Accessing QIAGEN OmicSoft Data using the R API

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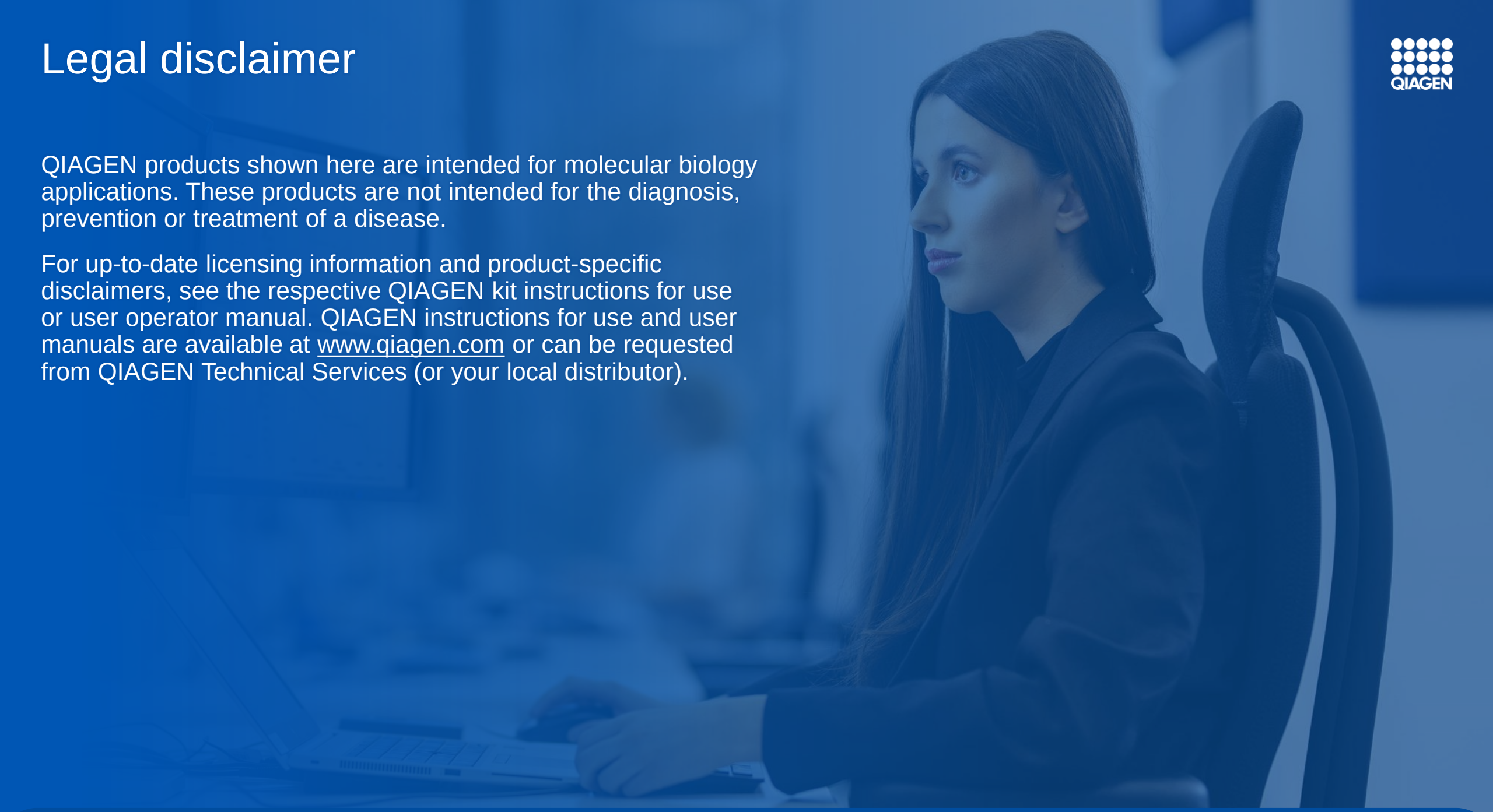
Legal disclaimer



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Agenda

Introduction to the QIAGEN OmicSoft dataset

- QIAGEN
- OmicSoft dataset
- Why detailed curation is essential for public data

Accessing Datasets from R example (Lung Cancer)

- Finding lung cancer datasets within the database
- Finding lung cancer datasets with a specific mutation in the database
- Finding lung cancer datasets involving a specific drug

Example Queries

- Identifying differentially expressed genes
- Accessing gene expression data
- Finding genes with correlated expression

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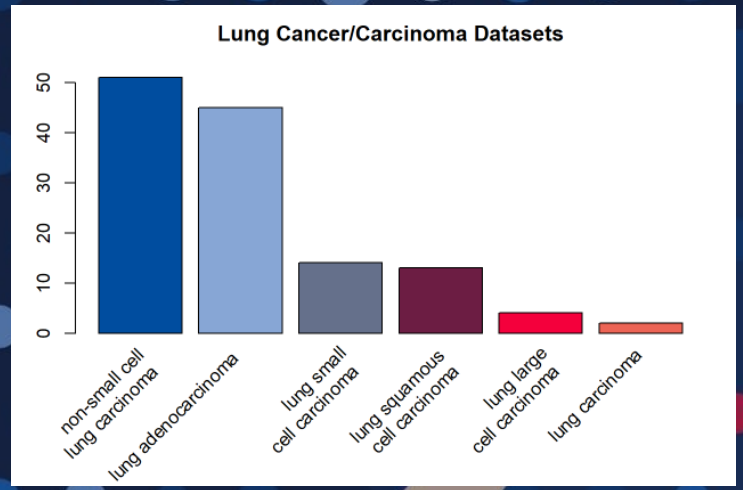

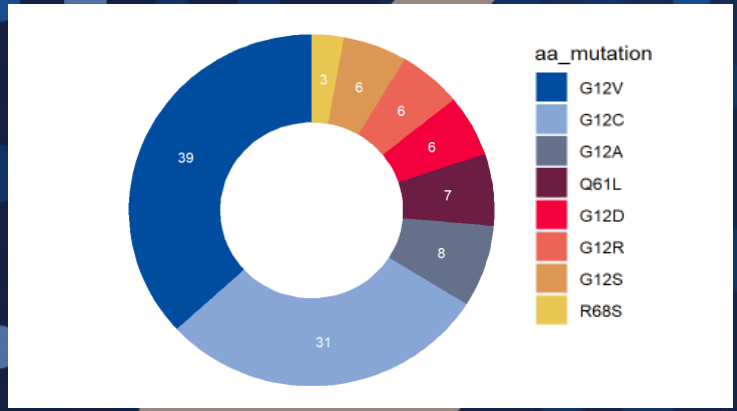

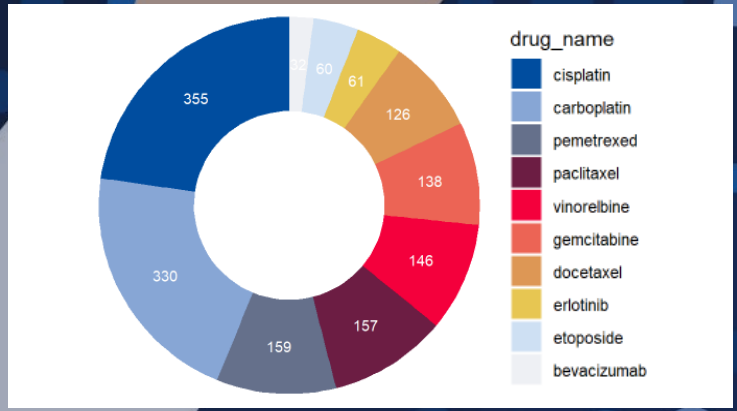

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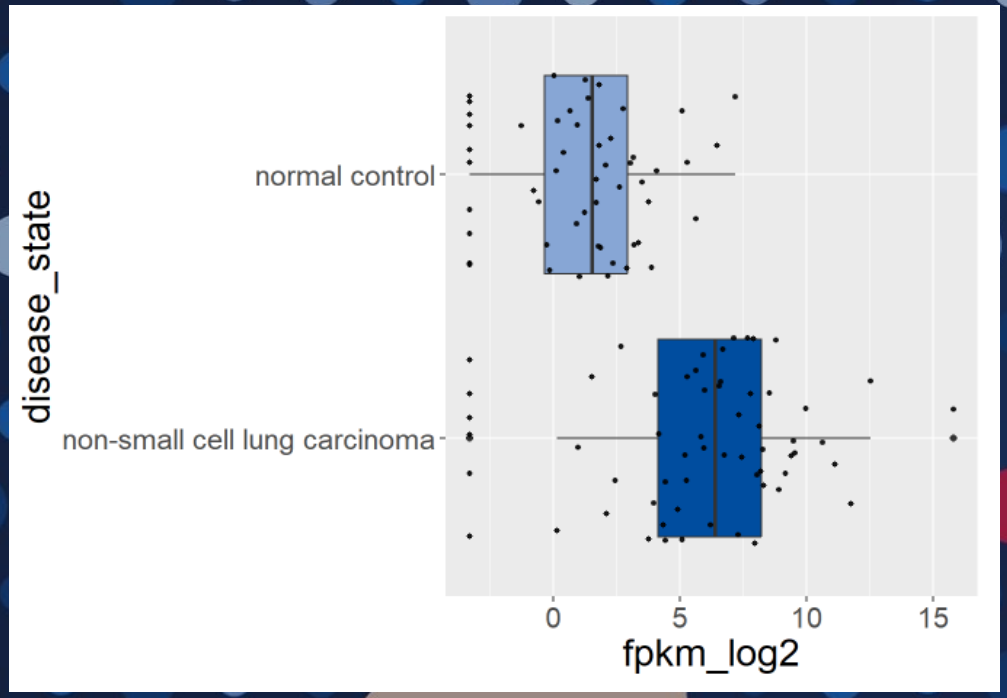
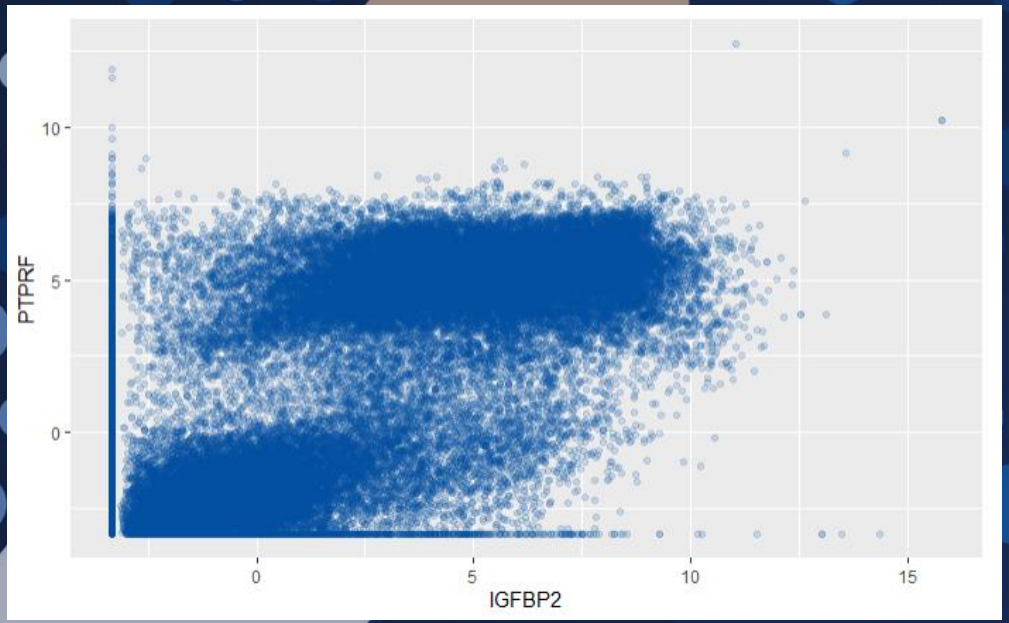
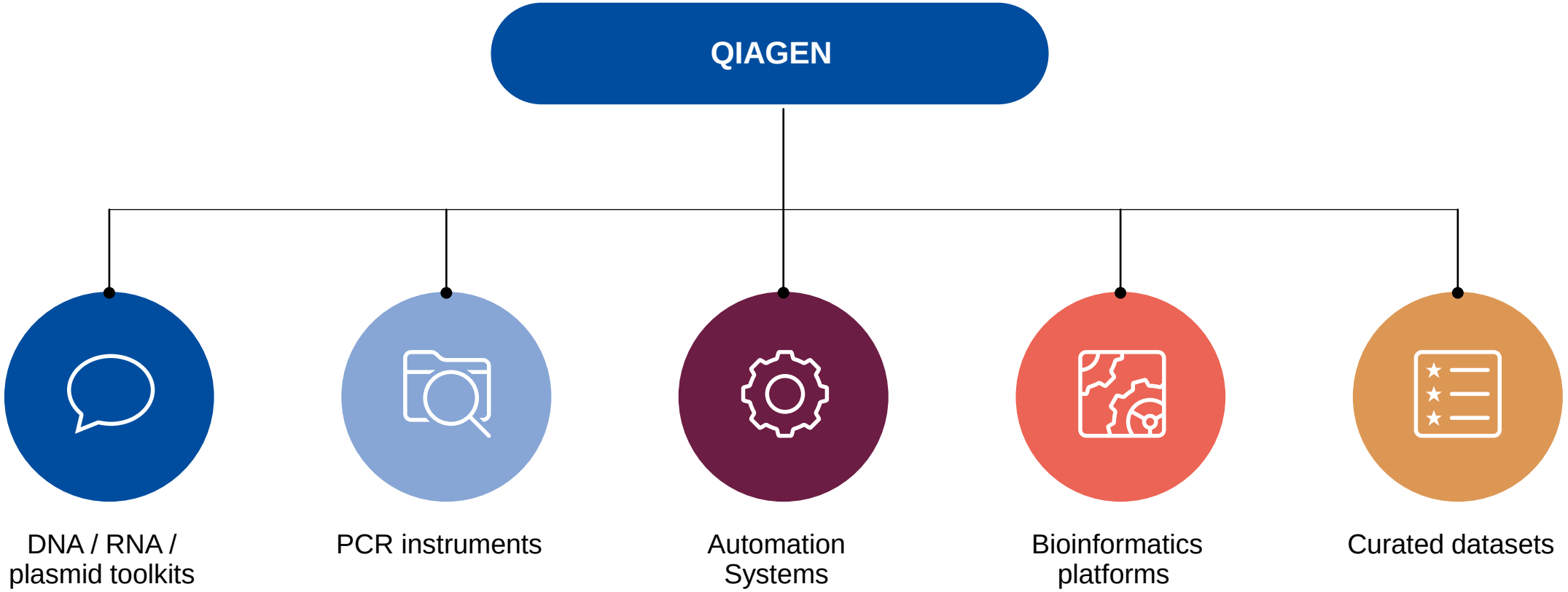




From sample to insight



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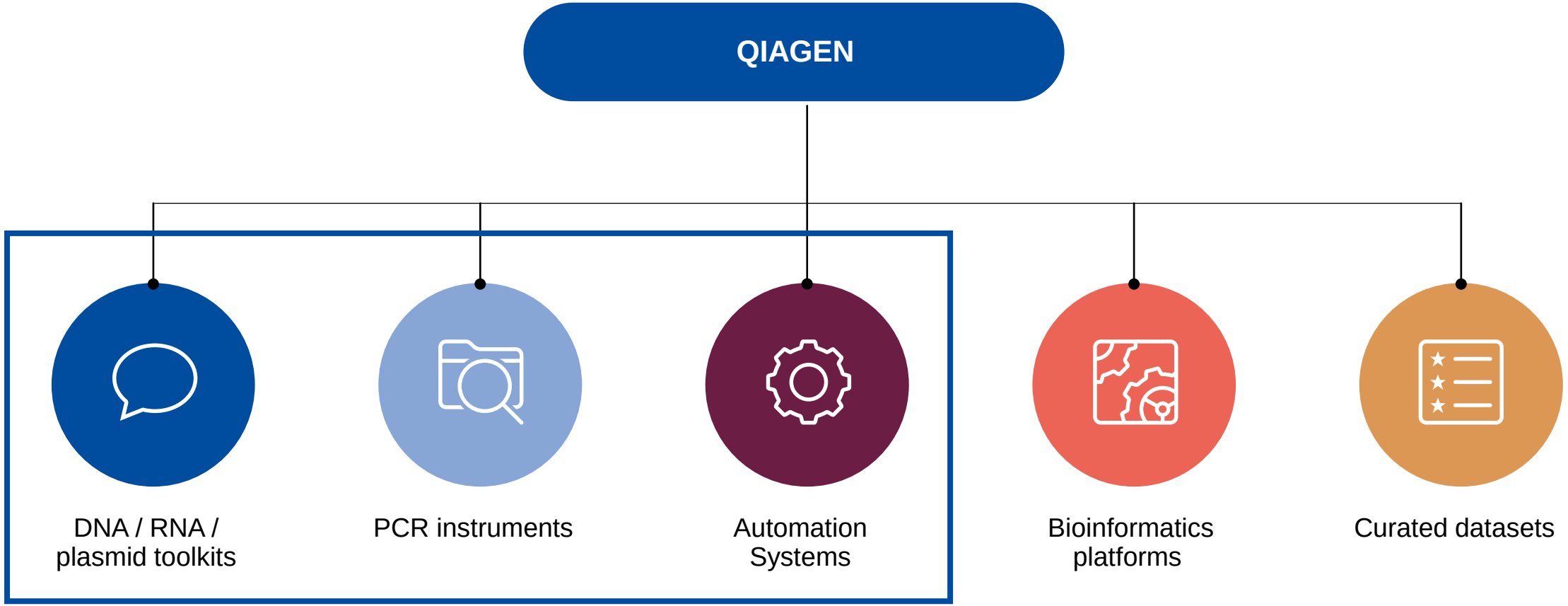
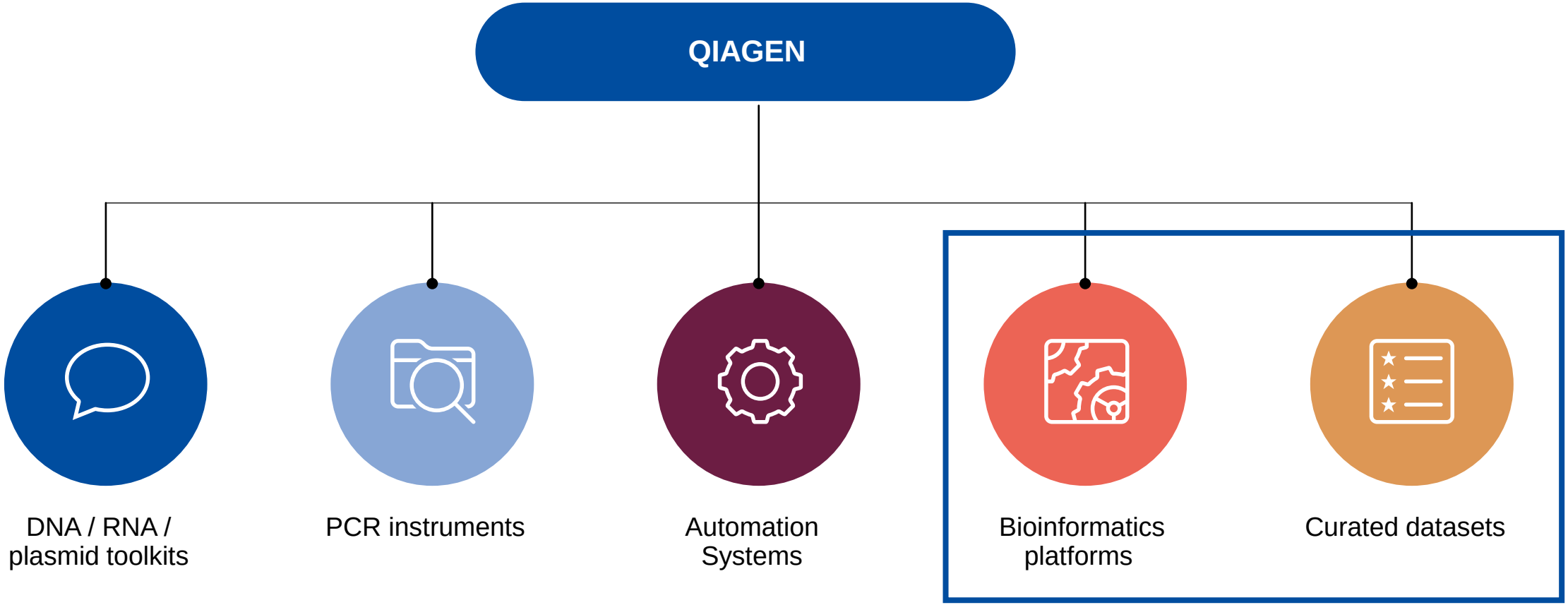
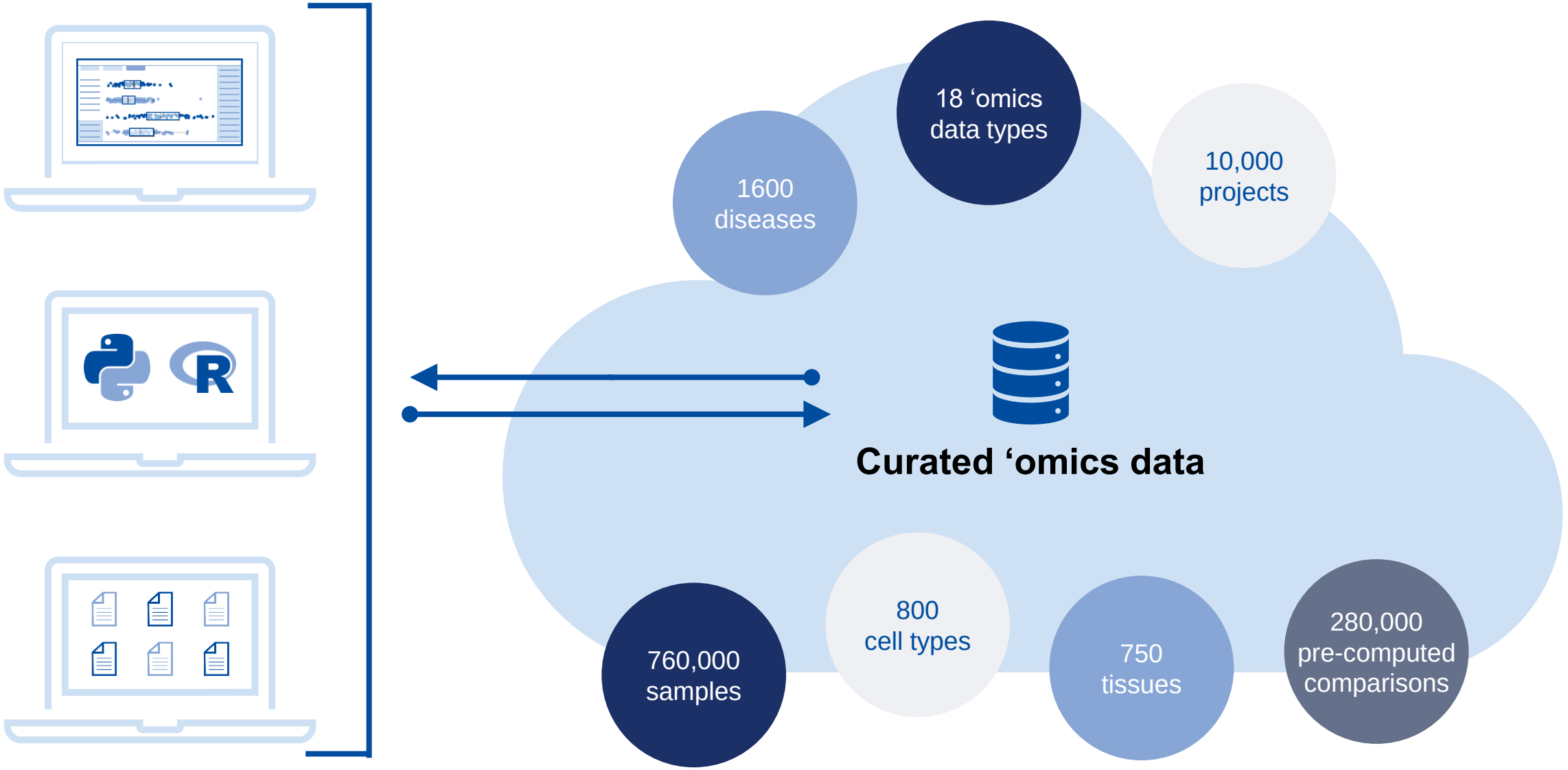


Process samples for Next Generation Sequencing

From sample to insight



OmicSoft Collection



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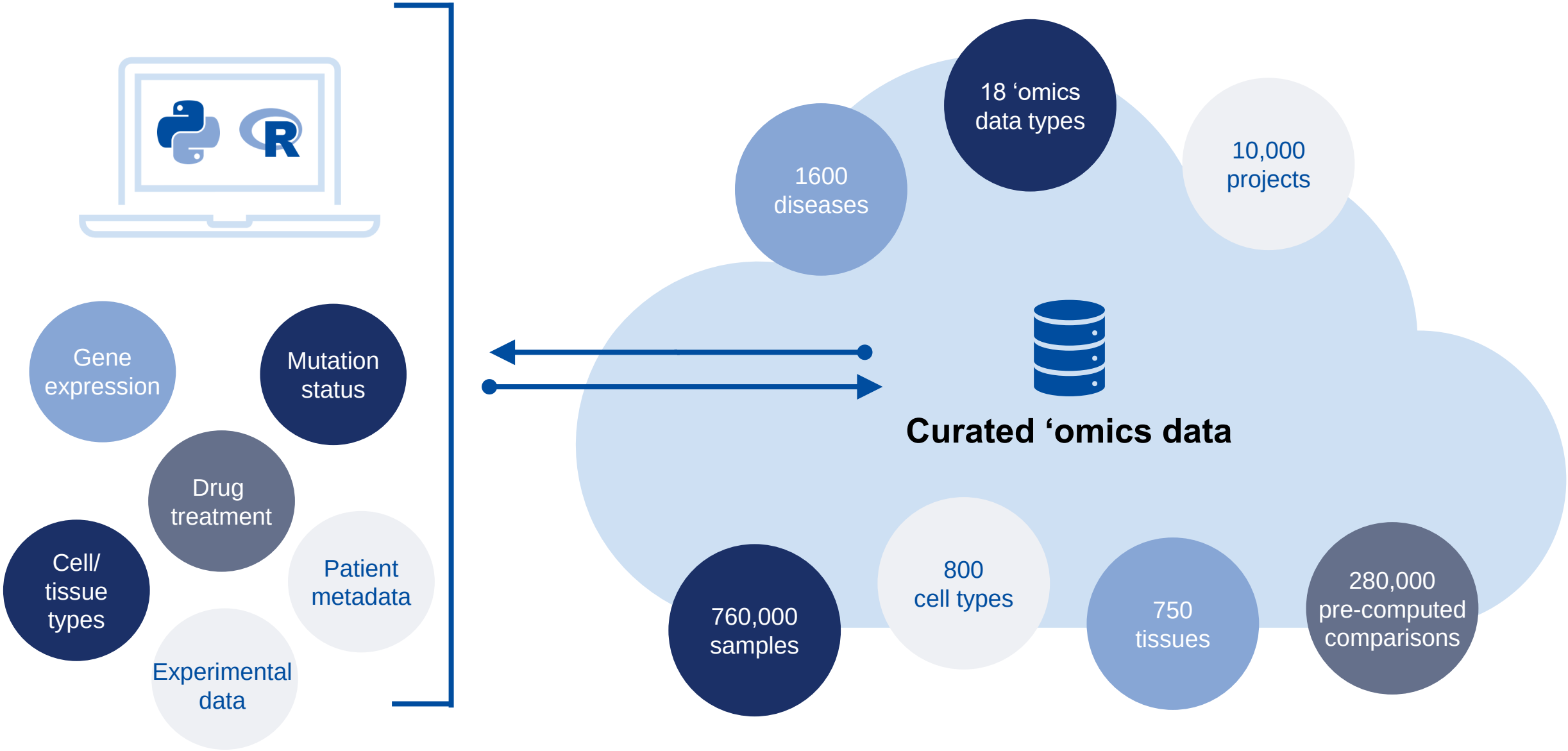
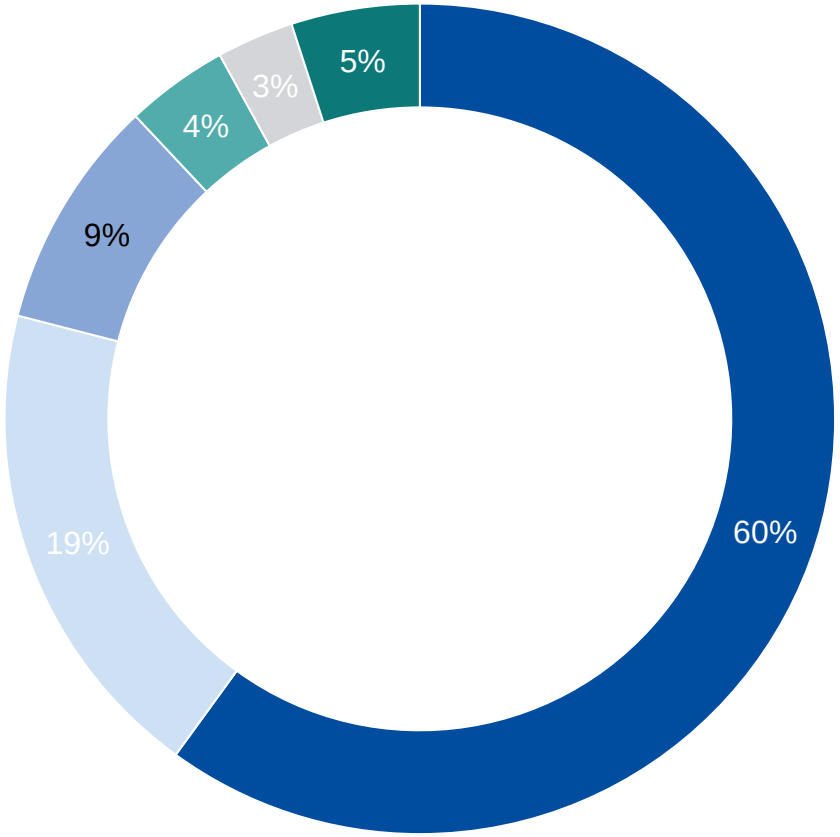


Why not use Open-Source Data?

Data scientists and bioinformaticians spend ~80% of their time collecting, cleaning and processing the data.



- Cleaning and organizing data: 60%
- Collecting datasets: 19%
- Mining data for patterns: 9%
- Refining algorithms: 4%
- Building training sets: 3%
- Others: 5%

Data source: Sarih, H., Tchangani, A. P., Medjaher, K. and Pere, E. (2019) Data preparation and preprocessing for broadcast systems monitoring in PHM framework. 6th International Conference on Control, Decision and Information Technologies (CoDIT). 1444–1449.

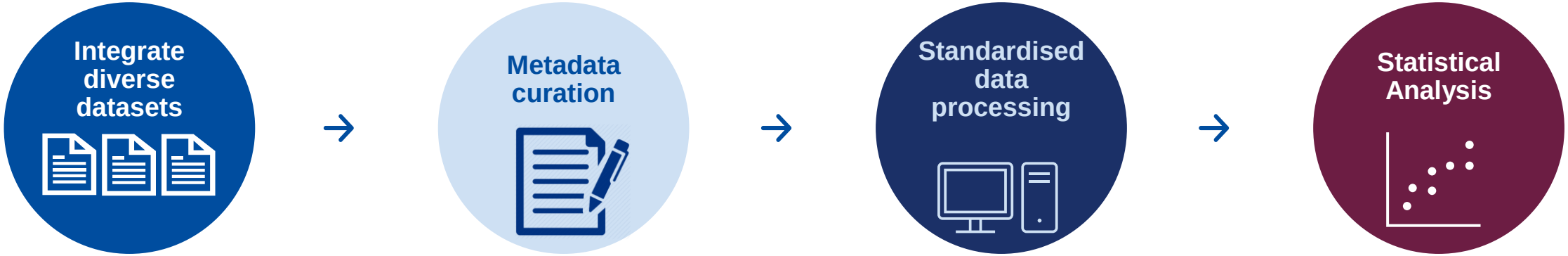
OmicSoft pipeline

Disease relevant **omics samples** are gathers from **hundreds of thousands of published projects** and popular **consortia**.

Manual metadata curation using controlled vocabularies

Extracted data is processed using **consistent bioinformatics pipelines**

All results are included in our models to generate **statistical analysis**



OmicSoft Land pipeline

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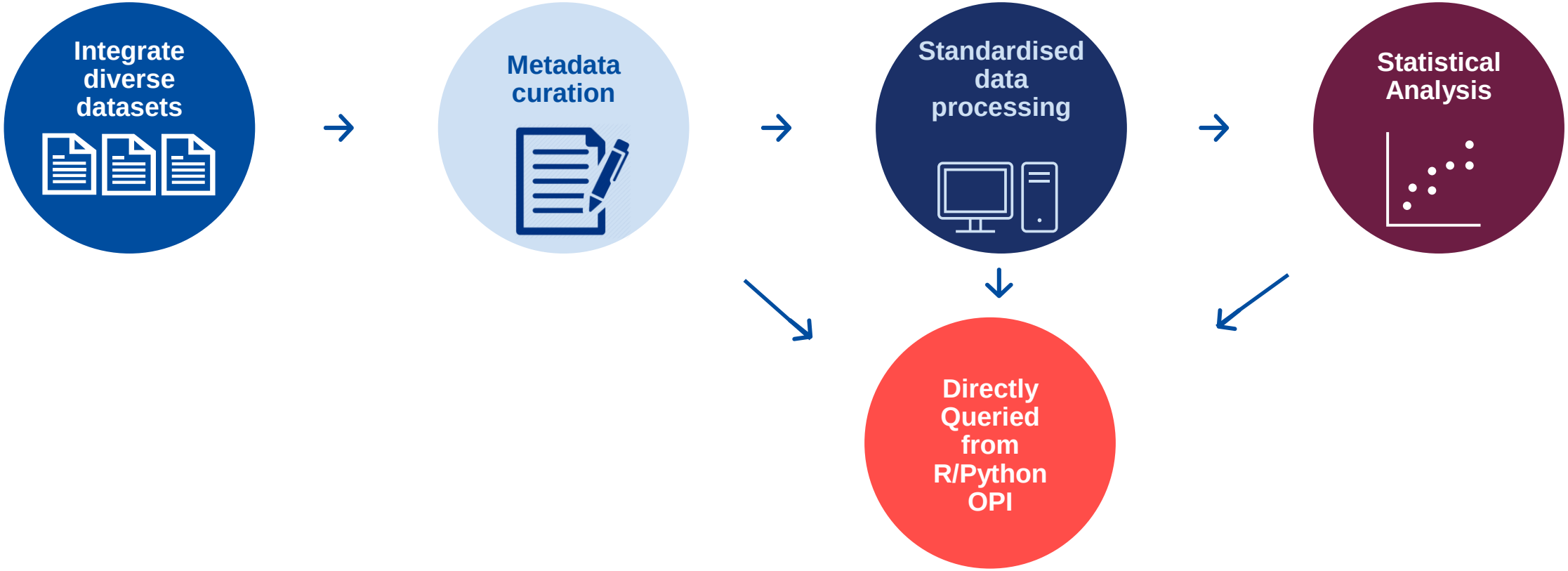

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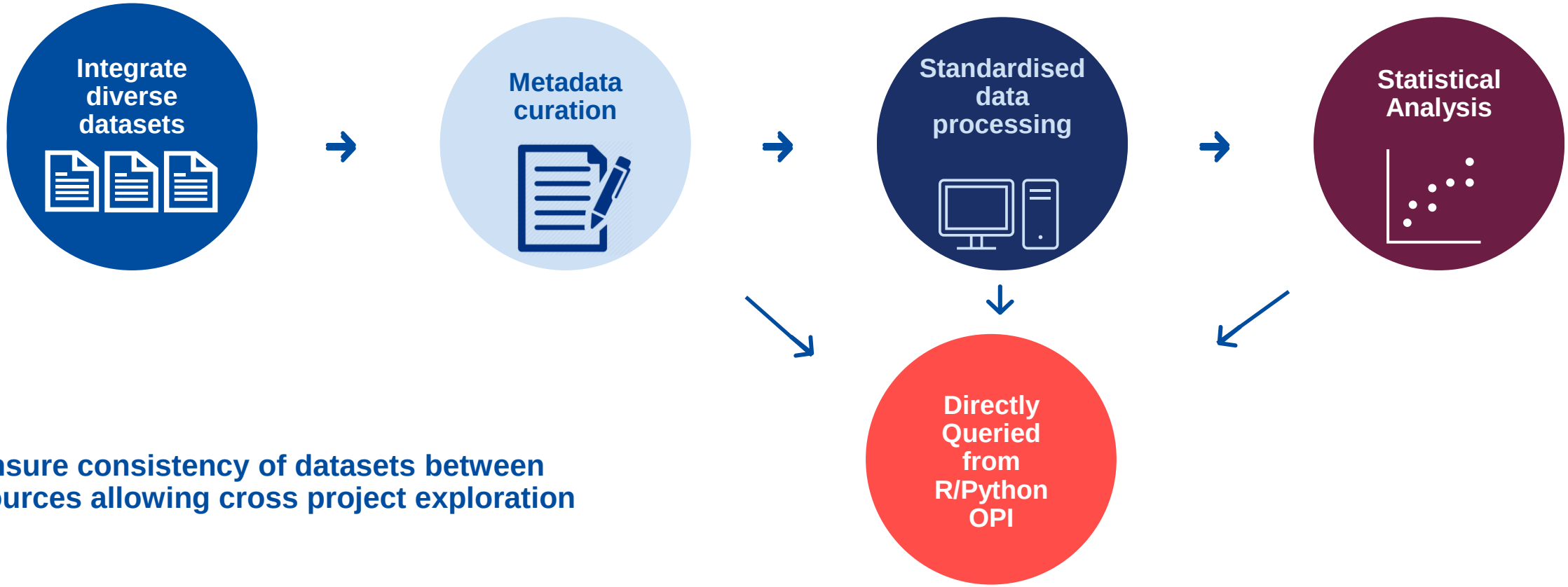
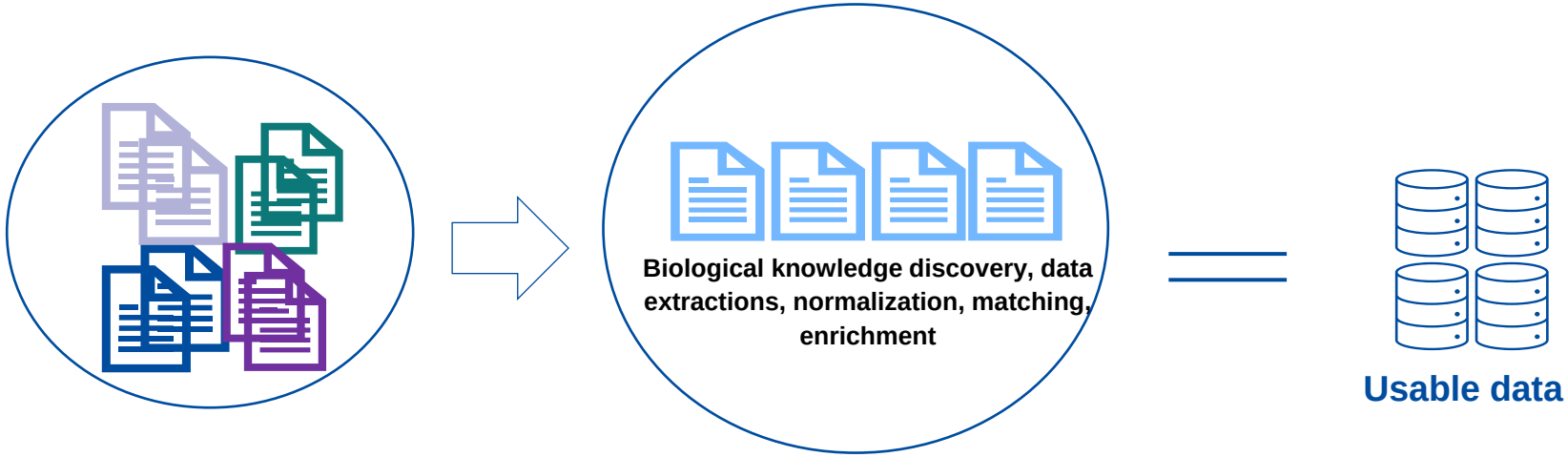


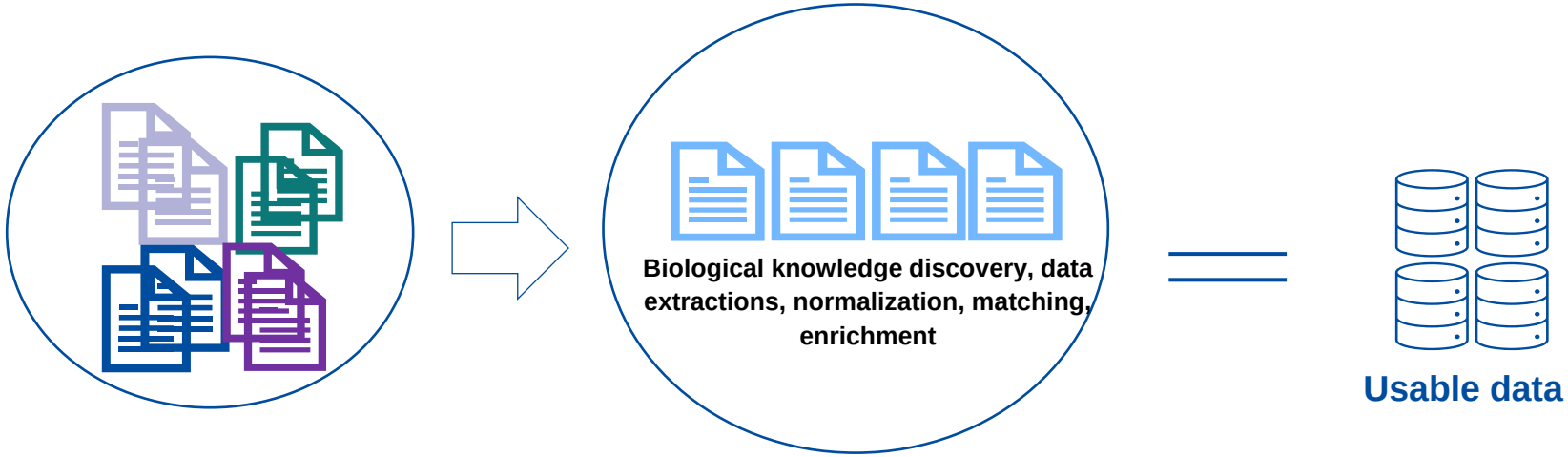
Ensure consistency of datasets between sources allowing cross project exploration

The OmicSoft collection

OmicSoft


Biological knowledge discovery, data extractions, normalization, matching, enrichment
Usable data
Heterogeneous data
Curation and processing

OmicSoft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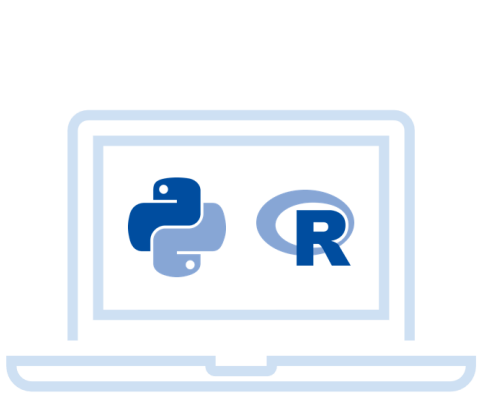
R example: Lung cancer

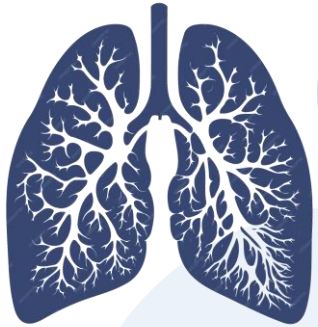


Gene expression

Mutation status

Cell/ tissue types

Drug treatment



18 ‘omics data types

1600 diseases

10,000 projects

Curated ‘omics data

760,000 samples

800 cell types

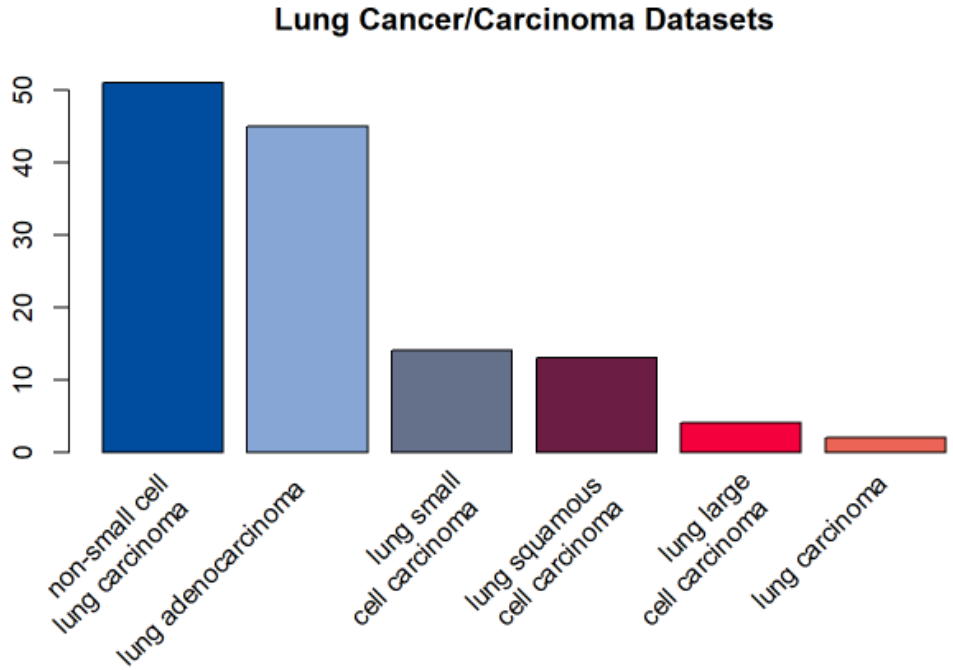
750 tissues

280,000 pre-computed comparisons

Finding Datasets related to Lung Cancer

```
datastore <- opi()
sql <- "
SELECT disease_state, _db_ as database, project_id, tissue, organism,
  count(*) AS no_samples
FROM samples
WHERE (LOWER(disease_state) LIKE '%lung%' AND
  LOWER(disease_state) LIKE  '%carcinoma%')
GROUP BY disease_state, _db_, project_id, tissue, organism
ORDER BY no_samples DESC
"

result<- datastore$query(sql)
counts <- sort(table(result[result$no_samples>30,'disease_state']),
               decreasing = TRUE)
```



Lung Cancer Datasets

disease_state	database	project_id	tissue	organism	no_samples
lung adenocarcinoma (LUAD)	lincs_b38_gc33	LINCS_B38_GC33	lung	human	19558
lung adenocarcinoma (LUAD)	tcga_b38_gc33	TCGA_LUAD	lung	human	767
lung squamous cell carcinoma (LUSC)	tcga_b38_gc33	TCGA_LUSC	lung	human	747
non-small cell lung carcinoma	trace_rx_b38_gc33	TRACERx_2020R3	lung	human	447
lung adenocarcinoma (LUAD)	onco_human_b38_gc33	GSE72094	lung	human	442

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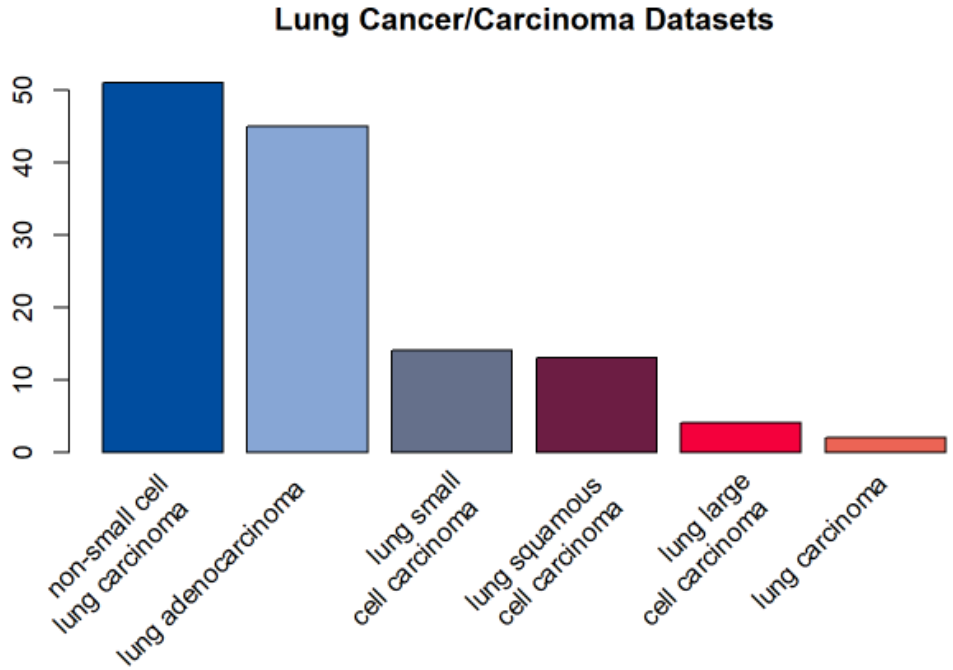

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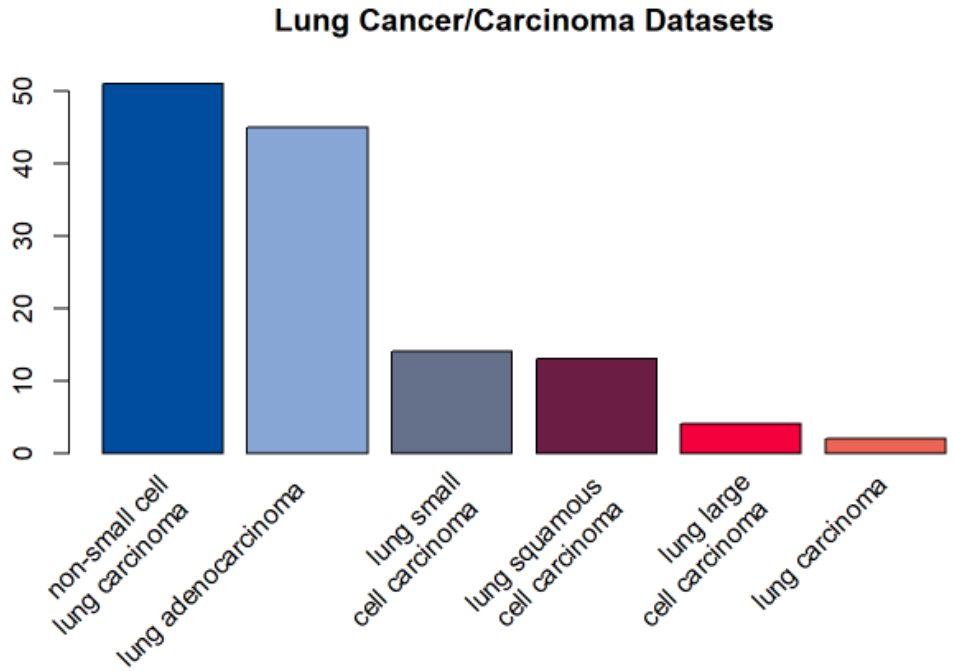

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  organism = 'human'AND
  tissue = 'lung'
GROUP BY disease_state, _db_, project_id, tissue, organism
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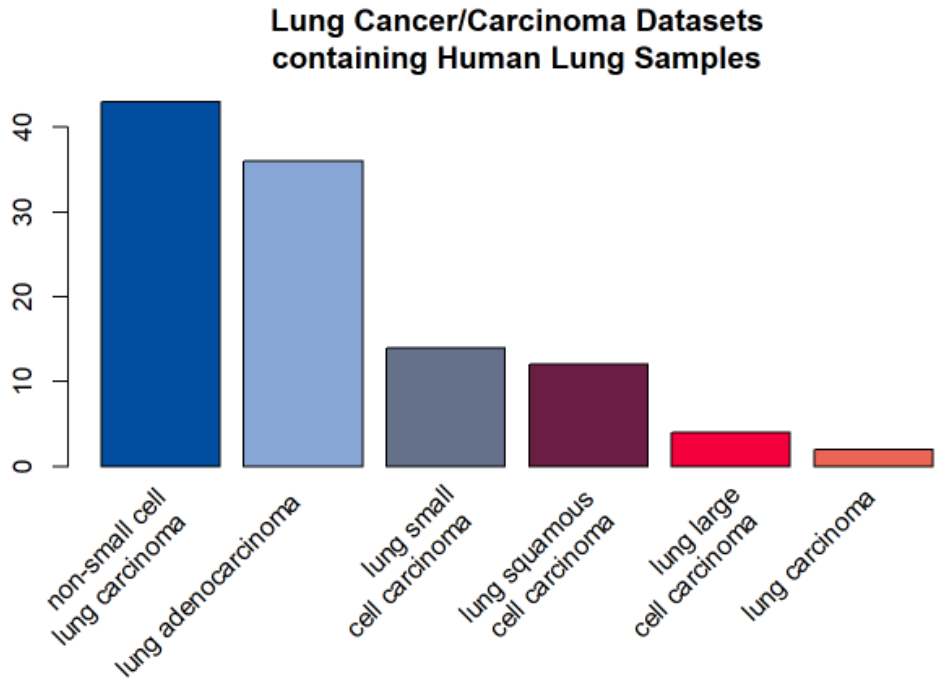

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Finding Drug Datasets

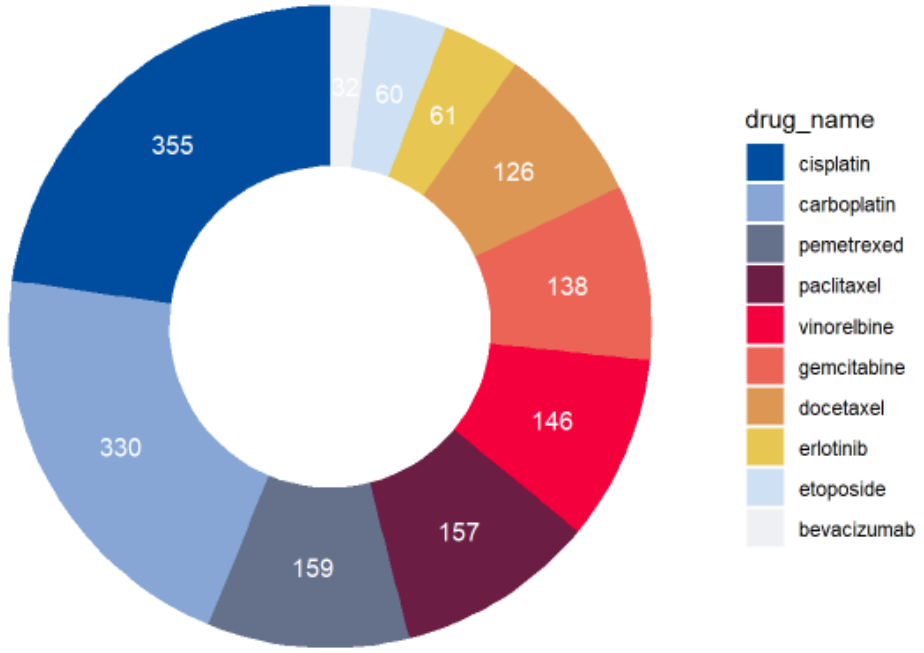
```
sql <- "
SELECT
     project_id, disease_state, tissue, drug_name,
     count(*) AS count
FROM
    samples
LEFT JOIN (
    SELECT sample_id, CAST(value as VARCHAR) AS drug_name
    FROM clinical_triplets
    WHERE attribute = 'drug_name'
    ) USING (sample id)
WHERE
    LOWER(disease_state) LIKE '%lung%carcinoma%' AND
    LOWER(drug_name) not LIKE 'NA'
GROUP BY
    project_id, disease_state, tissue, drug_name
ORDER BY count DESC
"

drugs<- datastore$query(sql)
drugs2 <- drugs %>%
  separate_rows(drug_name, sep=";")

result <- drugs2 %>%
  select(drug_name, count) %>%
  group_by(drug_name) %>%
  summarise(total_samples= sum(count)) %>%
  arrange(desc(total_samples))
```

```
result<- result[1:10,]
result$drug_name <- reorder(result$drug_name, - result$total_samples)

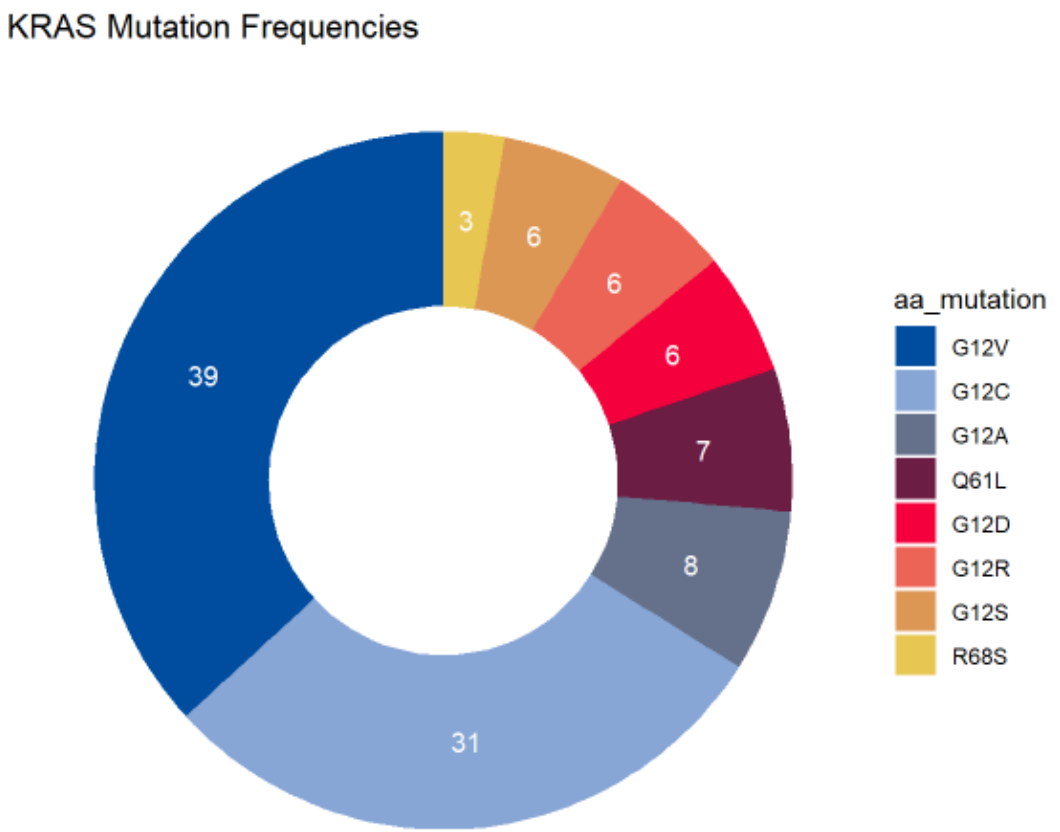
# Create the doughnut plot
ggplot(result, aes(x = 2, y =total_samples, fill = drug_name)) +
  geom_bar(stat = "identity", width = 1) +
  coord_polar(theta = "y") +
  xlim(0.5, 2.5) + theme_void() +
  theme(legend.position = "right") +
  geom_text(aes(label = paste0(total_samples)),
            position = position_stack(vjust = 0.5), color = "white") +
  scale_fill_manual(values = my_cols) + ggtitle("Drug Treatment Samples")
```



Finding NSCLC with KRAS Mutations

```
sql<- "
SELECT
    project_id, tissue, disease_state, mc.gene_name, mc.aa_mutation
FROM
    samples
JOIN
    dna_seq_somatic_mutation dssm ON samples.sample_index = dssm.sample_index
JOIN
    mutations_canonical mc on mc.mutation_index = dssm.mutation_index
WHERE
    LOWER(disease_state) = 'non-small cell lung carcinoma' AND
    mc.gene_name = 'KRAS'
"

mutations<- datastore$query(sql)
```



Identifying Differentially Expressed Genes
Pre-computed Comparison: Disease vs. Normal

```
sql <- "
SELECT  gene_name, log2_fold_change, adjusted_p_value, project_id
FROM human_disease_b38_gc33.comparison_data
JOIN human_disease_b38_gc33.comparisons USING (comparison_index)
JOIN human_disease_b38_gc33.gene_annotation USING (gene_index)
WHERE
     LOWER(case_disease_state) = 'non-small cell lung carcinoma' AND
     comparison_category = 'Disease vs. Normal' AND
     log2_fold_change > 3  AND
     p_value < 0.001 AND
     case_sample_size > 50 AND
     control_sample_size > 50 AND
     sample_data_mode = 'RnaSeq_Transcript'
ORDER BY  log2_fold_change DESC
"

result<- datastore$query(sql)
```

Lung Cancer Differential Expression - Gene vs Normal

gene_name	log2_fold_change	adjusted_p_value	project_id
AC000093.1	6.9448	0.00e+00	GSE68086
PRR7	5.6663	0.00e+00	GSE68086
GP1BB	5.3220	0.00e+00	GSE68086
IGFBP2	5.0468	0.00e+00	GSE68086
SH2B2	4.8870	0.00e+00	GSE68086
LYL1	4.4718	0.00e+00	GSE68086
EVA1B	4.2421	0.00e+00	GSE68086
NUDT4B	4.1178	0.00e+00	GSE68086
ANKRD9	3.9237	0.00e+00	GSE68086
TPGS1	3.8363	8.61e-05	GSE68086

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Pre-computed Comparisons

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JOIN human_disease_b38_gc33.comparisons USING (comparison_index)
JOIN human_disease_b38_gc33.gene_annotation USING (gene_index)
WHERE
     LOWER(case_disease_state) = 'non-small cell lung carcinoma' AND
     comparison_category = 'Disease vs. Normal' AND
     log2_fold_change > 3  AND
     p_value < 0.001 AND
     case_sample_size > 50 AND
     control_sample_size > 50 AND
     sample_data_mode = 'RnaSeq_Transcript'
ORDER BY  log2_fold_change DESC
"

result<- datastore$query(sql)
```

Lung Cancer Differential Expression - Gene vs Normal

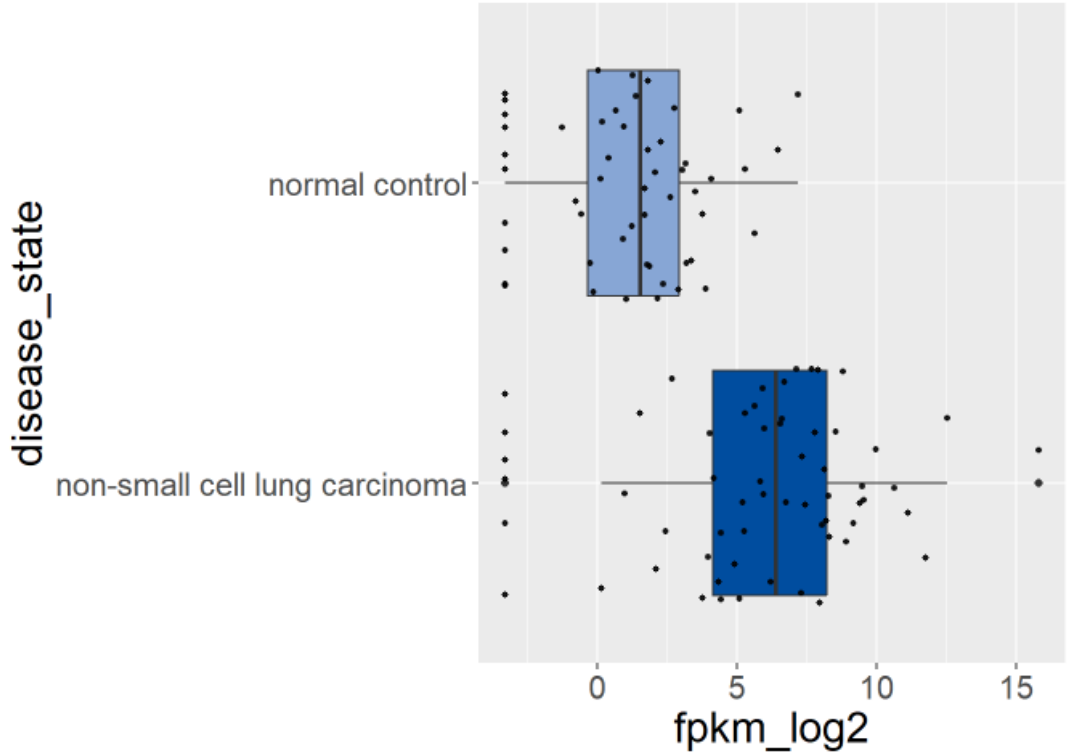
gene_name	log2_fold_change	adjusted_p_value	project_id
AC000093.1	6.9448	0.00e+00	GSE68086
PRR7	5.6663	0.00e+00	GSE68086
GP1BB	5.3220	0.00e+00	GSE68086
IGFBP2	**5.0468**	**0.00e+00**	**GSE68086**
SH2B2	4.8870	0.00e+00	GSE68086
LYL1	4.4718	0.00e+00	GSE68086
EVA1B	4.2421	0.00e+00	GSE68086
NUDT4B	4.1178	0.00e+00	GSE68086
ANKRD9	3.9237	0.00e+00	GSE68086
TPGS1	3.8363	8.61e-05	GSE68086

Accessing Gene Expression Data

```
sql <- "
SELECT _db_, gene_name, fpkm, disease_state, project_id
FROM gene_fpkm
JOIN samples USING (sample_index)
JOIN gene_annotation USING (gene_index)
WHERE
      gene_name = 'IGFBP2' AND
      project_id = 'GSE68086' AND
      (LOWER(samples.disease_state) = 'non-small cell lung carcinoma' OR
      LOWER(samples.disease_state) LIKE '%control%')
"

result <- as.data.frame(datastore$query(sql))
result$fpkm_log2 <- log2(result$fpkm + 0.1)
```

```
# plot boxplot
plot <- ggplot(result,
               aes(x=fpkm_log2, y=disease_state, fill=disease_state)) +
  geom_boxplot(show.legend = F) +
  geom_jitter(color="black", size=1, alpha=0.9, show.legend = F) +
  scale_fill_manual(values = my_cols[1:2]) +
  theme(axis.text.x= element_text(size = 15),
        axis.text.y= element_text(size = 15),
        axis.title.x= element_text(size = 20),
        axis.title.y= element_text(size = 20),
        )
```



Gene Co-expression

```
sql <- "
SELECT gene, gene_annotation.gene_name,
CORR(log_fpkm_1,log_fpkm_2) AS correlation
FROM
(
    SELECT
        gene1_fpmk.gene_index AS gene,
        log2(gene1_fpmk.fpkm+0.1) AS log_fpkm_1,
        log2(gene2_fpmk.fpkm+0.1) AS log_fpkm_2
    FROM
        human_disease_b38_gc33.gene_fpkm gene1_fpmk,
        human_disease_b38_gc33.gene_fpkm gene2_fpmk
    WHERE
        gene2_fpmk.gene_index = 9112 AND
        gene1_fpmk.sample_index = gene2_fpmk.sample_index
)
JOIN human_disease_b38_gc33.gene_annotation ON gene = human_disease_b38_gc33.gene_annotation.gene_index
GROUP BY gene, gene_annotation.gene_name, gene_annotation.gene_index
ORDER BY correlation DESC
LIMIT 11
"
result <- datastore$query(sql)
```

Lung Cancer Differential Expression - Gene vs Normal

gene_name	correlation
PTPRF	0.7213568
MDK	0.7185268
ADCY6	0.7088722
MMP15	0.7009866
TMEM98	0.6950555
BCAR1	0.6925772
SHROOM3	0.6871723
TSPAN6	0.6805749
EFNB2	0.6798894
VWA1	0.6788953

Gene co-expression

```
sql <- "
SELECT gene, gene_annotation.gene_name,
CORR(log_fpkm_1,log_fpkm_2) AS correlation
FROM
(
    SELECT
        gene1_fpmk.gene_index AS gene,
        log2(gene1_fpmk.fpkm+0.1) AS log_fpkm_1,
        log2(gene2_fpmk.fpkm+0.1) AS log_fpkm_2
    FROM
        human_disease_b38_gc33.gene_fpkm gene1_fpmk,
        human_disease_b38_gc33.gene_fpkm gene2_fpmk
    WHERE
        gene2_fpmk.gene_index = 9112 AND
        gene1_fpmk.sample_index = gene2_fpmk.sample_index
)
JOIN human_disease_b38_gc33.gene_annotation ON gene = human_disease_b38_gc33.gene_annotation.gene_index
GROUP BY gene, gene_annotation.gene_name, gene_annotation.gene_index
ORDER BY correlation DESC
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Gene co-expression

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        log2(gene2_fpmk.fpkm+0.1) AS log_fpkm_2
    FROM
        human_disease_b38_gc33.gene_fpkm gene1_fpmk,
        human_disease_b38_gc33.gene_fpkm gene2_fpmk
    WHERE
        gene2_fpmk.gene_index = 9112 AND
        gene1_fpmk.sample_index = gene2_fpmk.sample_index
)
JOIN human_disease_b38_gc33.gene_annotation ON gene = human_disease_b38_gc33.gene_annotation.gene_index
GROUP BY gene, gene_annotation.gene_name, gene_annotation.gene_index
ORDER BY correlation DESC
LIMIT 11
"
result <- datastore$query(sql)
```

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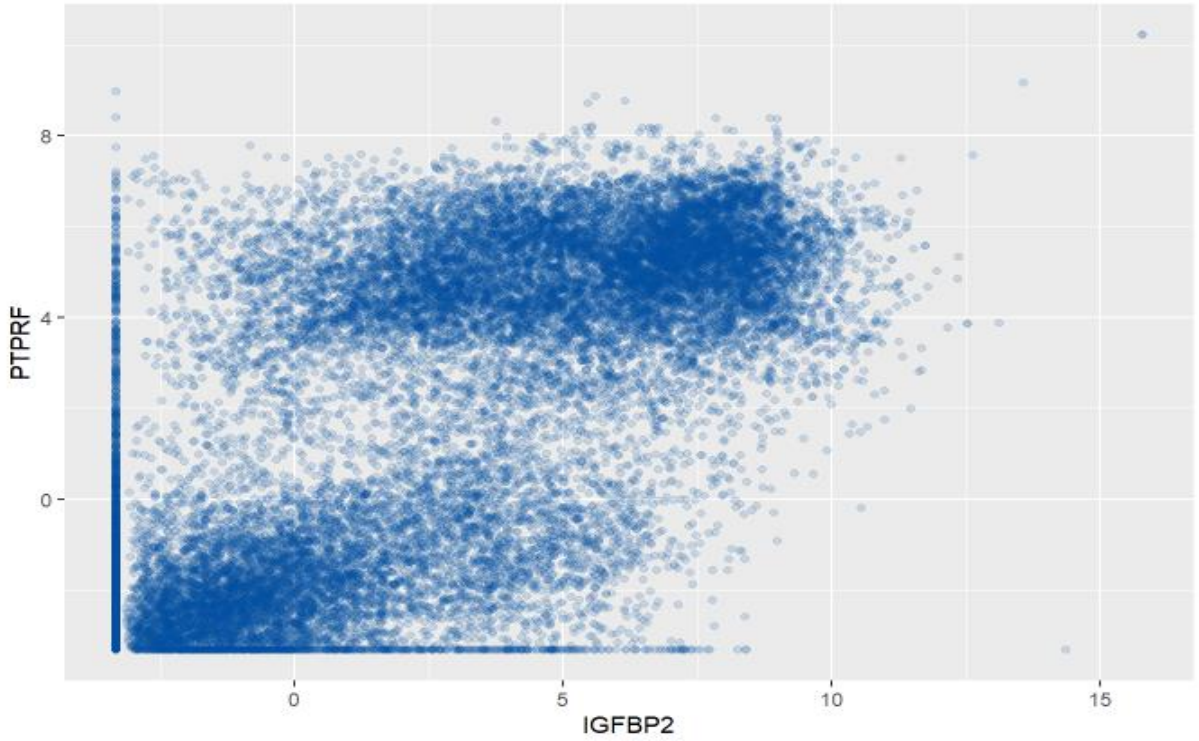
TSPAN6	0.6805749
EFNB2	0.6798894
VWA1	0.6788953

Gene co-expression

```
sql <- "
SELECT gene_name, log2(fpkm+0.1) AS log_fpkm, sample_index, project_id
FROM human_disease_b38_gc33.gene_fpkm
JOIN human_disease_b38_gc33.samples USING (sample_index)
JOIN human_disease_b38_gc33.gene_annotation USING (gene_index)
WHERE
      (gene_name = 'IGFBP2' OR gene_name = 'PTPRF') AND
      (LOWER(samples.disease_state) = 'non-small cell lung carcinoma' OR
      LOWER(samples.disease_state) LIKE '%control%')
"

result <- datastore$query(sql)
```



Lung Cancer Differential Expression - Gene vs Normal

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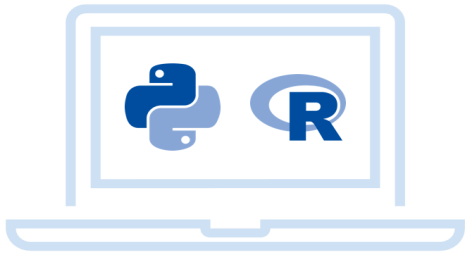
OmicSoft Summary

Extensive Database of Disease Relevant Omics Data



Gene expression

Mutation status

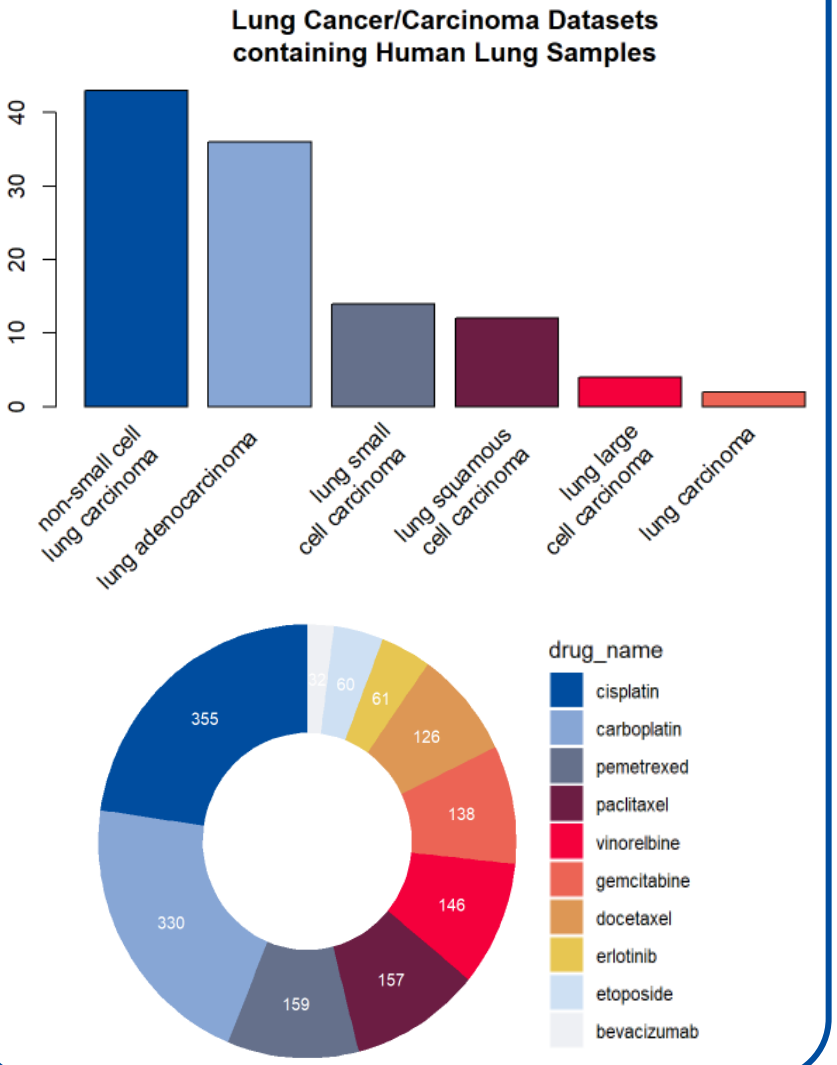
Drug treatment

Cell/ tissue types

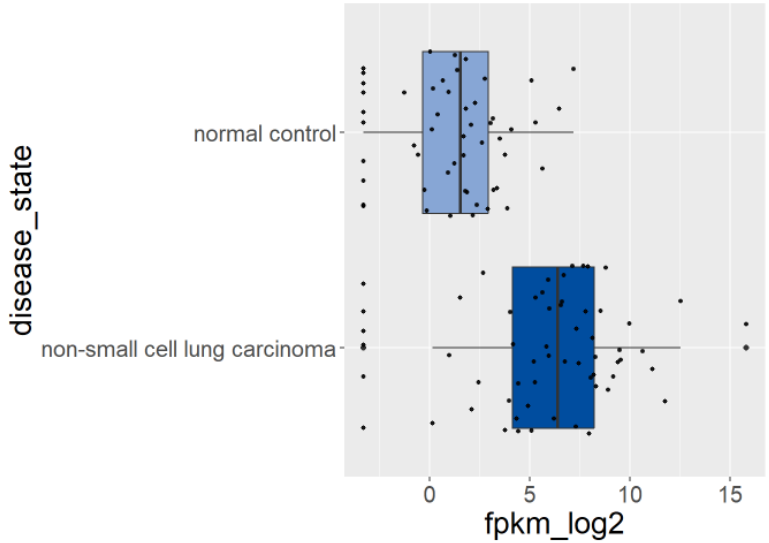
Patient metadata

Experimental data

Easy API Access to Datasets



Pre-computed Multi-dataset Analysis



Please get in touch

We are happy to provide training and participate in collaborative projects