Cancer Genomics: Integrative and Scalable Solutions in *R* / *Bioconductor*

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Bioconductor
OPEN SOURCE SOFTWARE FOR BIOINFORMATICS

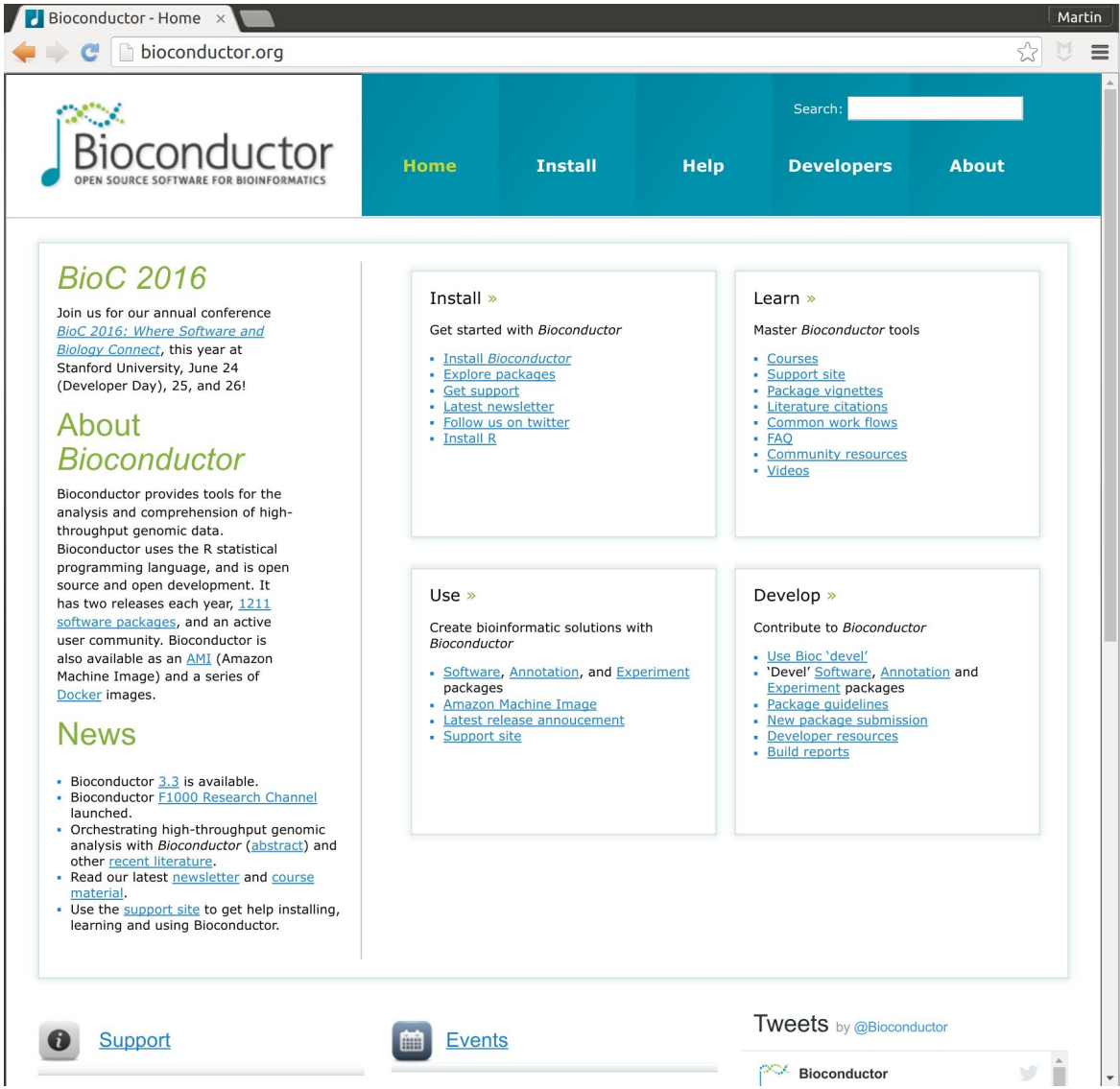
ROSWELL PARK CANCER INSTITUTE

Bioconductor

Statistical analysis and comprehension of high-throughput genomic data

Established 2002, widely used and well-respected

- https://bioconductor.org/
- https://support.bioconductor.org



Common *Bioconductor* tasks and packages

Differential gene expression

- RNA-seq: *DESeq2*, *edgeR, scde, …*
- Microarray: *limma*

Gene regulation

- ChIP-seq: *csaw, DiffBind*
- Methylation arrays: *minfi, missMethyl*
- Gene set enrichment: *topGO, limma*

Working with called variants

- *VariantAnnotation*
- *VariantFiltering*

Flow cytometry

- *flowCore*

Data access

- *GEOquery / SRAdb*
- *TCGAbiolinks*
- *AnnotationHub / ExperimentHub*

Annotation resources

- Identifier, gene model, and sequence packages: *org.**, *TxDb.**, *BSgenome.**
- Online queries: *biomaRt*, *...*

Visualization

- *Gviz, ComplexHeatmap, ggtree, ...*

Many other packages!

Bioconductor and ITCR

Three directions to further enable cancer genomics research

1. Multi-assay data representations
   - In-memory -- *MultiAssayExperiment*
   - On-disk (coming soon...)
2. Easy access to high-quality curated consortium-scale data
   - *AnnotationHub*
   - *ExperimentHub*
   - Emerging resources
3. Scalable performance
   - Large data representation -- *GenomicRanges*, *HDF5Array*
   - Core, cluster, cloud -- *BiocParallel*
   - Interactive and batch-iterative

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```
> ##
> ## Multi-assay experiments, 'devel' only
> ##
> library(MultiAssayExperiment)
> ovarian
MultiAssayExperiment with 13 experiments
Containing an Elist class object of length 13
 [1] RNASeqGene: ExpressionSet - 19990 rows, 299 columns
 [2] RNASeq2GeneNorm: ExpressionSet - 20501 rows, 307 columns
 [3] miRNASeqGene: ExpressionSet - 705 rows, 461 columns
 [4] CNASNP: RangedRaggedAssay - 873768 rows, 1145 columns
 [5] CNVSNP: RangedRaggedAssay - 254437 rows, 1141 columns
 [6] CNACGH: RangedRaggedAssay - 126479 rows, 472 columns
 [7] Methylation: ExpressionSet - 27578 rows, 591 columns
 [8] mRNAArray: ExpressionSet - 18632 rows, 575 columns
 [9] miRNAArray: ExpressionSet - 821 rows, 573 columns
 [10] RPPAArray: ExpressionSet - 208 rows, 427 columns
 [11] Mutations: RangedRaggedAssay - 20219 rows, 316 columns
 [12] gistica: ExpressionSet - 24776 rows, 573 columns
 [13] gistict: ExpressionSet - 24776 rows, 573 columns
To access slots use:
 Elist() - to obtain the "Elist" of experiment instances
 pData() - for the primary/phenotype "DataFrame"
 sampleMap() - for the sample availability "DataFrame"
 metadata() - for the metadata object of 'ANY' class
See also: subsetByAssay(), subsetByRow(), subsetByColumn()
```

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```
> library(AnnotationHub)
> (hub <- AnnotationHub())
AnnotationHub with 43720 records
…
> hub["AH30903"]$title
[1] "E129-H3K4me1.narrowPeak.gz"
> hub[["AH30903"]]
...

> library(ExperimentHub)
> hub <- ExperimentHub()
> tcga <- hub[["EH1"]]
see ?GSE62944 and browseVignettes('GSE62944') for documentation
loading from cache '/home/mtmorgan/.ExperimentHub/1'
> table(tcga$CancerType)

BLCA BRCA COAD  GBM HNSC KICH KIRC KIRP LAML  LGG LIHC LUAD LUSC
 273 1082  468  170  481   66  540  226  164  528  212  514  490
  OV PRAD READ SKCM STAD THCA UCEC
 344  423  164  373  146  506  536
> tcga[, tcga$CancerType == "OV"]
ExpressionSet (storageMode: lockedEnvironment)
...
```

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```
> ##
> ## Emerging resources
> ##
> library(GenomicDataCommons)  # not yet public
> endpoints()
available endpoints:
    status, projects, cases, files, annotations, data, manifest,
    slicing, submission
> files()
class: files_list
cases: 10
names:
    6acecceb-7d71-4c50-bd76-781dffe13060,
    8361f2f1-8d30-444b-be70-6aa3e7557c8b,
    3414c8e2-21f4-41b6-ba1d-cfa7e83f30f7, ...,
    dd7c8b01-6173-40a1-abc1-04d195d7cee7,
    43eb57cc-7e99-40f0-83ca-9a0208de0531
```

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```
> ##
> ## Large data representation and processing
> ##
> library(GenomicRanges)
> gpos <- GPos(seqinfo(bfl)["chr14"])

> ##
> ## Parallel evaluation -- cores, clusters, clouds
> ##
> library(BiocParallel)
> library(RNAseqData.HNRNPC.bam.chr14)
> bfl <- BamFileList(RNAseqData.HNRNPC.bam.chr14_BAMFILES)
> cvg <- bplapply(bfl, coverage)
> mcols(gpos) <- DataFrame(lapply(cvg, "[[", "chr14"))
> gpos
GPos object with 107349540 positions and 8 metadata columns:
             seqnames       pos strand | ERR127306 ERR127307
                <Rle> <integer>  <Rle> |     <Rle>     <Rle>
         [1]    chr14         1      * |         0         0
 …
  [107349540]    chr14 107349540      * |         0         0
```

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```
> ##
> ## Integration with existing 'containers'
> ##
> library(SummarizedExperiment)
> gpos <- GPos(seqinfo(bfl)["chr14"])
> df <- DataFrame(lapply(cvg, "[[", "chr14"))
> (se <- SummarizedExperiment(list(cvg=df), rowData=gpos))
class: RangedSummarizedExperiment
dim: 107349540 8
metadata(0):
assays(1): cvg
rownames: NULL
rowData names(0):
colnames(8): ERR127306 ERR127307 ... ERR127304 ERR127305
colData names(0):
```

Learn, use, and contribute to *Bioconductor*

Learn

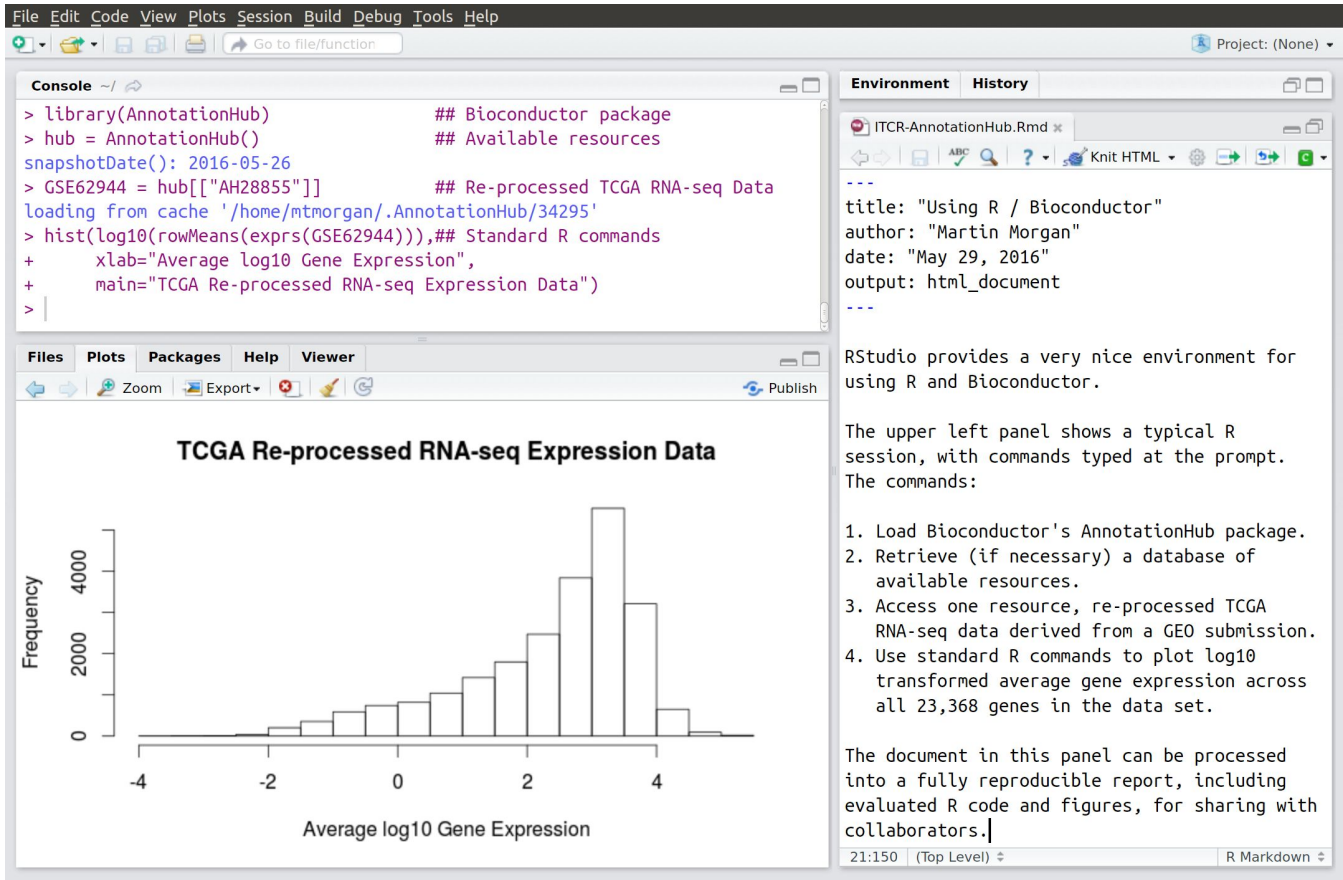
- Package vignettes (e.g., *DESeq2*)
- Training material
- Scientific literature

Use

- Package discovery
- Support site

Contribute

- Developer resources
- Submission and technical review process



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SOUND

FRED HUTCH
40 YEARS OF CURES 1975–2015

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