Adaptive Genomics of *Acinetobacter pittii* on the ISS: Distinct Clade Formation, Stress Tolerance, and Antimicrobial Phenotypes

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Executive summary

ISS-derived *A. pittii* isolates form a **genetically distinct clade** relative to terrestrial strains, marked by unique accessory genes, ISS-associated SNPs/indels, and enrichment of **oxidative/osmotic stress**, **DNA repair**, and **metal homeostasis** functions. Phenotypically, they display **enhanced resistance** to extended-spectrum cephalosporins **without canonical ARG expansion**, implying alternative resistance mechanisms. Temporal data suggest **ecological succession** and persistence within the closed ISS habitat, underscoring the need for continuous surveillance and harmonized protocols.

Key findings

- **Phylogenomics & population structure:** Spaceborne isolates cluster into a **ISS-specific clade**, separated by defined **GWAS-linked** variants (≥175 genes; >200 SNPs/indels).
- **Functional enrichment:**
  - **Stress defenses:** methionine sulfoxide reductases; toxin–antitoxin (RelBE); osmoprotection.
  - **DNA repair: UmuC, RecF** and related pathways potentially countering radiation/oxidative stress.
  - **Metal handling:** siderophore uptake (**FhuE**), **arsenate reductase**.
- **Drug response:** Increased **cephalosporin resistance** without clear expansion of classic β-lactamases—points to **cell envelope remodeling, e ux, or regulatory rewiring**.
- **Ecology:** Rising relative abundance across missions suggests **adaptation/persistence** in spacecraft microbiomes.

Knowledge gaps

- **Causality:** Which **flight-specific variables** (microgravity, radiation spectra, humidity, cleaning chemistries) most strongly drive adaptation?
- **Mechanisms of resistance:** Structural/biophysical basis for **cephalosporin tolerance** absent canonical ARG changes.
- **Transferability:** Potential for **HGT** within habitat microbiomes and **reversion** dynamics after return to 1g.

Consensus or disagreement

- **Consensus:** Space habitats can select for **stress-tolerant lineages** with distinctive genomic signatures.
- **Debate:** Extent to which **microgravity vs. closed-system ecology** governs the observed phenotypes.

Actionable insights

- **Surveillance design:** Pair **in-flight omics** with **onboard 1g controls (centrifuge)** to isolate gravity effects; maintain **strict hardware/media parity** to remove confounders.
- **Antimicrobial stewardship:** Screen ISS isolates with **mechanism-focused assays** (outer membrane permeability, e ux activity) rather than relying solely on ARG catalogs.
- **Habitat hygiene:** Tune **cleaning regimens** and environmental parameters (humidity, surfaces) to disrupt persistence.

Recommended next steps

1. **Functional validation:** CRISPRi/knockouts of ISS-linked genes (e.g., **UmuC, FhuE, RelBE**) to test fitness in **low-shear bioreactors** and radiation analogs.
2. **Biophysics:** Measure **OM porins, LPS architecture, and envelope stiffness**; quantify **e ux kinetics** under altered shear.
3. **Community dynamics:** Longitudinal co-culture with **human-associated species** to probe **competition/HGT** under habitat-relevant stresses.

N. **Countermeasures:** Evaluate **non-traditional adjuvants** (membrane permeabilizers, ionophore combinations) against ISS isolates.

Relevant sections

- Comparative genomics and **GWAS** of ISS vs. clinical isolates;
- Functional enrichments (stress, DNA repair, metals);
- **AST** profiles to extended-spectrum cephalosporins;
- Temporal **abundance trends** across missions.

Context

Papers used:

- *Acinetobacter pittii adapts to space environments with multidrug resistance* (Tierney et al., Microbiome, 2022)
- *Bacterial Genome Sequences from International Space Station Isolates* (Simpson et al., Microbiology Resource Announcements, 2021)