# Analysis of MBD-Seq data of Korean CLL patients:

## As an example of KOBIC Research Support Service

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kobic Korean Bioinformation Center

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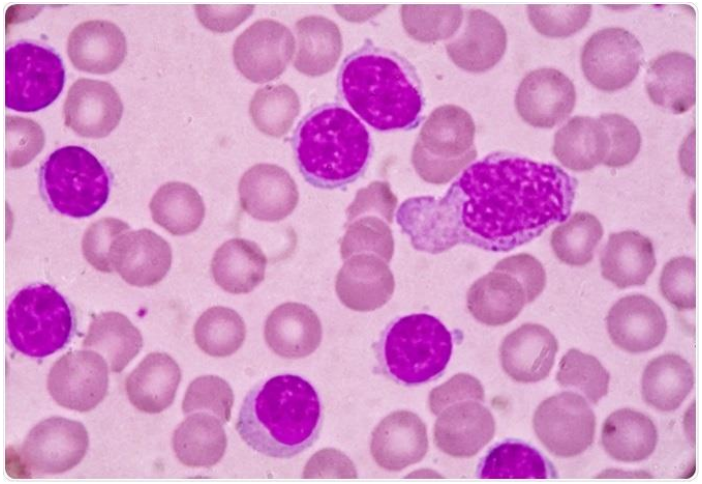
KRIBB Korea Research Institute of Bioscience & Biotechnology

# CLL (Chronic Lymphocytic Leukemia)



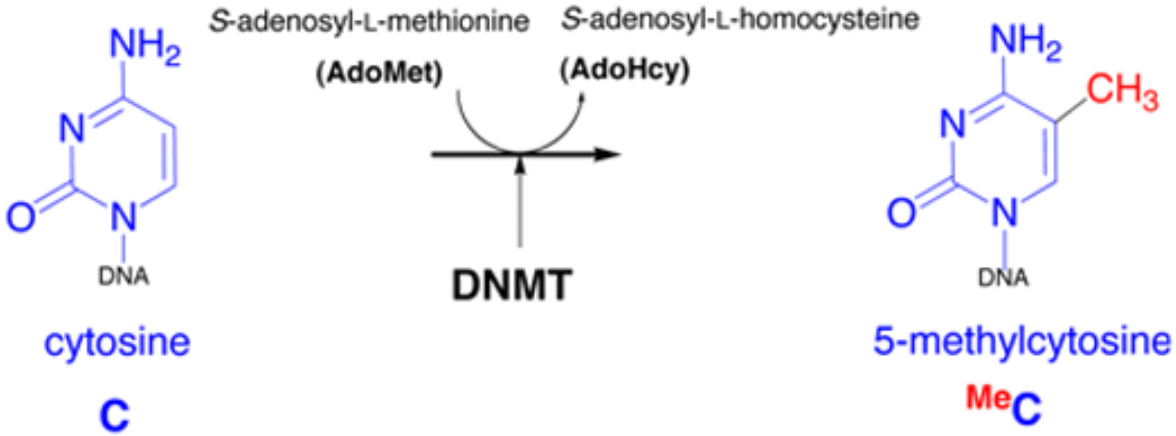
- CLL is a cancer of the blood; the bone marrow makes too many lymphocytes ⇨ the buildup of premature B-cell lymphocytes, which do not function well ⇨ crowd out healthy blood cells

- Ethnic differences in CLL

| | Incidence rate (per 100,000 person-years) | Median age of initial diagnosis |
|---|---|---|
| Western countries | High (3.83) | Late (70) |
| Korea | Low (0.04) | Early (61) |

# DNA methylation

- DNA methylation refers to the addition of a methyl group to the cytosine ring.

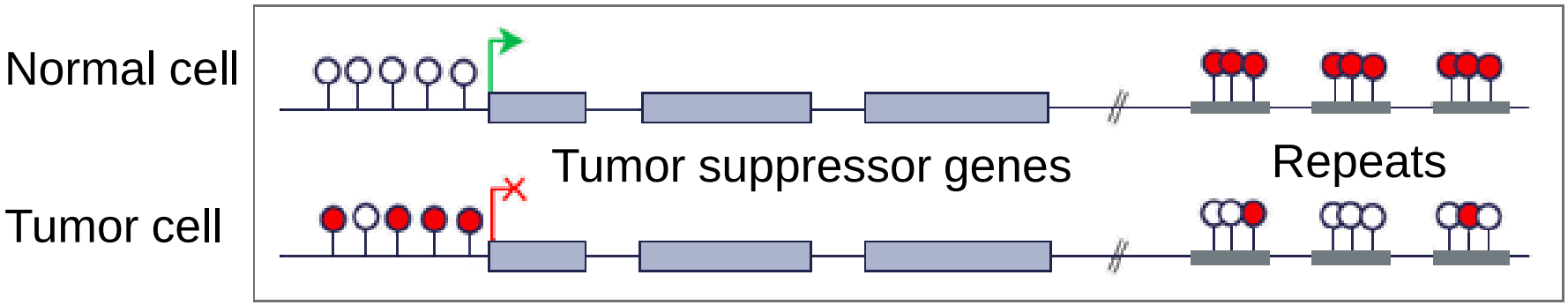



- DNA methylation controls gene transcription by changing chromatin structure and, in turn, influences the affinity and accessibility of TFBSs.

- In normal cells, DNA methylation plays a useful role in embryonic development, X-chromosome inactivation, genomic imprinting, maintaining genome integrity (by repressing transcription at repeated sequences), and tissue-specific gene expression.

# Aberrant DNA methylation in cancer

- A simplified view

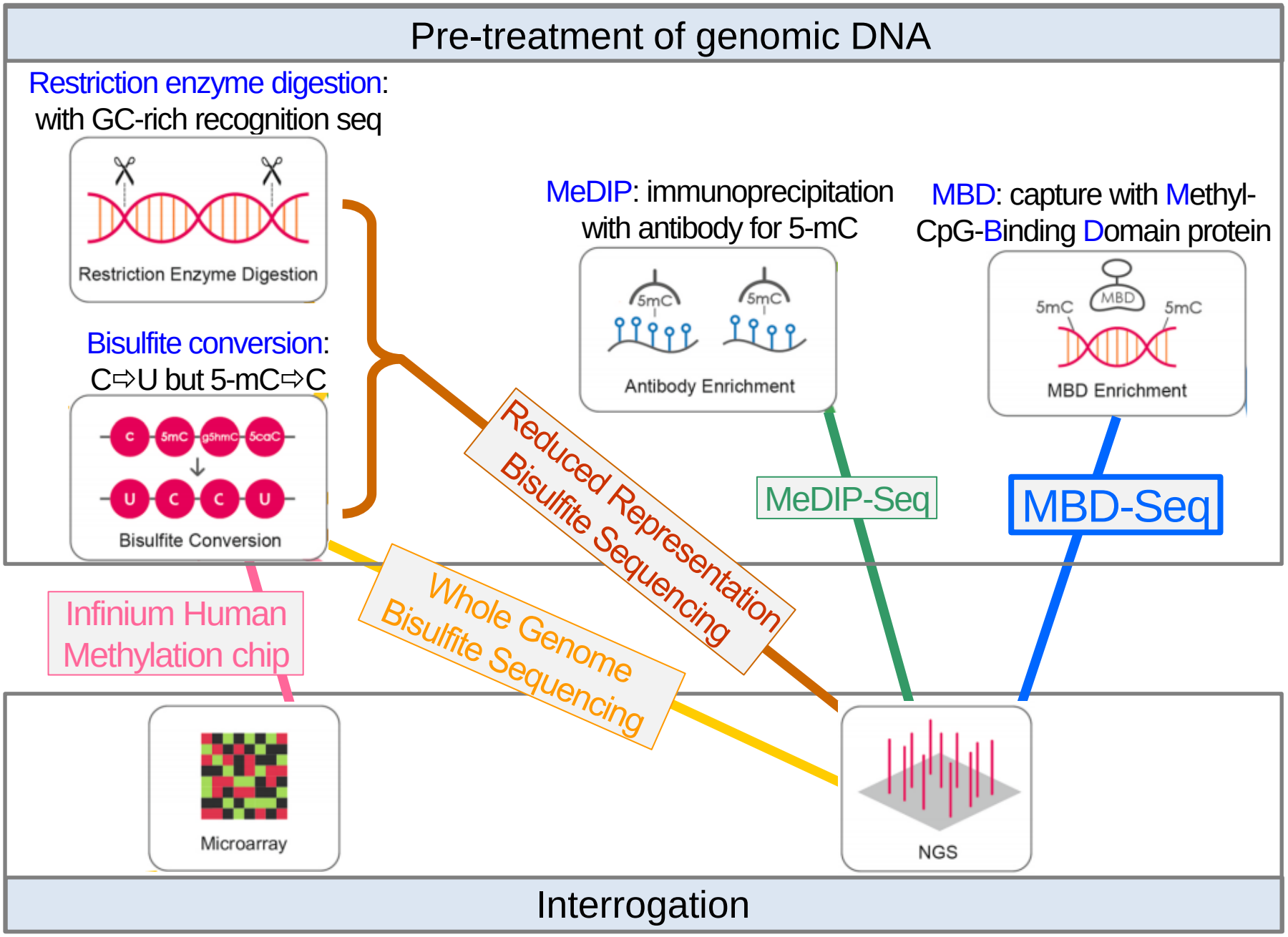



↑Hyper-methylation in TSG promoter
⇨ TSG silencing

↓Hypo-methylation in repeats
⇨ genomic instability

- The association between DNA methylation and gene expression is much more ambiguous and controversial
  - The role of DNA methylation in non-promoter regions (inter-genic, intra-genic)
  - The role of DNA methylation in noncoding RNA (miRNA, lncRNA) promoters
  - The role of DNA methylation in pseudogenes
  - ...

# Platforms for genome-wide DNA methylation profiling



# Three routes for genome data analysis

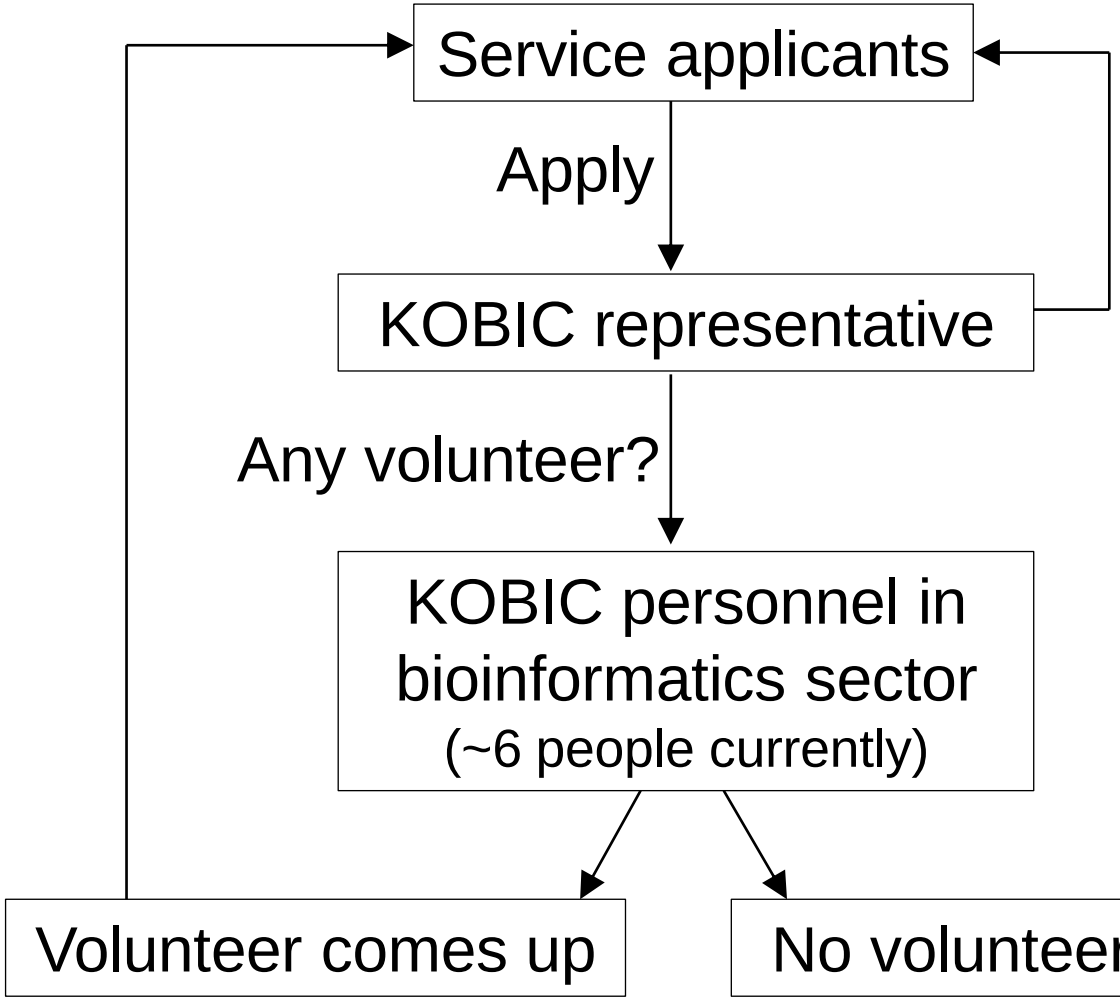
- In-house
  - Best, but works for large labs only
- Collaboration with bioinformatics experts
  - Finding a reliable collaborator is not easy
  - There is a luck factor (collaboration with a prominent bioinformatics group, but the actual work done by a novice graduate student)
  - There is a potential credit dispute
    - (Extreme) view from biology: You are just support personnel
    - (Extreme) view from bioinformatics: I am the one who magically pulled out science from your junky data
- Outsourcing to an NGS service company
  - Customer's perspective: OK to pay for sequencing. Resistant to pay extra for data analysis. Even with extra payment, not sure about full support until publishable results come out.
  - Company's perspective: Going beyond an automated analysis takes time and money. In-depth analysis may not be much of s profitable business model.



**We have KOBIC, a friendly neighborhood of Korean biologists**

# KOBIC Research Support Service

# Process




No

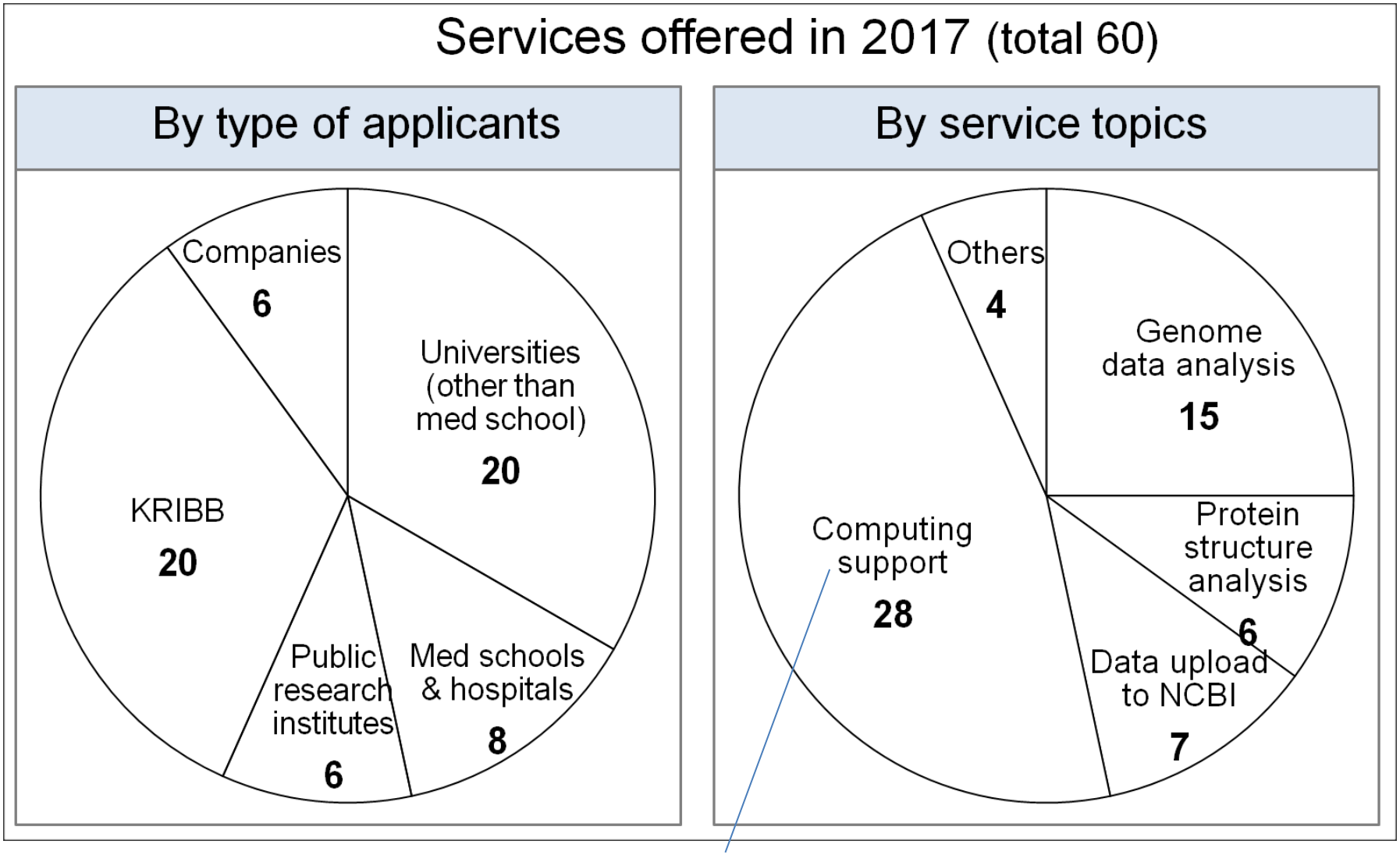
- When it is a full-blown long-term research project without a clear end-goal

- No expertise to the requested task
- Busy (everyone, always)

# Methods for the MBD-Seq data analysis

| Task | Software |
|---|---|
| Alignment | Bowtie2 |
| Differential methylation analysis | MEDIPS |
| Annotation of differentially methylated windows | ChIPseeker |
| GO/Pathway analysis | clusterProfiler |
| Network analysis | Cytoscape with BisoGenet and ReactomeFIViz apps (for retrieval of protein-protein and protein-DNA interaction data) |
| Gene-Disease relation analysis | DisGeNET |

# Service requests come in all varieties




Mostly about providing computer servers

(web server, DB server, servers for bioinformatics short courses)

# Conclusion and some thoughts

- Need for a change of perception for bioinformatics support
  - Perception as just a support ↔ yet sometimes the responsibility to get something useful out of data is put on the shoulders of bioinformaticians
  - Perception that bioinformatics does not cost a lot, or at least customer's emotional resistance (inkjet printer – ink cartridge scam)


Cheap


Expensive


- Need for appropriate price tag for bioinformatics support
  - Very hard to quote a price: all projects are different
- Should KOBIC start to commercialize the service?
  - Currently: Free of charge. We don't owe them anything. We may work at our own convenience.
  - Commercialization: An age-old internal discussion in KOBIC