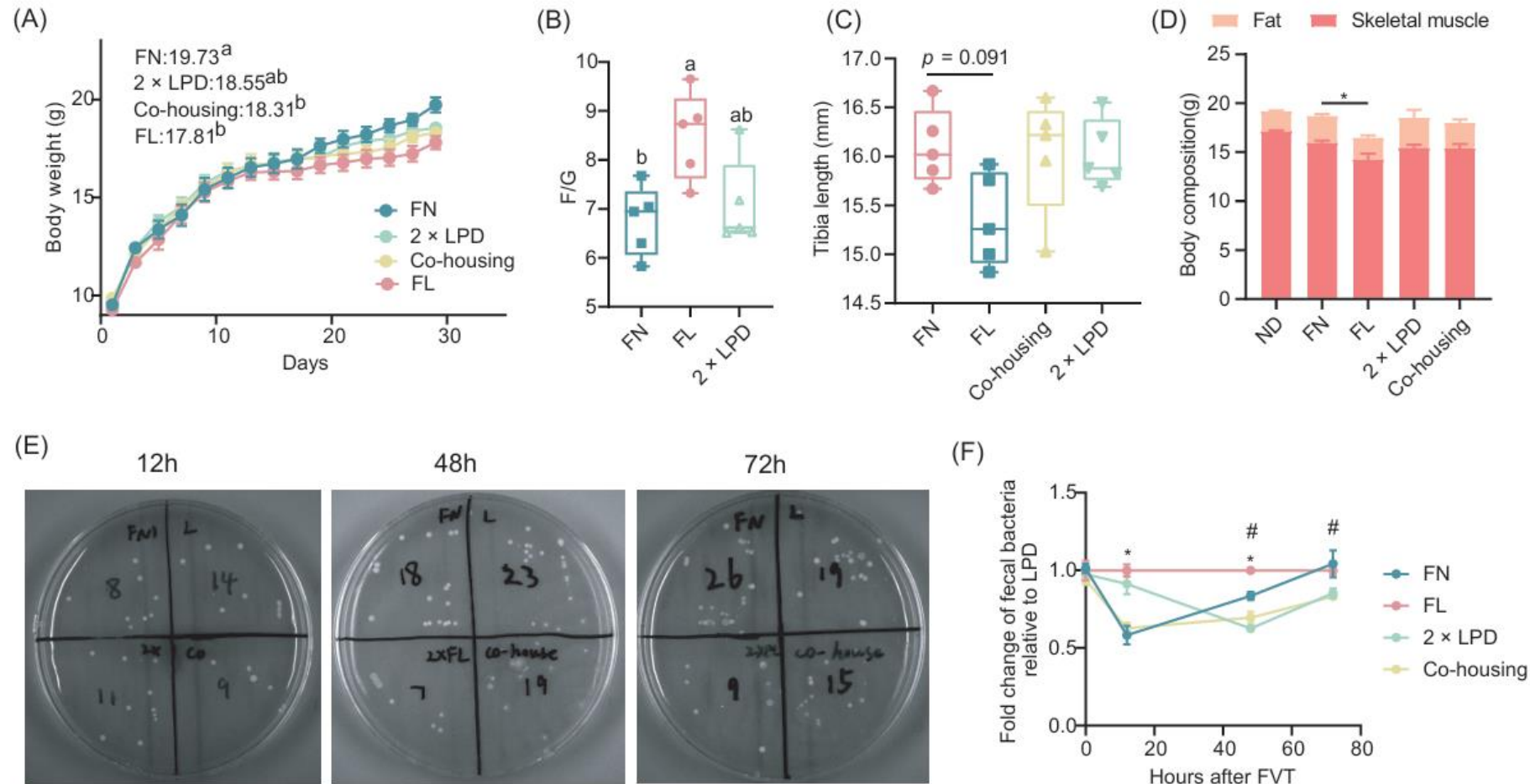


Fig.5. Effects of virome preparations with different abundances on recipient mouse growth.

- ND-derived virome improved LPD mouse growth, whereas LPD-derived virome showed the poorest growth, with 2×LPD and co-housing showing intermediate phenotypes.



Phage-Released Bacterial Protein Supports Host Nutrition

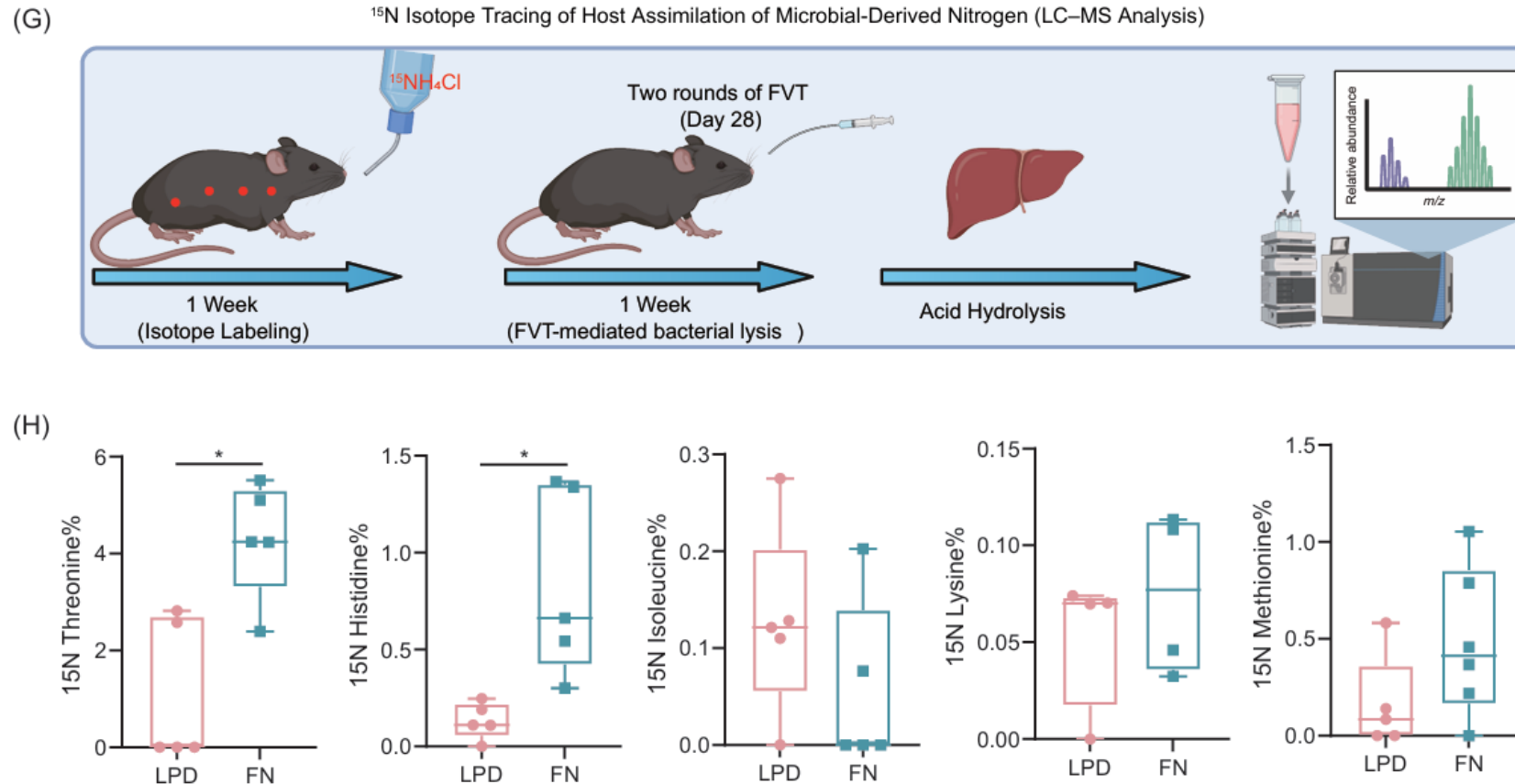


Fig.5. High-dose virome transplantation increases bacterial-derived threonine and histidine.

- ¹⁵N tracing showed bacterial nitrogen entered the host amino acid pool, especially threonine and histidine.



Summary

- ❑ Normal Diet: Phages promote bacterial lysis and microbial protein release, facilitating microbial nitrogen transfer to the host.
- ❑ Low-Protein Diet: Nutritional stress suppresses phage release, reducing free phage abundance and bacterial lysis. This increases bacterial load, enhances carbohydrate metabolism, and impairs urea nitrogen recycling, leading to microbial nitrogen retention and limiting host nitrogen utilization and growth.

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