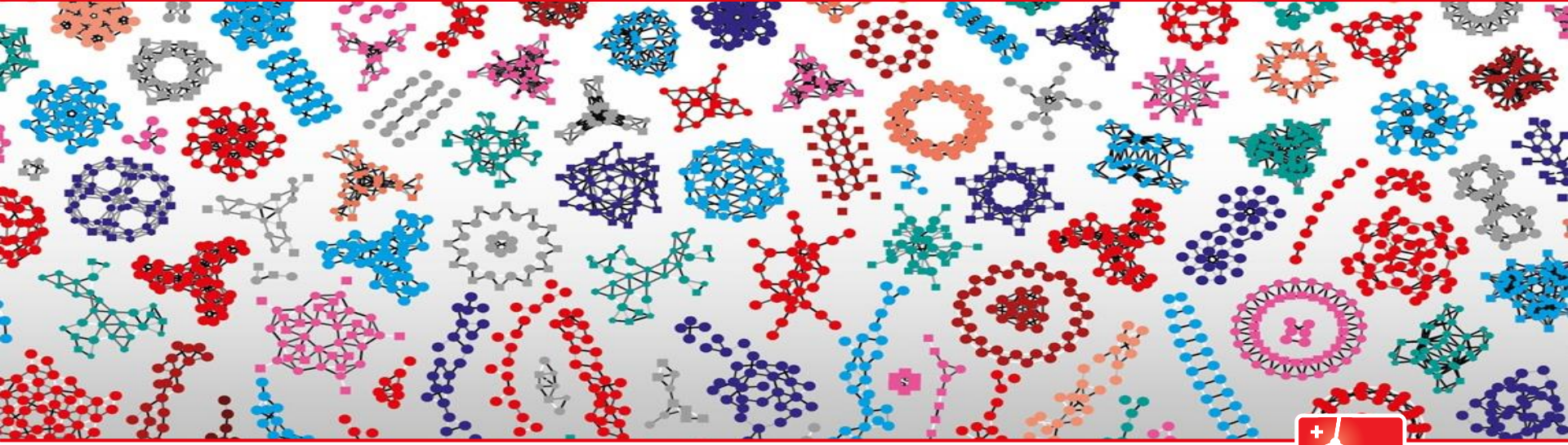


Swiss Institute of Bioinformatics

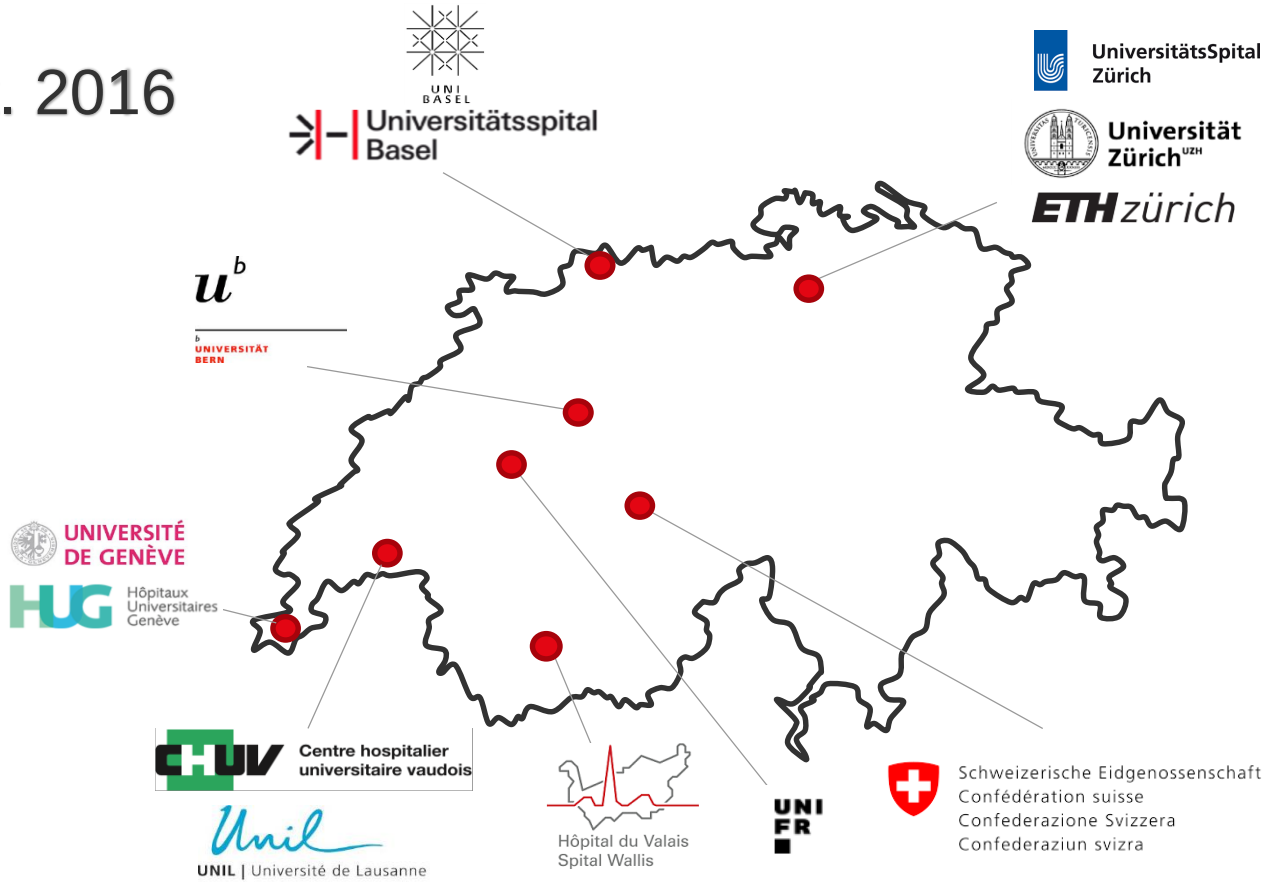
Viral metagenomics in the clinical realm: lessons learned from a Swiss-wide ring trial

International Conference on Clinical Metagenomics (ICCMg)

Dr Aitana Lebrand | Geneva, 17 October 2019

NGS microbes typing and characterization WG

- Since Sept. 2016

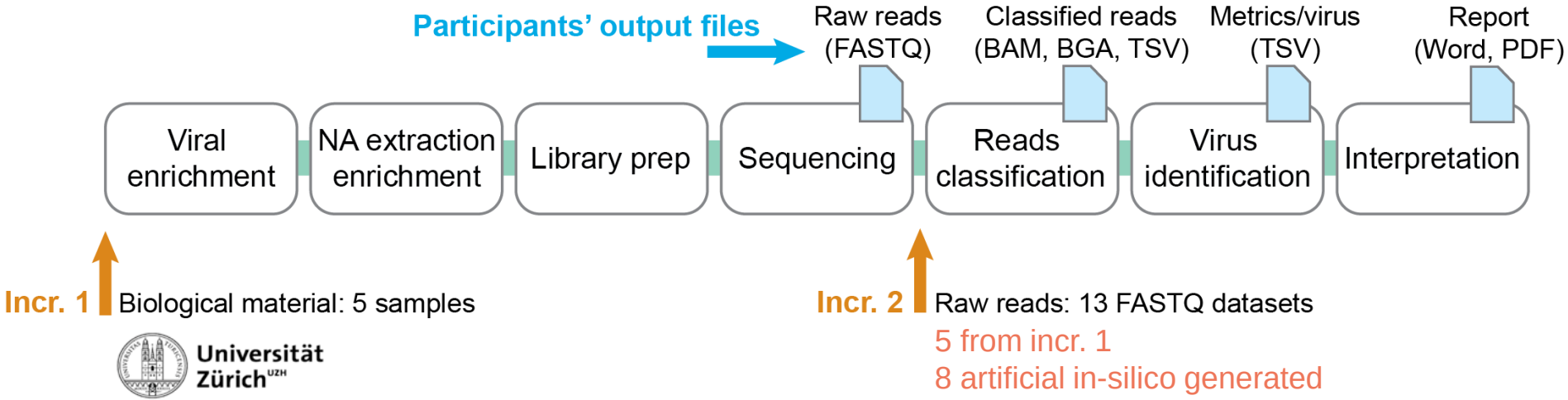


Need for harmonization?

Survey shows different pipelines are used in each clinical laboratory

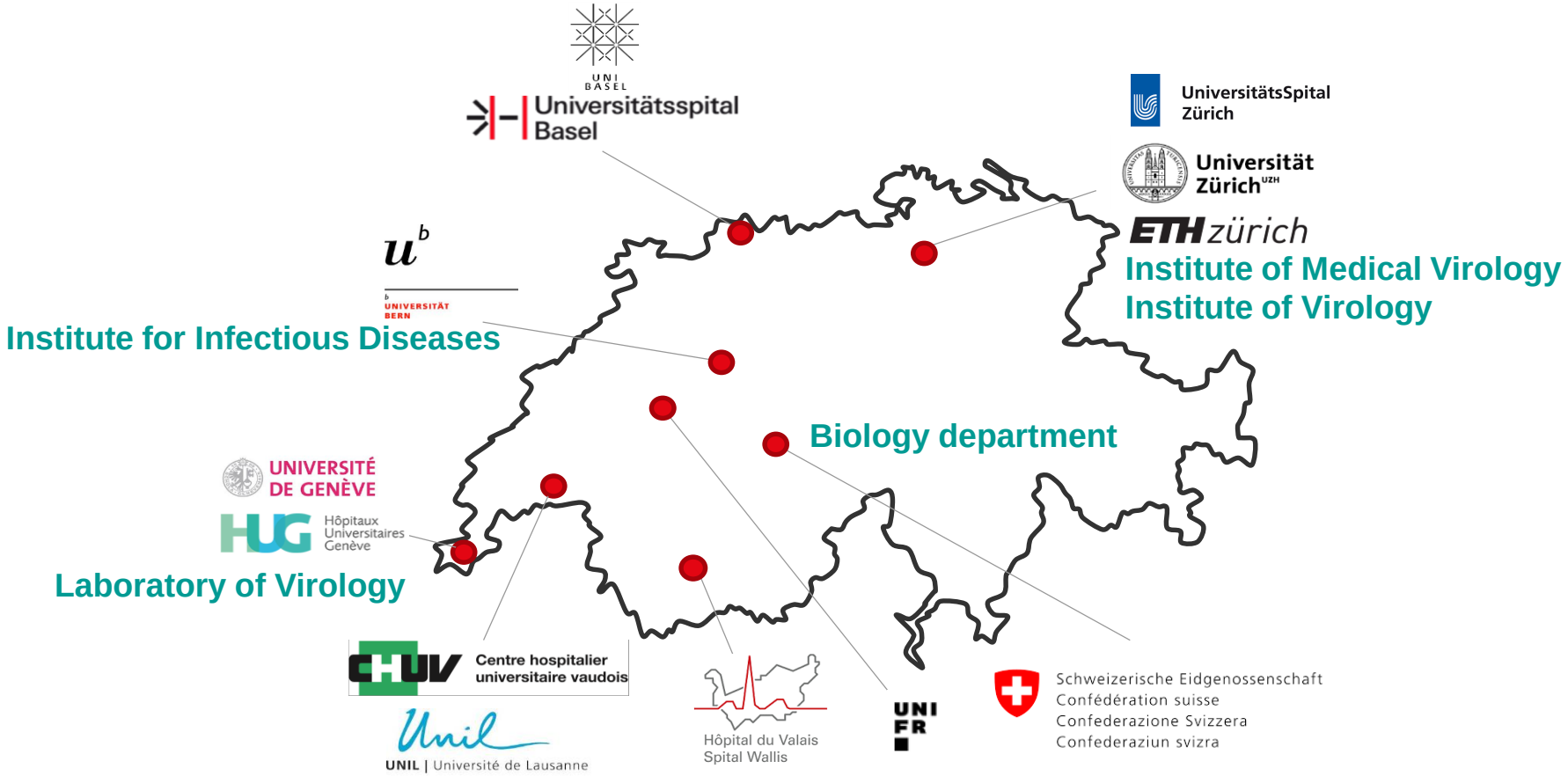
- Would they agree on interpretation if starting from the same sample?
- Is there a need for harmonizing NGS practices
  (i.e. same answer, independent of workflow used)?
- Organize ring trials as quality controls (end 2017 - 2018)

Ring trial with two increments: ground truth known



Universität Zürich[UZH]

Ring trial participants: 5 labs, 8 pipelines in total



Evaluation of pipeline performance

- Identified viruses at the species level, per pipeline, per sample ➔ TP, FP, FN
- For the negative control, false positives were mapped at the family level
- Sensitivity, precision, F1

Nomenclature matters

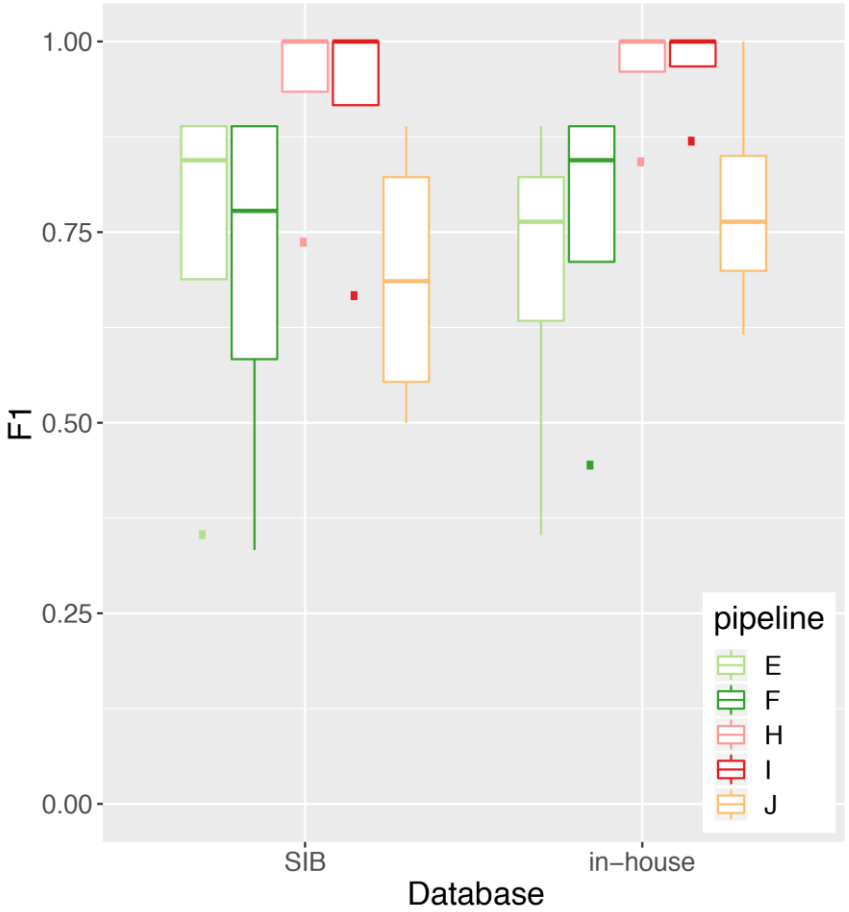
- **Problem:** the following names
  - *human adenovirus A*
  - *Adenovirus 12*
  - *Mastadenovirus type 31*

  all refer to the **same** species

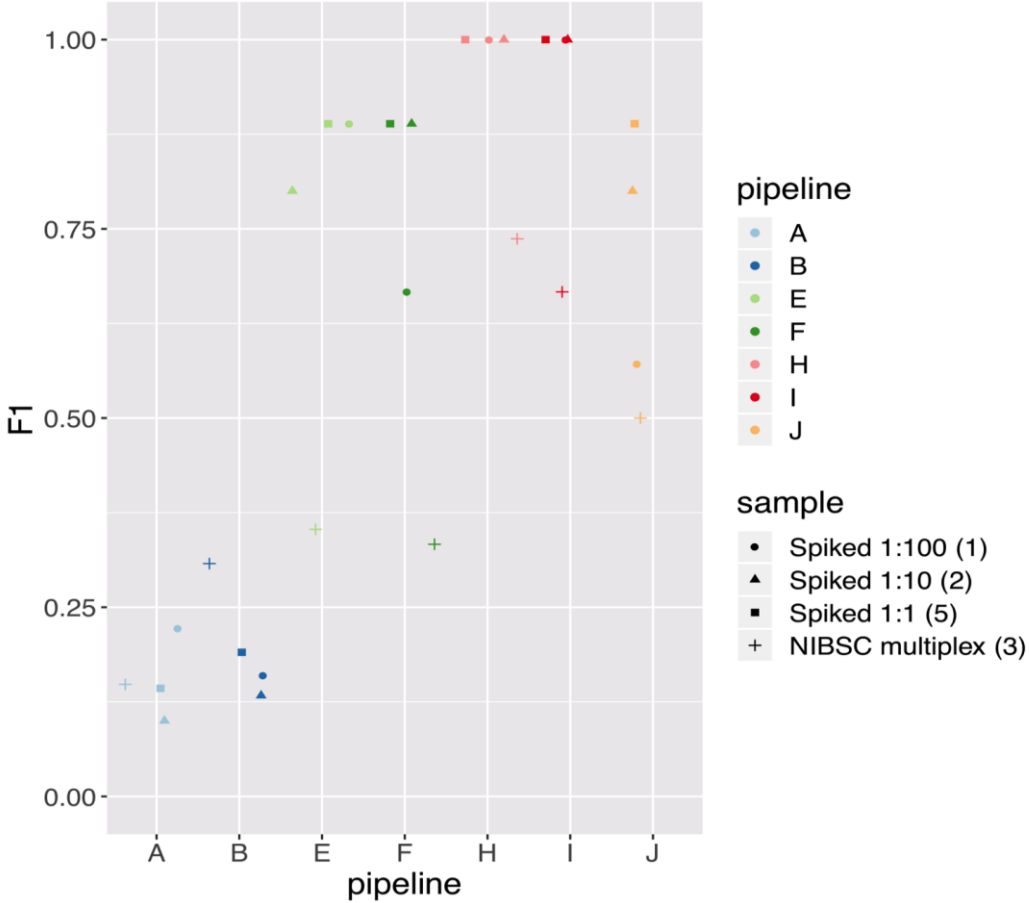
  This is the *rule*, not an exception...

- **Solution :**
  - Define a resolution level for the trial (e.g. species)
  - Map all possible names at that resolution, e.g.
    /human (mast)?adenovirus (type)?(A|12|31)\b/i
    → HAdV-A

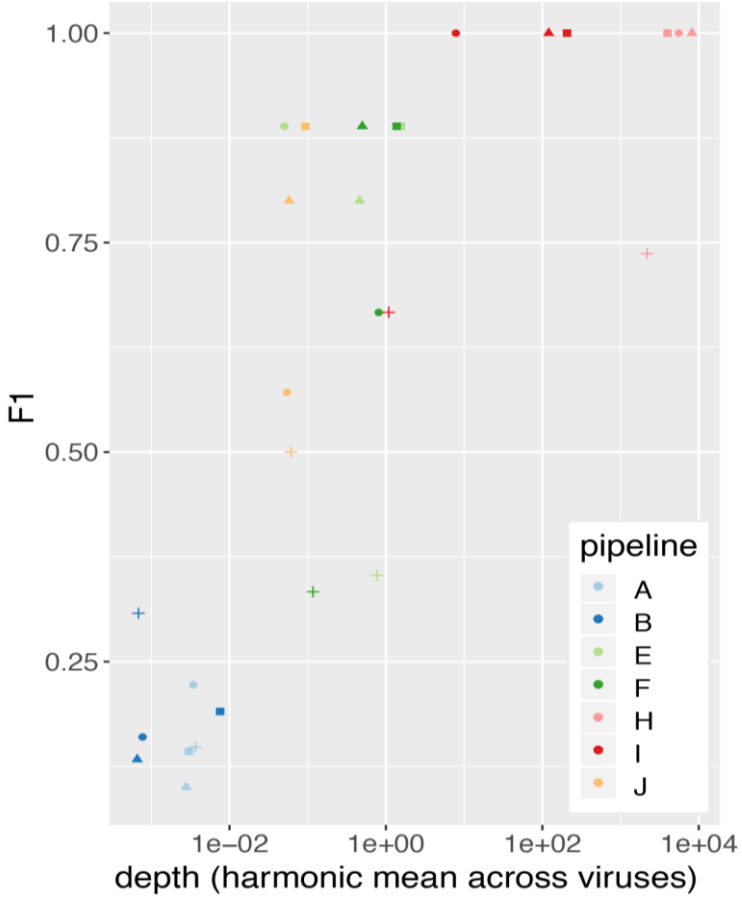
Impact of database (incr-1)



F1 varies strongly across pipelines (incr-1)



Coverage helps… up to a point (incr-1)

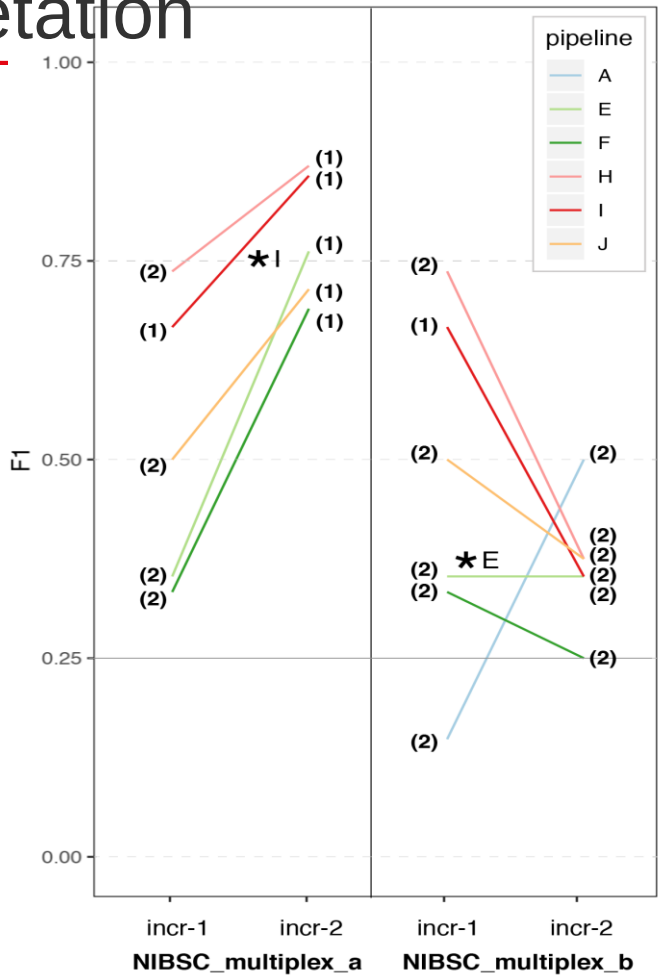


sample

- Spiked 1:100 (1)
- Spiked 1:10 (2)
- Spiked 1:1 (5)
- \+ NIBSC multiplex (3)

Impact of sample prep and interpretation

- **Same sample present twice** (sequenced by 2 centers)
- In incr-2, all started with same FASTQ
  => performance is poor for sample “b”
  => sample preparation has an impact
- In incr-2, sample “a” was provided by pipeline I (red). Its results improved!
  => impact of human review for reproducibility of results



More information

- **Read more details in our publication**
  Junier *et al. Viral metagenomics in the clinical realm : Lessons learned from a Swiss-wide ring trial.*
  Genes, 2019, 10, 655; doi:10.3390/genes10090655

- **Download in-silico datasets (zenodo)**

Next step

Partner with ISO17043 certified organizations for production-level EQAs

Swiss Institute of Bioinformatics

Special thanks to the EQA Team
Dr Thomas Junier (SIB & EPFL)
Dr Michael Huber (Medical Virology, Uni Zh)

And to **the RT participants!**

Dr. Aitana Lebrand
SIB Clinical Bioinformatics
aitana.lebrand@sib.swiss