

DPC 2026 - Freiburg

Distangling contaminants from true intratumoural microbial signals in pancreatic ductal adenocarcinoma – A benchmarking approach

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Intratumor Microbiome

Background

- PDAC tumors harbor their own bacteria community,
- New biomarkers for diagnoses, prognoses and therapy.

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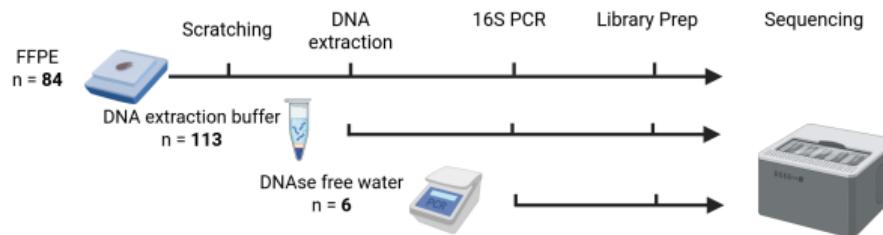
Cubersome!!

- Low bio-mass samples, prone to contamination.

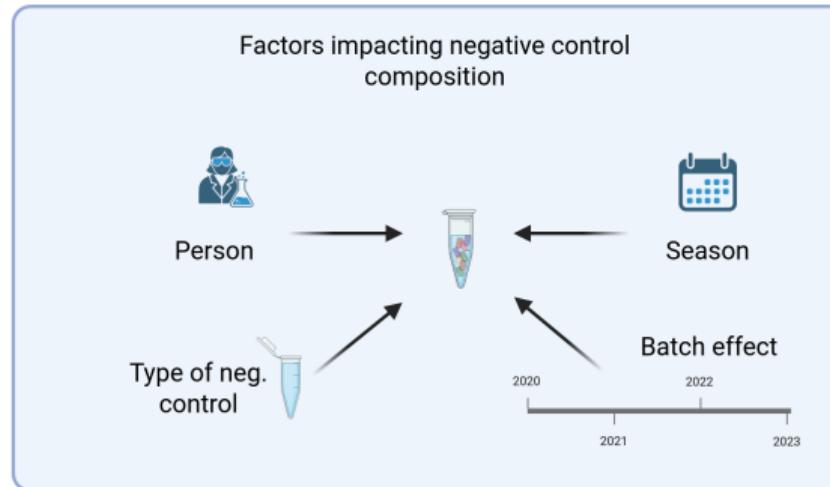
Section 1

Negative Control Survey in the Lab

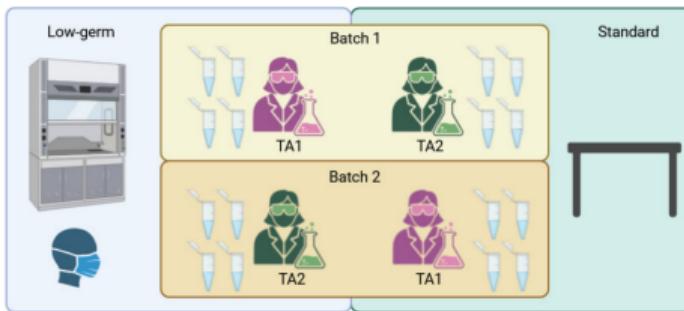
Negative Sample Collection



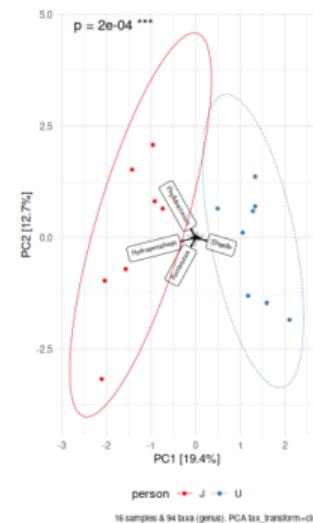
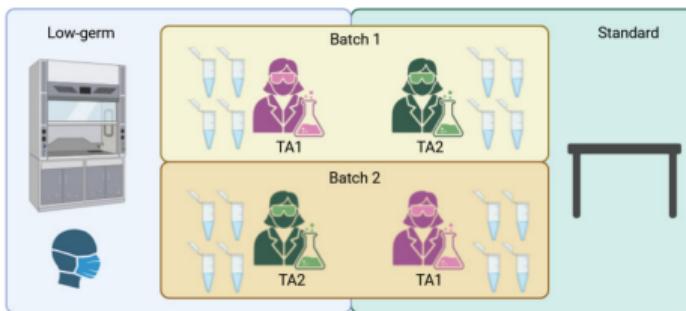
- In total 203 negative control samples over 4 years
 - 113 buffer controls,
 - 84 paraffin controls,
 - 6 PCR control.



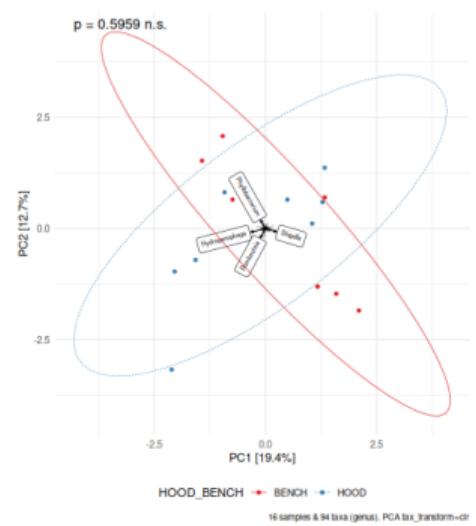
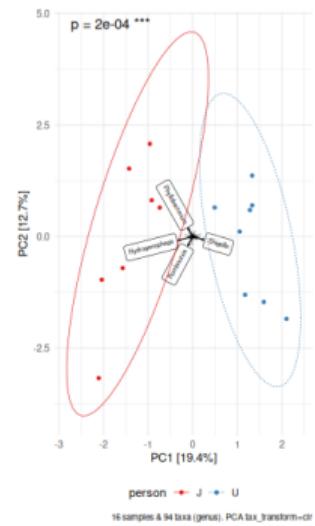
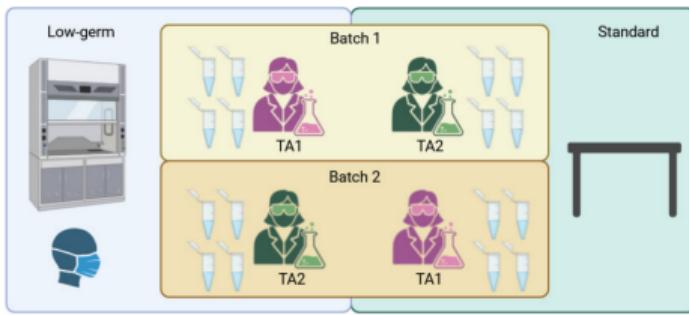
Example



Example



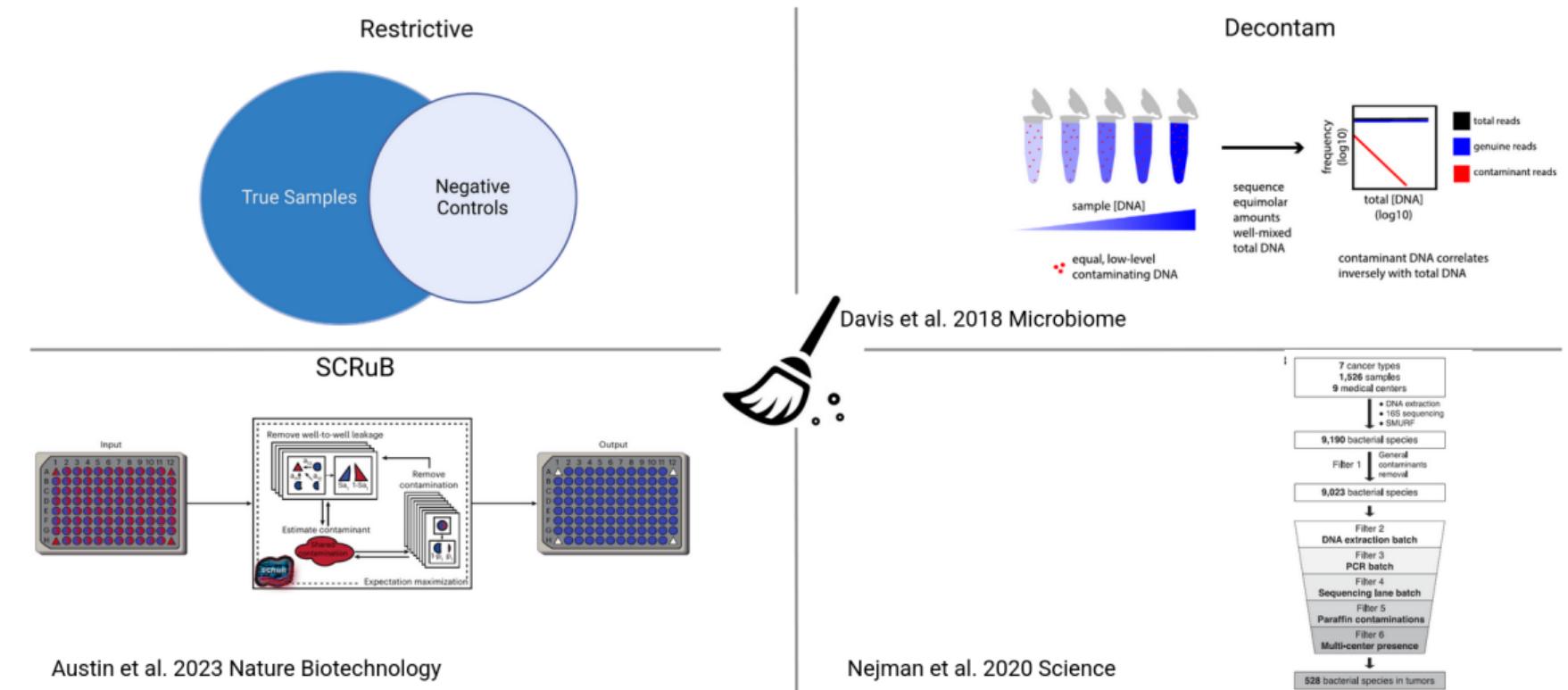
Example



Section 2

Assessment of Decontamination Methods and Intratumor Microbiome
in PDAC

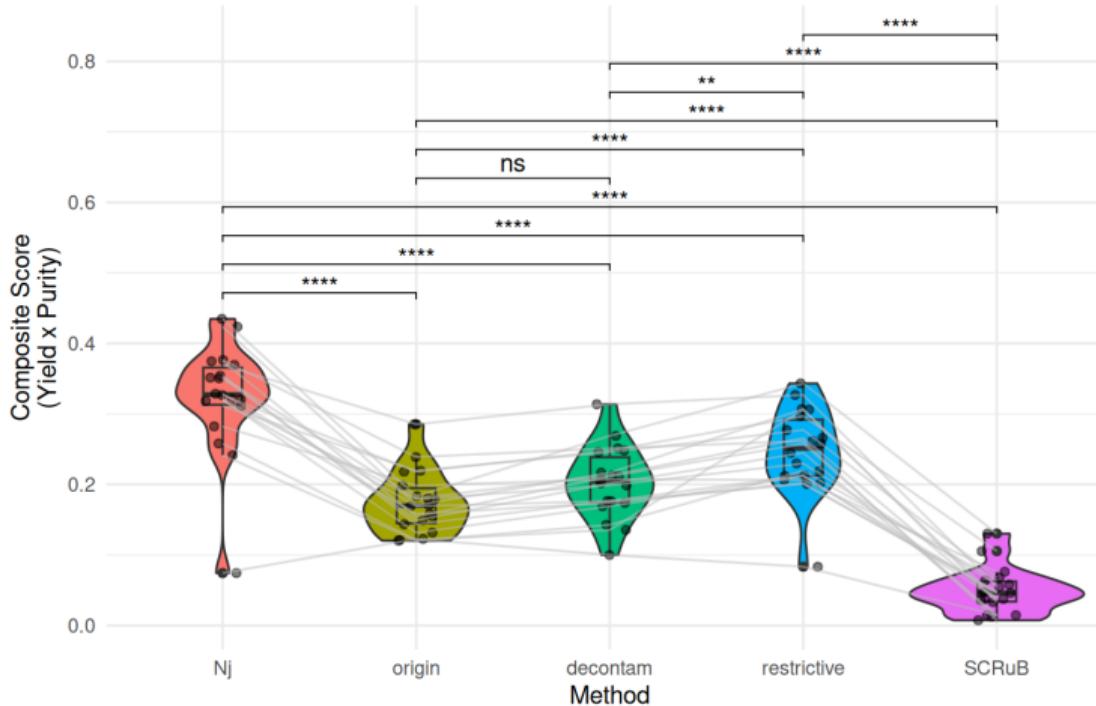
Decontamination Strategies



Assessment of Decontamination Approach

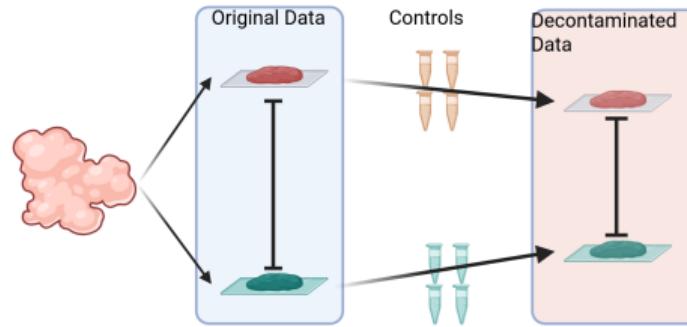
Comparison of Decontamination Methods - LMM

Metric: Penalized Clean Yield (Higher is Better)



Involving Technical Replica

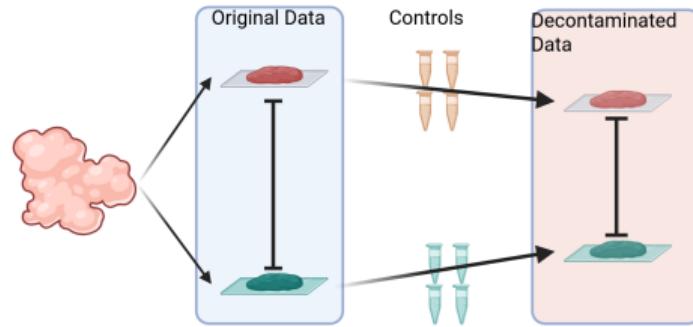
Utilize Replica for Assessment



- 10 PDAC sample, each with 2 replica
- Aichison distance with paired Wilcox test.

Involving Technical Replica

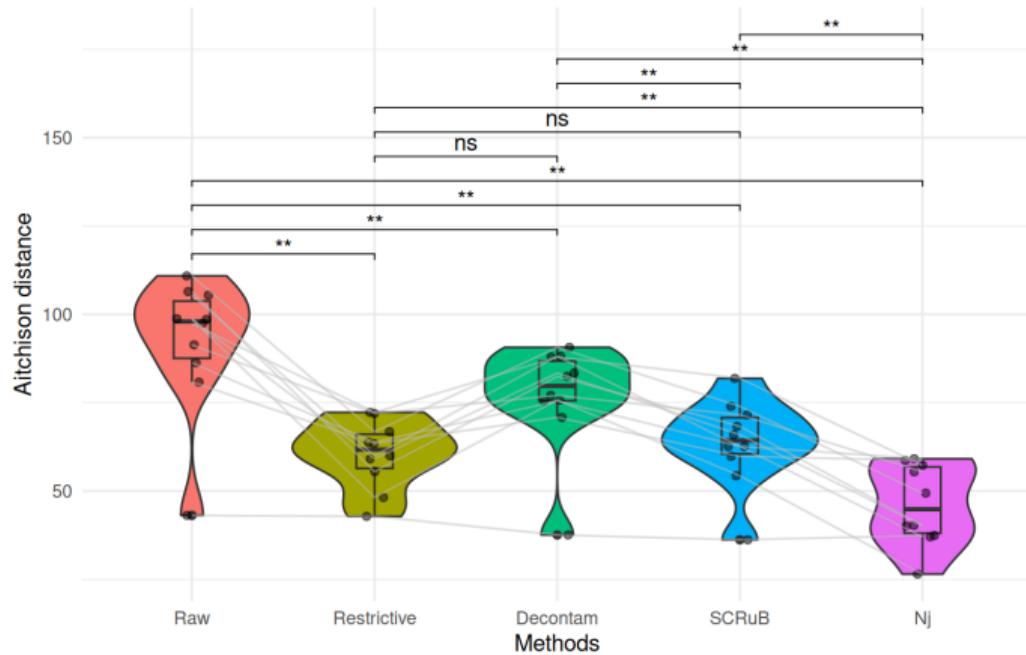
Utilize Replica for Assessment



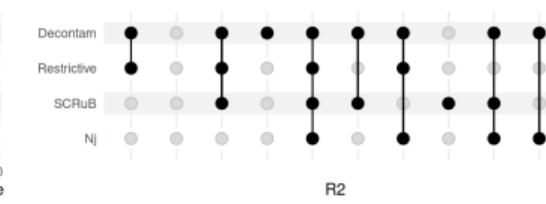
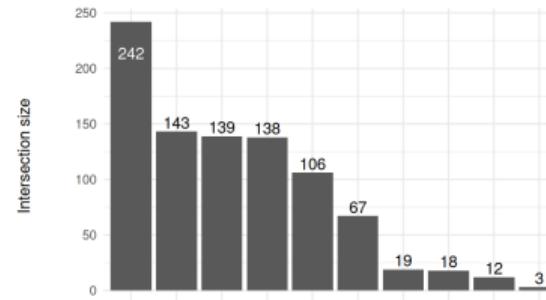
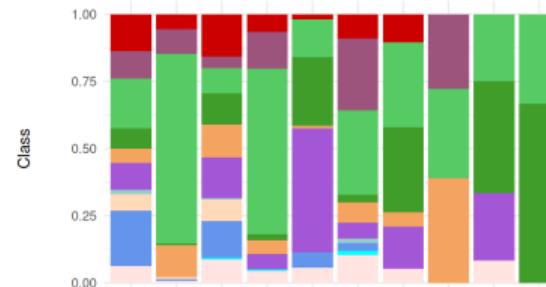
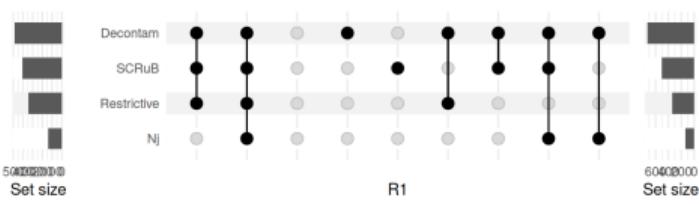
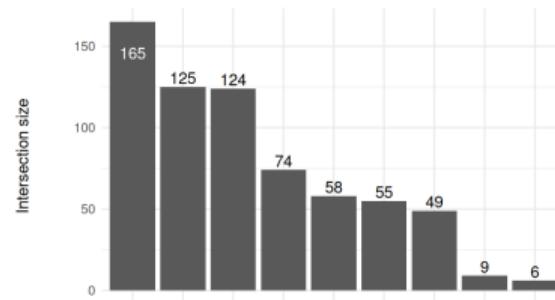
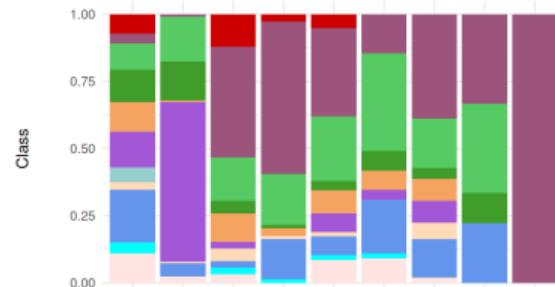
- 10 PDAC sample, each with 2 replica
- Aitchison distance with paired Wilcox test.

Paired Wilcox test

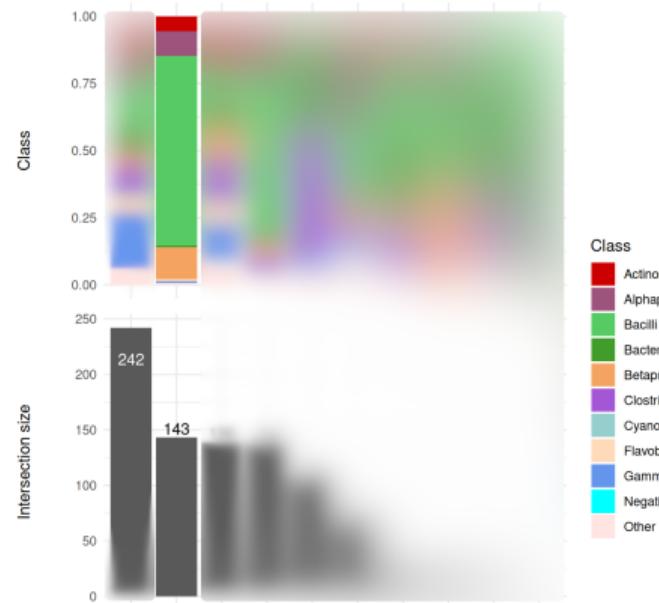
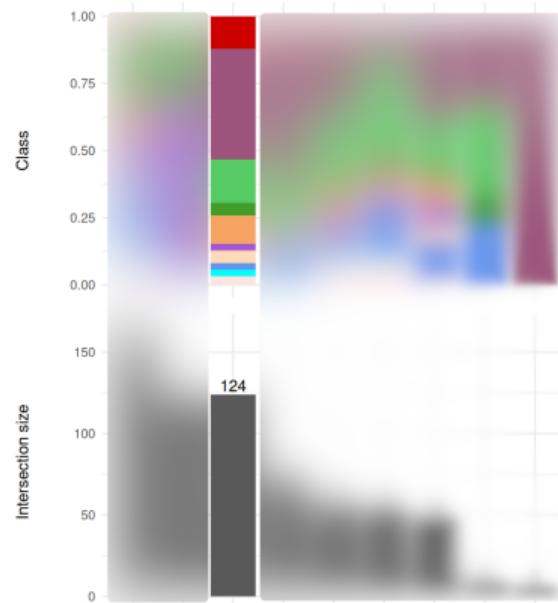
The lower the better



Overlap - Microbial profile of Mice-model PDAC

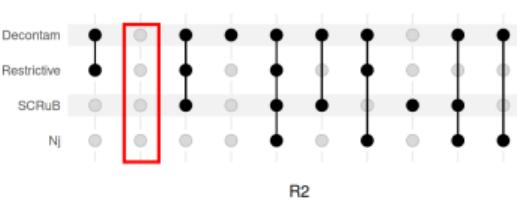
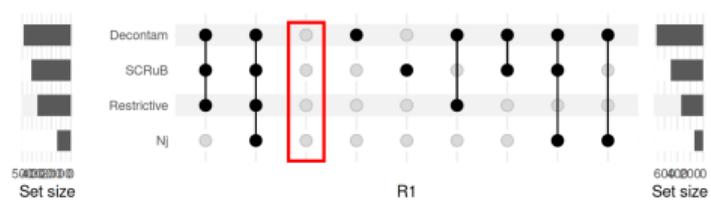


Overlap - Microbial profile of Mice-model PDAC

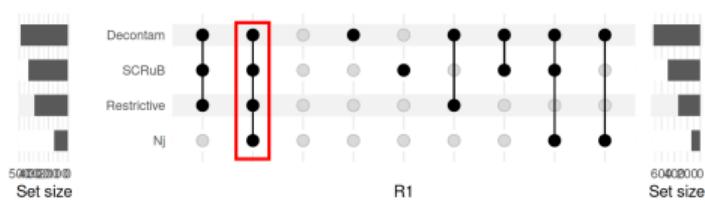
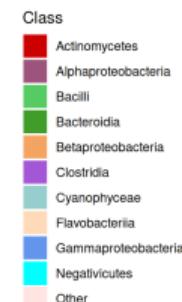
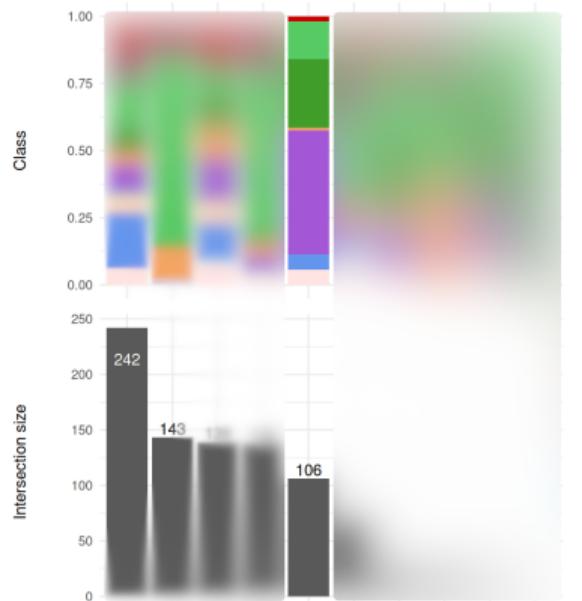
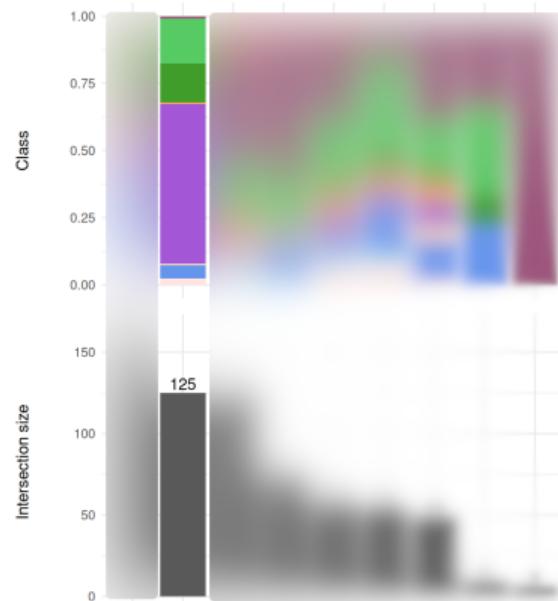


Class

- Actinomycetes
- Alphaproteobacteria
- Bacilli
- Bacteroidia
- Betaproteobacteria
- Clostridia
- Cyanophyceae
- Flavobacteriia
- Gammaproteobacteria
- Negativicutes
- Other



Overlap - Microbial profile of Mice-model PDAC



Conclusions

Decontamination Methods

- Negative control samples are essential to avoid spurious taxa.
- Each batch has its own contaminant profile.
- In our study, thoroughly removing contaminant such as Nejman et al. procedure outperforms others.

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- Negative control samples are essential to avoid spurious taxa.
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Intratumor microbiome in PDAC

- Technical replica and various decontamination methods with proper negative controls could yield a reliable set of intratumor microbiota.
- Most of identified taxa are well-known gut microbiota.

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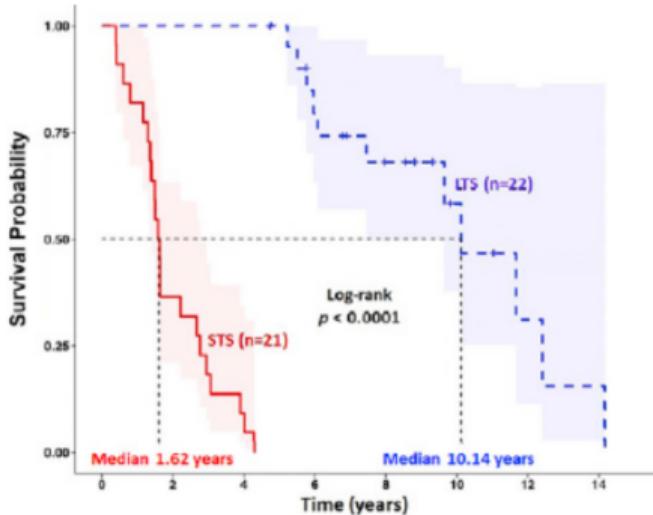
Section 3

Backup Slides

Contamination in Microbiome Study

Cell

Tumor Microbiome Diversity and Composition Influence Pancreatic Cancer Outcomes



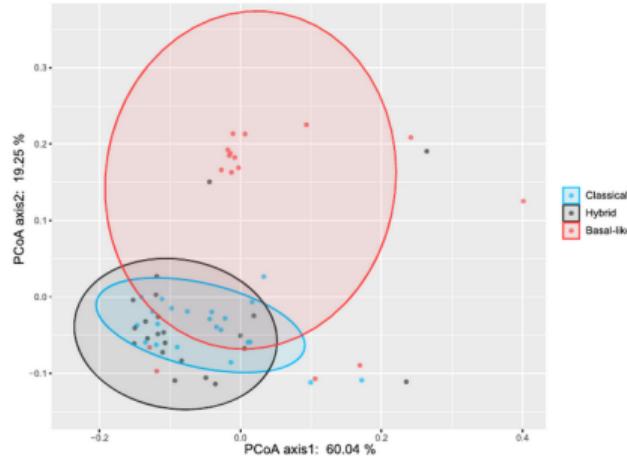
Riquelme et al. Cell 2019

Key taxa: Streptomyces, Pseudoxanthomonas, Saccharopolyspora

Article | Open access | Published: 31 August 2021

Tumor microbiome contributes to an aggressive phenotype in the basal-like subtype of pancreatic cancer

Wei Guo, Yuchao Zhang, Shiwei Guo, Zi Mei, Huiping Liao, Hang Dong, Kai Wu, Haocheng Ye, Yuhang Zhang, Yufei Zhu, Jingyu Lang, Landian Hu, Gang Jin & Xiangyin Kong



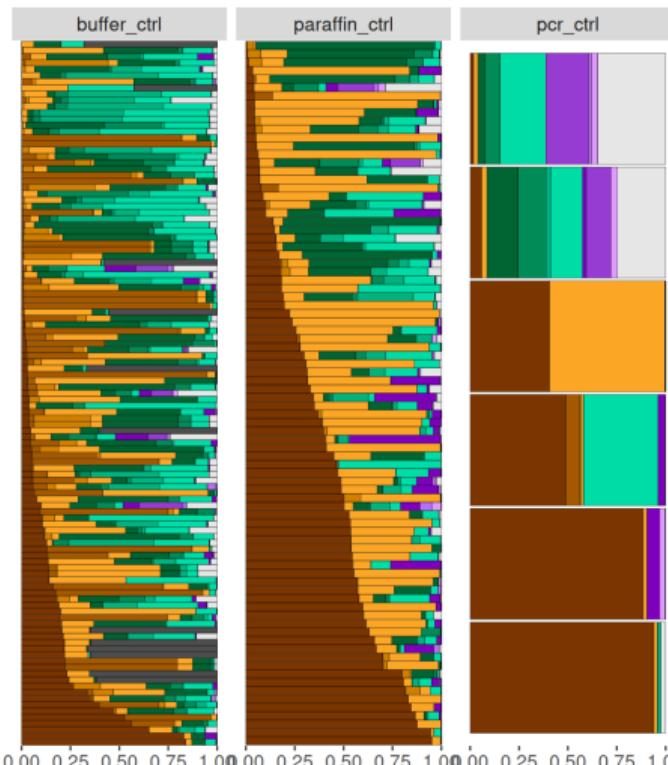
Guo Communication biology 2021

Key taxa: Acinetobacter, Pseudomonas, Sphingopyxis

Bacterial Composition

Composition of NCT Samples

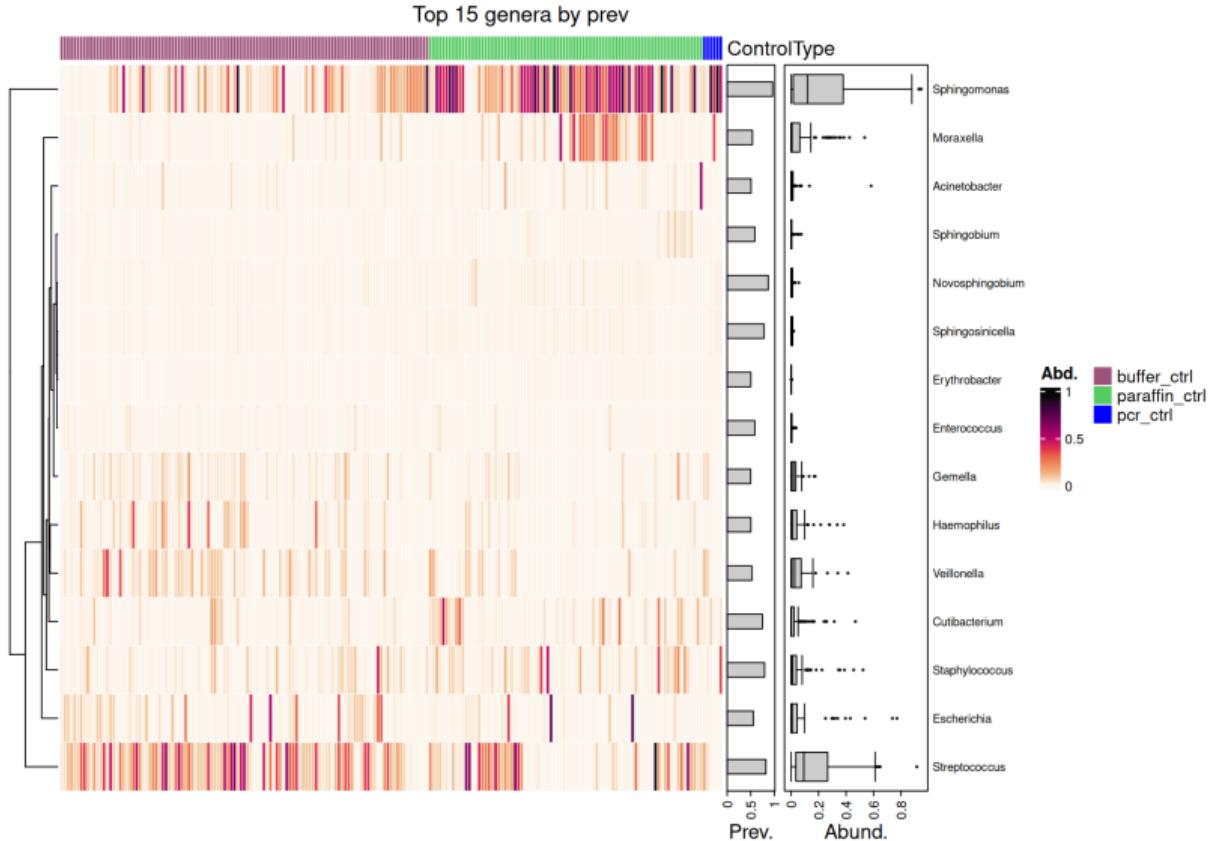
Order by sum



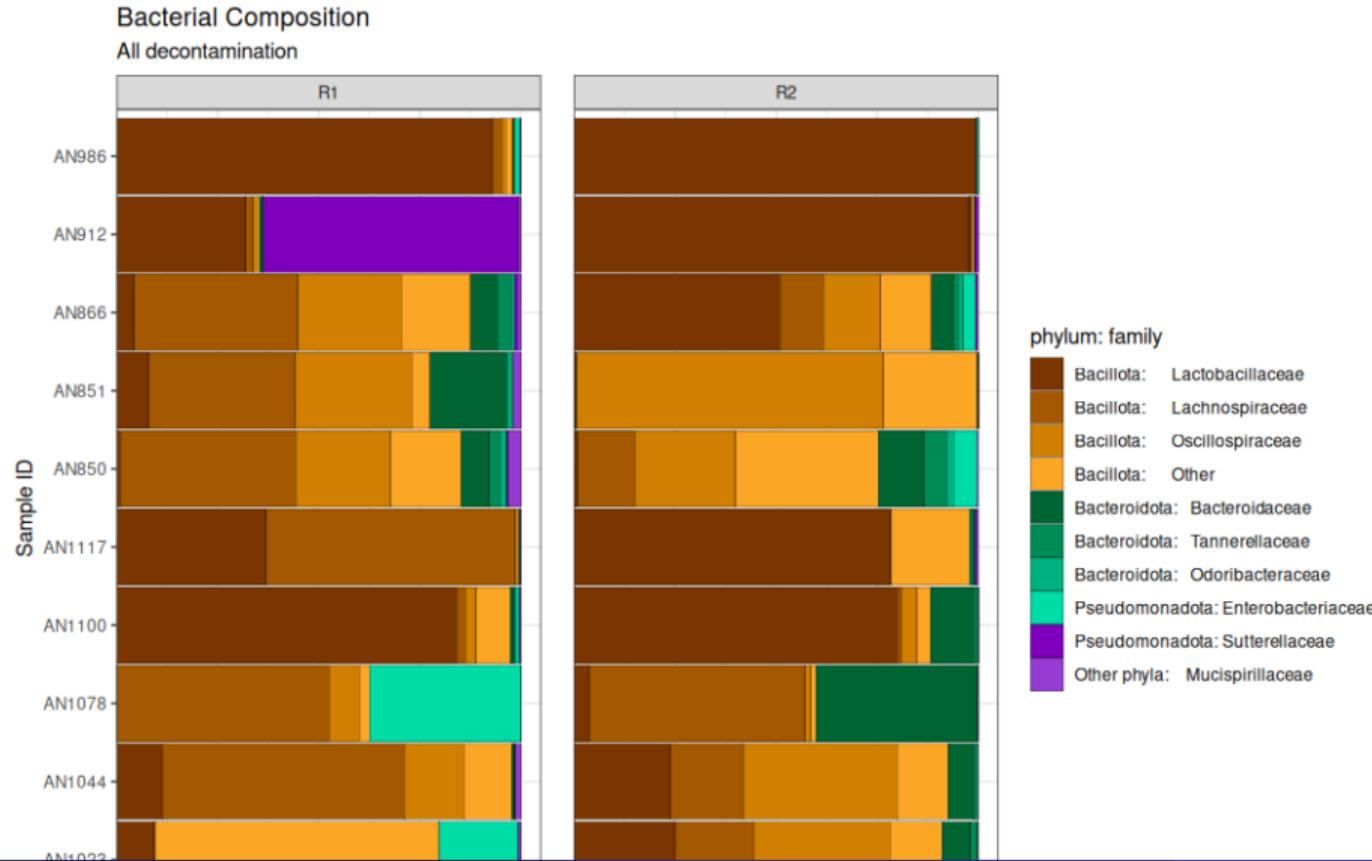
phylum: family

- Pseudomonadota: Sphingomonadaceae
- Pseudomonadota: Burkholderiaceae
- Pseudomonadota: Pasteurellaceae
- Pseudomonadota: Other
- Bacillota: Streptococcaceae
- Bacillota: Veillonellaceae
- Bacillota: Peptoniphilaceae
- Bacillota: Other
- Actinomycetota: Propionibacteriaceae
- Actinomycetota: Actinomycetaceae
- Actinomycetota: Micrococcaceae
- Actinomycetota: Other
- Other phyla: Bacteria_unclassified_superkingdom
- Other phyla: Candidatus Babeliaceae
- Other phyla: Deltaproteobacteria_unclassified_class
- Other phyla: Other

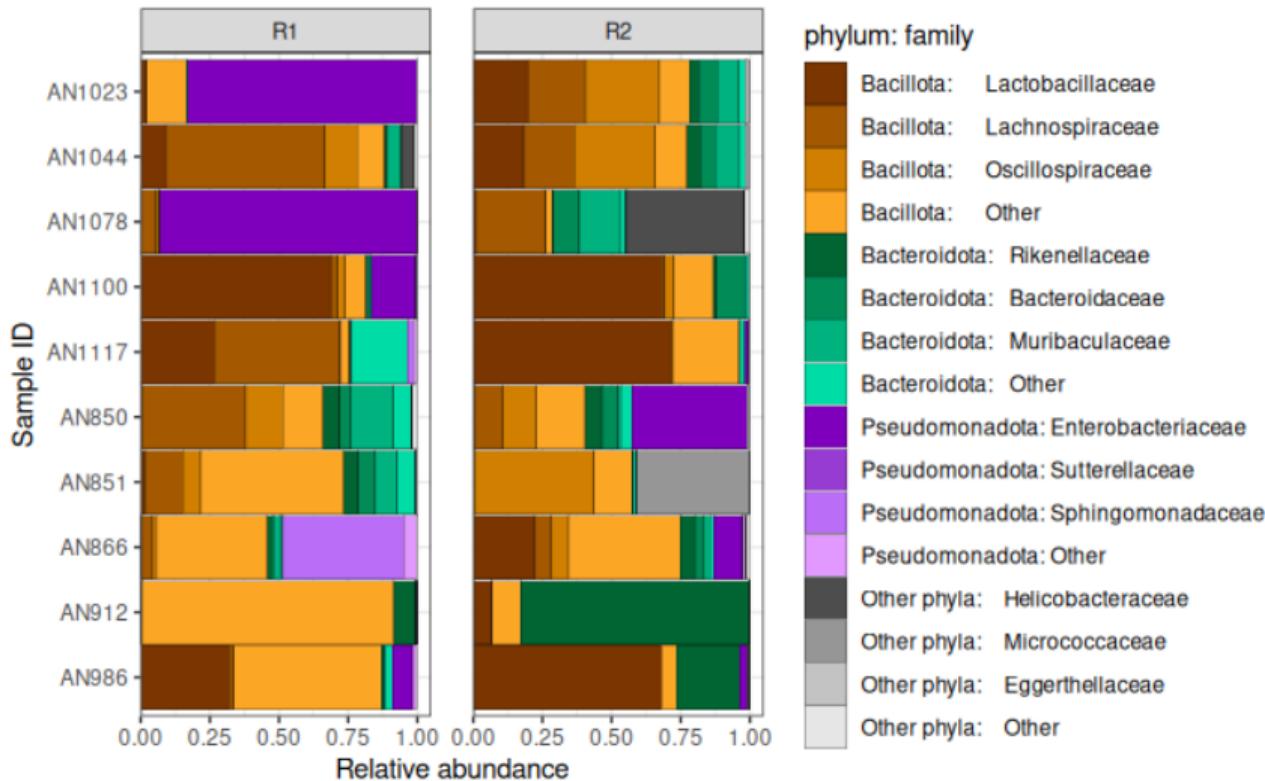
Heatmap from Negative Controls



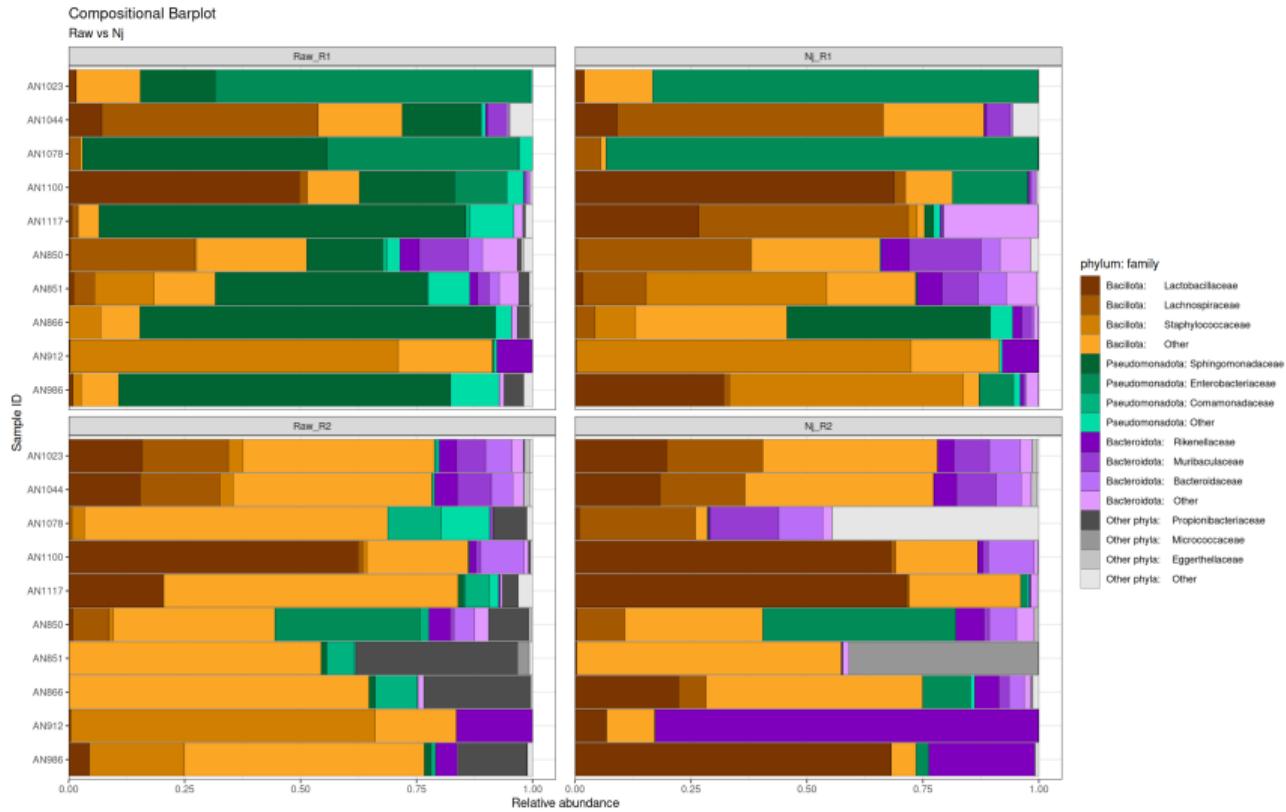
Core microbiome - All decontamination method - phylum: family



Core microbiome after Nj approach



Core microbiome after Nj approach



Assessment of Decontamination Approach

- **Yield:**

$$\frac{\# \text{ putative true taxa} \notin \text{NCT}}{\# \text{ observed species}}$$
 - **Purity:**

$$\frac{\# \text{ putative true taxa} \notin \text{NCT}}{\# \text{ putative contaminants}}$$
 - **Composite Score =**

$$\text{Yield} \times \text{Purity}$$

