

Apple (Malus domestica)



Alligator (Alligator mississippiensis)



Cow (Bos taurus)



Barrel Clover (Medicago truncatula)



Platypus (Ornithorhynchus anatinus)



 $(Salmo\ salar)$ 



(Rattus norvegicus)



(Gallus gallus domesticus)

Mouse (Mus musculus)

# **Epigenetics Services**

Explore with Next-Gen Sequencing





Human (Homo sapien)



Wheat (Triticum)



Dog (Canis lupus familiaris)



Opossum (Didelphimorphia)



Soybean (Glycine max)



(Sus scrofa domesticus)



(Phaseolus vulgaris)



Wine Grape (Vitis vinifera)



Fruit Fly (Drosophila melanogaster)



Rockcress (Arabidopsis)



Baboon (Papio anubis)



Guinea Pig (Cavia porcellus)



Earthworm (Lumbricina)



Cod (Gadus morhua)



Sheep (Ovis aries)



Zebrafish (Danio rerio)



Zebra Finch (Taeniopygia guttata)



## **Overview**

## Epigenetic Analysis



## Epigenetic Biomarker Discovery Program

Start to finish development for your diagnostic test



### DNA Methylation

Platforms for genome-wide and targeted single-base resolution DNA methylation analysis



### MethylCheck™ Bisulfite Sequencing

Validate epigenetic markers from a large sample cohort or specific gene region



### DNA Hydroxymethylation: RRHP™

Single-base resolution platforms for detection of 5-hydroxymethylation in DNA



#### ChIP-Seq

Genome-wide analysis of protein-DNA interactions

## **Expression Services**



#### RNA-Seq

Transcriptome-wide analysis of total RNA or small RNA (miRNA)

## Epigenetic Aging Clock Service



### **Epigenetic Aging Clock**

Gauge the biological age from a wide variety of human samples

## Additional Services



### Mass Spectrometry

Global quantitative analysis of DNA methylation and hydroxymethylation levels



### **Custom Bioinformatics**

Fully customizable bioinformatics solutions for the analysis of raw data from any of your Next-Generation Sequencing experiments



#### Microbiomics Services

Next-Generation Sequencing services for microbiomics, including discovery, identification, and characterization of microbial communities

# **Epigenetic Biomarker Discovery Program**



#### From Collection to Conclusion

Zymo Research offers a new Epigenetic Biomarker Discovery Program for the development of epigenetic lab diagnostic tests. Whether you are interested in developing epigenetic tests for cancer, developmental disorders, autoimmune diseases, obesity and other anomalies, Zymo Research provides a solution for sample collection through to commercial development. The experts at Zymo Research can help you at any step in the development pipeline by offering a portfolio of products and services for sample collection and purification, biomarker discovery, biomarker validation, platform selection and commercial development.

### **Sample Collection & Purification**

Zymo Research offers specialized collection devices and purification kits for tissues, feces, urine, blood, and other biological specimens. Sample collection begins with DNA/RNA Shield™, which is an innovative stabilization reagent that allows samples to be stored and transported at ambient temperatures. DNA/RNA Shield™ does not require the need for refrigeration or specialized equipment, and makes shipping your precious specimens to Zymo Research easy.



### **Biomarker Discovery: Epigenetic NGS Services**

With the latest Next-Generation Sequencing technologies for DNA methylation analysis, Zymo Research provides comprehensive services and bioinformatics analysis to help discover epigenetic biomarkers in your specific sample set. Zymo Research's Illumina® certified MethylSeq® platforms are each designed to suit your specific coverage needs.



### **Epigenetic Biomarker Validation**

Zymo Research offers the simplest way to validate epigenetic biomarkers with our MethylCheck™ sequencing platform. Whether you have genome-wide DNA methylation (450K/EPIC array or RRBS) data or a particular gene region in mind, our scientists will design, validate, and evaluate site-specific DNA methylation changes.



#### **Platform Selection**

Once you have your specific biomarkers narrowed down and validated, Zymo Research will help you select the most sensitive and cost-effective platform for your lab diagnostic test. A wide range of citation-leading bisulfite and bisulfite-free methods are available to implement your test.



Zymo Research's associates, Pangea™ CLIA-certified lab, will help you to bring your lab diagnostic test to the market.



# **DNA Methylation Services**



Zymo Research offers three platforms for genome-wide DNA methylation analysis at single nucleotide resolution, each designed to suit your specific coverage needs. The main difference between the platforms is the percentage of the total genome actually being sequenced. All platforms accommodate a wide range of sample types, including any species with a reference genome, low-input (>10 ng), and FFPE samples.

Classic RRBS (Reduced Representation Bisulfite Sequencing) combines restriction enzyme digestion with bisulfite sequencing to enrich for a CpG-dense fraction of the genome. The Classic RRBS platform allows for a maximum amount of methylation data using a minimal amount of sequencing at a significantly reduced cost. This combination makes Classic RRBS the perfect platform for pilot studies. Classic RRBS covers ≥70% all CpG islands, >75% all gene promoters, and detects 1.5-2 million unique CpG sites at 5-10x average minimum coverage\*.

**Methyl-MiniSeq®** is an expanded version of Classic RRBS. The system is extremely robust and the read depth is impressive, making it ideal for biomarker discovery using identification of differentially methylated regions. The low cost of this platform relative to the sequence data it produces also makes Methyl-MiniSeq® a good platform for pilot studies. Methyl-MiniSeq® covers ≥85% all CpG islands, >80% all gene promoters, and captures approximately 4 million unique CpG sites at 5-10x average minimum coverage\*.

**Methyl-MaxiSeq**® is a whole-genome bisulfite sequencing (WGBS) option that provides DNA methylation information at single nucleotide resolution in a CpG context, as well as in the less common CHG and CHH contexts, across all regions of the genome.

The Basic Service package for each platform includes sample standardization, library construction, sequencing, and raw data alignment. The Full Service package offers additional down-stream bioinformatics processing and statistical analysis.

Service Option	Classic RRBS	Methyl-MiniSeq®	Methyl-MaxiSeq®
Capable with low DNA input?	Yes	Yes	Yes
Single-base Resolution?	Yes	Yes	Yes
Methylome Coverage*	1.5 - 2 million sites	3 - 4 million sites	Entire methylome
Quantitative Analysis?	Yes	Yes	Yes
Genomic Regions covered	Nearly all CpG islands and gene promoters	Twice as many unique CpG sites compared to Classic RRBS	Entire methylome
Notes	Efficient genome-wide analysis	Robust biomarker discovery	Complete methylation analysis

<sup>\*</sup> coverage estimates based on the human genome

<sup>\*\*</sup> depends on capture efficiency and methylation levels

# MethylCheck™

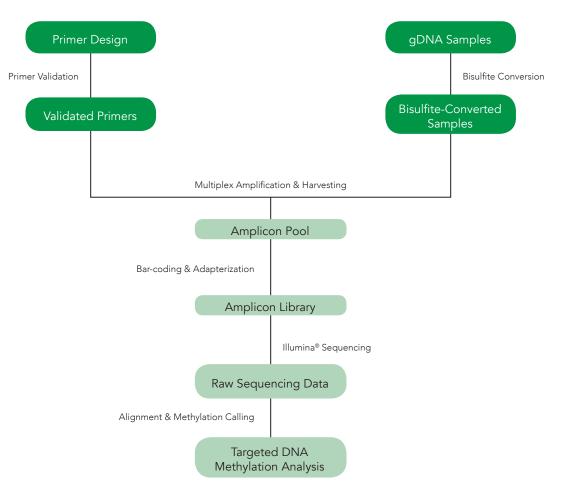


Zymo Research makes epigenetic biomarker validation simple with our MethylCheck™ platform. Whether you have methylation array (450K/EPIC) data that you would like to validate in a large sample cohort or have a specific gene region in mind, our scientists are available to design, validate, and evaluate site-specific DNA methylation changes. Simply send us your samples and regions of interest, and we will perform every step through data analysis, sending you back publication-quality graphs and figures.

The Targeted Bisulfite Sequencing service includes:

- Primer Design and Validation
- Targeted Amplification
- Adapterization and Barcoding
- Sequencing with Illumina® Technology
- Sequence Alignment to Reference Genome
- DNA Methylation Analysis





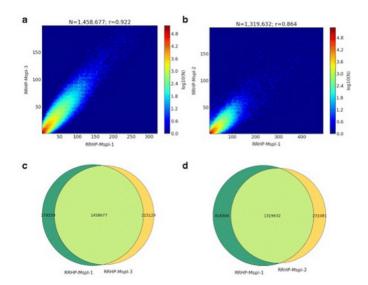
# **DNA Hydroxymethylation**



Zymo Research's platform for the analysis of DNA hydroxymethylation have unparalleled sensitivity and coverage of 5-hydroxymethylcytosine (5-hmC). With traditional bisulfite-conversion methods, 5-hmC cannot be distinguished from 5-mC. Therefore, Zymo Research has developed Reduced Representation Hydroxymethylcytosine Profiling (RRHP®), combined with Next-Generation sequencing to ensure high coverage and sensitivity for the detection of 5-hmC at single-base resolution. RRHP® allows genome-wide profiling for 5-hmC with reduced sequencing requirements.

### Reduced Representation Hydroxymethylation Profiling - RRHP®

This service is for genome-wide profiling of 5-hydroxymethylcytosine in DNA at single-nucleotide resolution. RRHP® also allows strand-specific determination of the location of the 5-hmC modification, as well as relative quantification of 5-hmC levels. Data from RRHP® can be combined with DNA methylation data from Methyl-MiniSeq®, allowing for direct comparison of DNA methylation and hydroxymethylation in the same sample. RRHP® is compatible with low DNA inputs and has the added advantage of providing read data for simultaneous SNP detection.



Replicate sample 5-hmC levels show very strong correlation when assessed using the RRHP® platform.

(Petterson A, Chung TH, Tan D, Sun X, Jia XY. Genome Biol. 2014 Sep 24;15(9):456.)

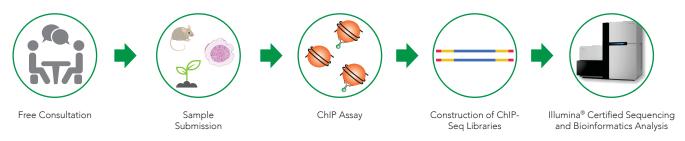
# ChIP Seq

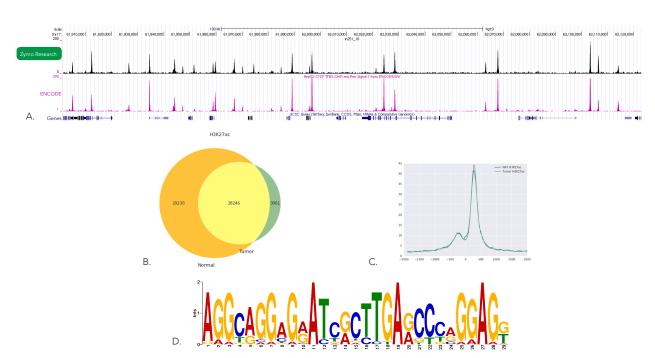


Chromatin Immunoprecipitation Sequencing (ChIP-Seq) is a technique that combines chromatin immunoprecipitation with the quantitative power and genome-wide coverage of Next-Generation Sequencing. It is a powerful tool for genome-wide mapping of DNA interactions with transcription factors, histone modifications, and chromatin binding proteins and is essential for understanding the effect of DNA-protein interactions on gene regulation.

With the ChIP-Seq service from Zymo Research, you can either perform the ChIP assay yourself and send us the enriched DNA for library construction and Next-Gen Sequencing, or we can process your samples using our proprietary chromatin shearing and enrichment procedures. We also perform the bioinformatics and statistical analyses, and send you the publication-ready results.

### Simply send us your samples and we will handle the rest!





**Example of Zymo Research's ChIP-Seq Services Data Output:** A. Browser tracks for visualization of peak regions. B. Venn diagram showing sample comparison data. C. Peak density profile to analyze peak locations relative to transcriptional start sites. D. Motif analysis to analyze bound genomic regions.

# **RNA-Seq Services**



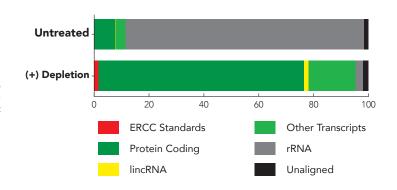
Zymo Research's RNA-Seq service makes transcriptome analysis available to every researcher, without the need for expensive equipment or bioinformatics expertise. Now you can achieve transcriptome-wide coverage of total RNA or small RNA with the latest Next-Gen Sequencing technology.

#### Let Zymo Research do the work for you!

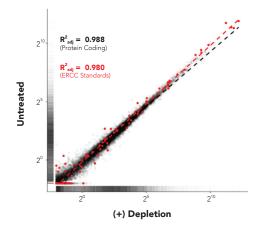
- **Simple and customizable:** All RNA purification, sample prep, sequencing, and bioinformatics analysis is included. Each project is customizable and delivers publication-ready figures.
- **Maximize Coverage:** Proprietary depletion method minimizes bias during rRNA removal, allowing for cost effective sequencing to increase coverage of relevant transcripts, no matter the sample type.
- Stringent QC: Each library is assessed using standards to ensure that quality data is generated.
- Available Services: Total RNA-Seq and miRNA-Seq.

#### Maximize Coverage

**All RNA-Seq services projects use cutting-edge methods to prepare your libraries.** Shown here is a proprietary depletion method to eliminate rRNA transcripts from your sample with virtually zero bias. Stacked bar plot represents read classification by gene biotype of Universal Human Reference RNA samples using the Zymo Research RNA-Seq analysis pipeline.

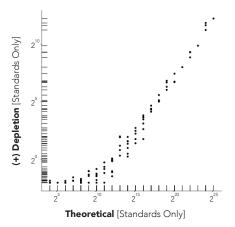


### **Unbiased Depletion**



Have confidence in your data every time with increasing read depth of relevant transcript coverage. Scatterplot demonstrates that rRNA Depletion (Y-axis) vs Untreated (X-axis) RPKM show virtually no bias in both gene expression (black) and spike-in standards (red).

#### Stringent QC Using Standards



Empirical quality control ensures reliable data generation and interpretation. RNA-seq pipelines are optimized using spike-in standards to deliver data of the highest quality and rigor, with the lowest bias. Scatterplot comparing measured (Y-axis) vs theoretical (X-axis) RPKM for spike-in standards

# **Epigenetics Aging Clock**



#### Highlights

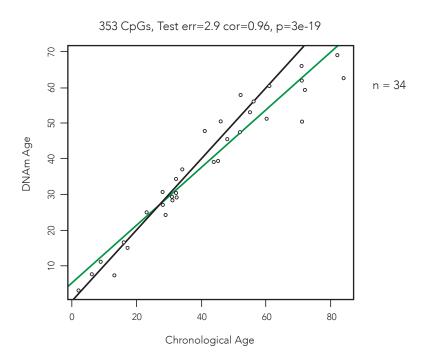
- Reliably determine the true biological age of any human sample.
- Quantify changes in biological age following lifestyle interventions or drug treatments.
- Identify disease associated aging alterations.

A growing number of studies have highlighted the strong correlation of DNA methylation changes with aging. Additionally, accelerated biological aging, as determined by DNA methylation profiling, has been associated with disease phenotypes including Down Syndrome and HIV-1-infection. DNA methylation-based biological age is a valuable surrogate biomarker of molecular aging.

The Epigenetic Aging Clock Service allows you to effectively gauge the biological age of any human tissue sample. With this easy to use service, the only thing you have to do is provide us with the sample. Starting with DNA purification all the way through bioinformatics analysis, Zymo Research scientists will do the work for you and provide you with an accurate biological age estimate along with a comprehensive report. Enhance any aging study or satisfy your intellectual curiosity with this multi-tissue age predictor.

This profiler is designed to:

- Detect methylation changes at highly informative CpG sites
- Use optimized data analysis workflow to provide an accurate biological age



Predicted epigenetic age of urine samples from healthy donors.

## **Additional Services**



### **Mass Spectrometry**

Zymo Research offers DNA composition analysis with LC/MS analysis. Please inquire for more information.



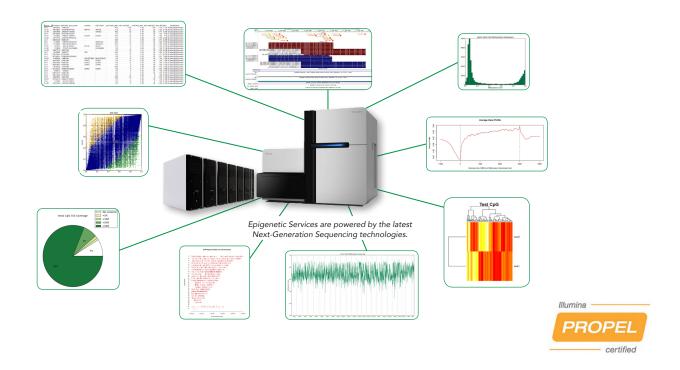
### **Custom Bioinformatics**

Do you have Next-Generation Sequencing data that you need analyzed? Zymo Research offers complete bioinformatics solutions to fulfill your needs. Whether it is whole-genome bisulfite sequencing data or ChIP-Seq data, we can help make sense of your overwhelming data sets. We use established as well as customizable bioinformatic pipelines to transform raw sequence data into manageable and interpretable figures and data sets. Simply provide the raw (FASTQ) or aligned (SAM or BAM) data and we will provide you with your desired downstream analyses.

# **Service Packages**

Basic Service Packages for all of the platforms include sample standardization, library construction, Next-Generation Sequencing, and raw data alignment.

Full Service Packages offer additional down-stream bioinformatic processing and statistical analysis specifically tailored to fit your needs.



## **Microbiomics Services**

### A Complete Solution for Unbiased Microbiome Profiling

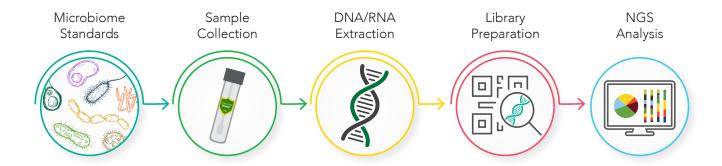
- Simply submit samples and receive a comprehensive, customizable, and user-friendly report
- Unbiased & contamination-free sample processing validated using microbial standards

### **Quick Turnaround**

- Results in ≤ 2 weeks for 16S rRNA gene sequencing
- Results in ≤ 6 weeks for shotgun metagenomic sequencing

### **Superior Taxonomic Resolution**

- Species-level resolution with 16S rRNA gene sequencing
- Strain-level resolution with shotgun metagenomic sequencing



All ZymoBIOMICS® Services include comprehensive bioinformatics and statistical analyses for each microbiomics project. The report can be customized according to each unique project or application. Let Zymo Research do the bioinformatics so that you don't have to!

## **Typical Analyses Include:**

- Composition Barplots
- Taxonomy Heatmap
- Alpha-Diversity
- Beta-Diversity

- LEfSe Biomarker Discovery
- Taxa2SV Decomposer



The **BEAUTY** of **SCIENCE** is to Make Things **SIMPLE**®



