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Explore how researchers are using a range of high-throughput, next-generation sequencing (NGS) methods to drive their discoveries. Whether your research focus is studying the epigenetic changes in breast cancer, identifying variants in rare and undiagnosed diseases, or applying integrative genomics, NGS enables you to push the boundaries and advance science at an unprecedented pace.

What will you discover?

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ctDNA	Epigenetics	Exome sequencing	Integrative genomics	Whole-genome sequencing	Whole-transcriptome sequencing	Single-cell sequencing

Circulating tumor DNA detection

Detection of circulating tumor DNA (ctDNA) in early- and late-stage human malignancies

Findings

- Researchers were able to detect ctDNA in early- and late-stage subject malignancies in > 75% of subjects with metastatic pancreatic, ovarian, colorectal, bladder, gastroesophageal, breast, melanoma, hepatocellular, and head and neck cancers.
- Lower malignancy percentages were detected in < 50% of subjects with primary brain, renal, prostate, and thyroid cancers.
- ctDNA was identified in ~55% of subjects with localized tumors with significant variability between cancer type and stage.
- The authors also identified relevant V-Ki-ras2 (KRAS) mutations with a sensitivity of 87.2% and a specificity of 99.2% in a separate sample of 206 metastatic colorectal cancer subjects.
- Mutations in the MAPK pathway were found in 23 of 24 subjects who developed resistance to EFGR.

Method

The authors applied high-throughput sequencing to detect cell-free ctDNA in a sample of 640 subjects with multiple cancer types that were at different stages.

Source

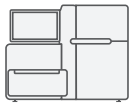
Bettegowda C, Sausen M, Leary RJ, et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. *Sci Transl Med.* 2014;6:224ra224.

Supporting publications

Newman AM, Lovejoy AF, Klass DM, et al. Integrated digital error suppression for improved detection of circulating tumor DNA. *Nat Biotechnol.* 2016;34:547-555.

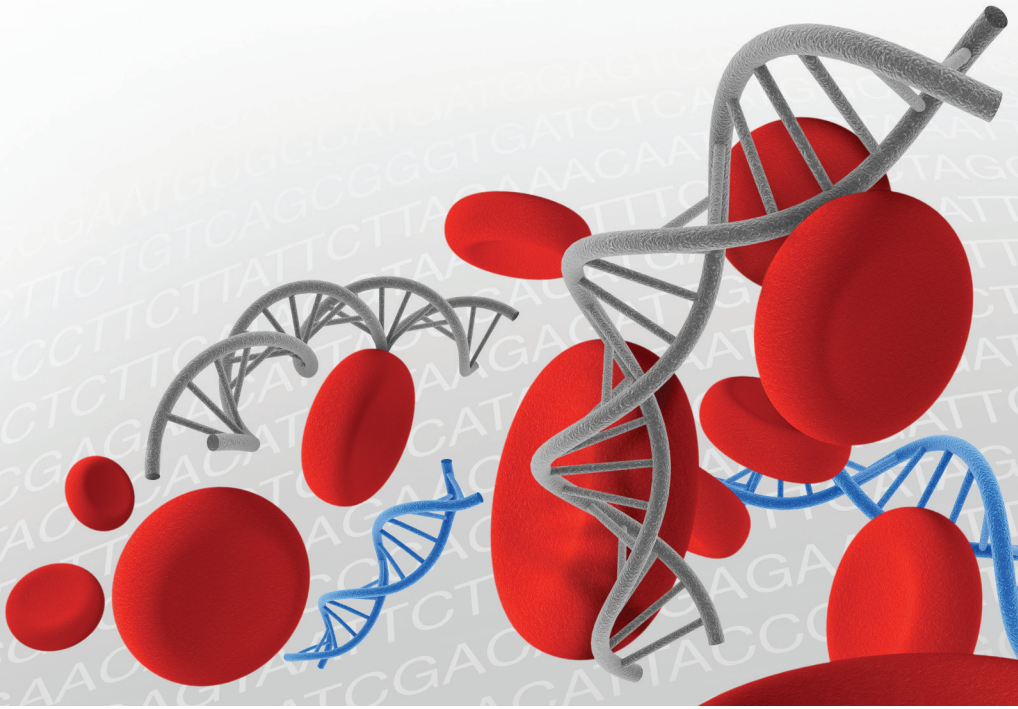
De Mattos-Arruda L, Mayor R, Ng CK, et al. Cerebrospinal fluid-derived circulating tumour DNA better represents the genomic alterations of brain tumours than plasma. *Nat Commun.* 2015;6:8839.

Recommended Illumina workflow



Sequencing
HiSeq® 2500 System, HiSeq 3000 System, HiSeq 4000 System

Analysis
BWA Whole Genome Sequencing BaseSpace® App, Tumor Normal BaseSpace® App



Epigenetics

Studying the methylome of B cells

Findings

- Extensive CpG methylation changes during B cell maturation while non-CpG methylation disappeared upon B cell commitment.
- B cell neoplasms frequently acquire methylation changes in regions already undergoing dynamic methylation during normal B cell differentiation.

Method

The authors used bisulfite sequencing and methylation arrays to study the methylome of 10 B cell subpopulations spanning the entire differentiation program. An average of 22.7 million CpG sites were measured per sample.

Source

Kulis M, Merkel A, Heath S, et al. Whole-genome fingerprint of the DNA methylome during human B cell differentiation. *Nat Genet.* 2015;47:746-756.

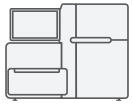
Supporting publications

Fan R, Toubal A, Goni S, et al. Loss of the co-repressor GPS2 sensitizes macrophage activation upon metabolic stress induced by obesity and type 2 diabetes. *Nat Med.* 2016;22:780-791.

Fang D, Gan H, Lee JH, et al. The histone H3.3K36M mutation reprograms the epigenome of chondroblastomas. *Science.* 2016;352(6291):1344-1348.

Recommended Illumina workflow

Library prep
TruSeq® DNA Methylation Kit,
TruSeq Methyl Capture EPIC Library Prep Kit



Sequencing
HiSeq® 2500 System, HiSeq 3000 System,
HiSeq 4000 System, HiSeq X Ten System

Analysis
MethylSeq BaseSpace® App,
MethylKit BaseSpace App

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Exome sequencing

Brain somatic mutations in MTOR cause focal cortical dysplasia type II leading to intractable epilepsy

Findings

- Researchers identified a *de novo* brain somatic mutation in the gene encoding the MTOR, along with 8 more somatic missense mutations from the focal cortical dysplasia type II (FCDII) cases studied.

Method

A whole-exome sequencing approach was utilized to determine if FCDII is associated with brain somatic mutations. They subsequently sequenced paired brain-blood DNA from 4 individuals with FCDII (read depth, 412-668X) and then performed deep sequencing of the MTOR gene in 73 additional subjects.

Source

Lim JS, Kim WI, Kang HC, et al. Brain somatic mutations in MTOR cause focal cortical dysplasia type II leading to intractable epilepsy. *Nat Med.* 2015;21:395-400.

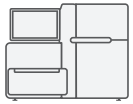
Supporting publications

Chubb D, Broderick P, Dobbins SE, et al. Rare disruptive mutations and their contribution to the heritable risk of colorectal cancer. *Nat Commun.* 2016;7:11883.

Huang L, Zhang H, Cheng CY, et al. A missense variant in FGD6 confers increased risk of polypoidal choroidal vasculopathy. *Nat Genet.* 2016;48:640-647.

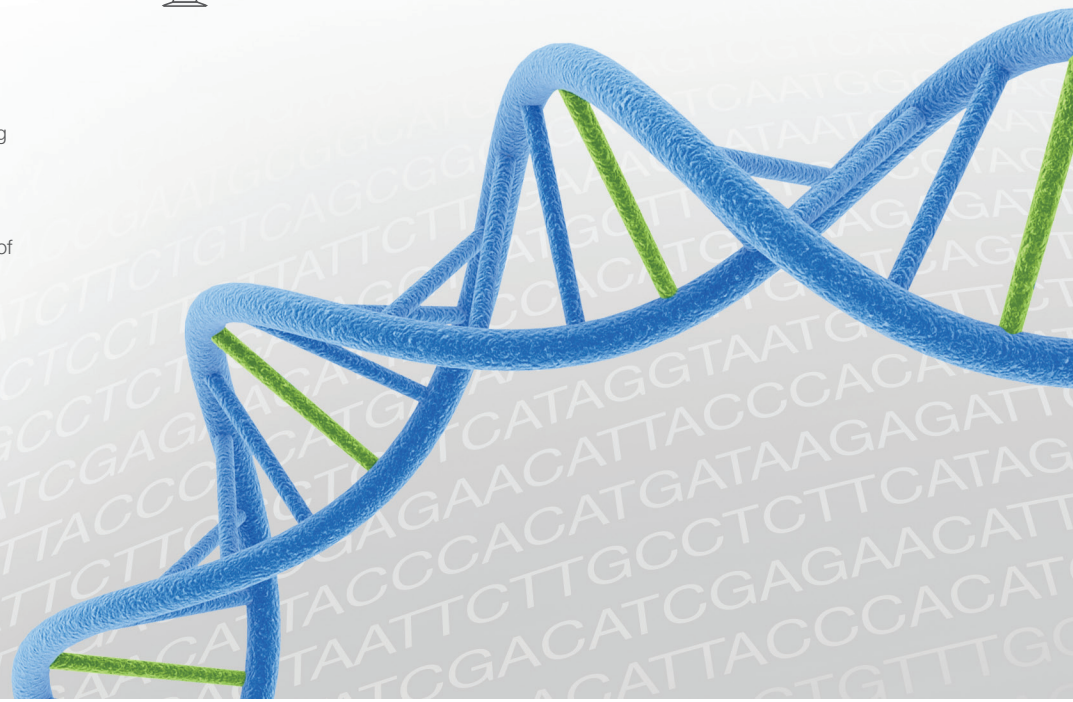
Recommended Illumina workflow

Library prep
TruSeq® Exome Library Prep Kit,
TruSeq Rapid Exome Library Prep Kit



Sequencing
HiSeq® 2500 System, HiSeq 3000 System,
HiSeq 4000 System

Analysis
Enrichment BaseSpace® App



Integrative genomics

Genomic analyses identify molecular subtypes of pancreatic cancer

Findings

- Identified 32 recurrently mutated genes that aggregated in 10 pathways and 4 tumor subtypes.
- Demonstrated that each tumor subtype is enriched for different mutations and has different histopathological, epigenetic, and transcriptional characteristics.

Method

The authors combined exome sequencing, whole-genome sequencing, methylation, and RNA sequencing to study 456 pancreatic ductal adenocarcinomas.

Source

Bailey P, Chang DK, Nones K, et al. Genomic analyses identify molecular subtypes of pancreatic cancer. *Nature.* 2016;531:47-52.

Supporting publications

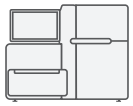
Patch AM, Christie EL, Etemadmoghadam D, et al. Whole-genome characterization of chemoresistant ovarian cancer. *Nature.* 2015;521(7553):489-494.

Gascard P, Bilenky M, Sigaroudinia M, et al. Epigenetic and transcriptional determinants of the human breast. *Nature.* 2015;6(6351).

Recommended Illumina workflow

Library prep

TruSeq® Exome Library Prep Kit, TruSeq Rapid Exome Library Prep Kit, TruSeq DNA PCR-Free Library Prep Kit, TruSeq Nano DNA Library Prep Kit, TruSeq DNA Methylation Kit, TruSeq Methyl Capture EPIC Kit, TruSeq Stranded Total RNA Library Prep Kit, TruSeq Stranded mRNA Library Prep Kit



Sequencing

HiSeq® 2500 System, HiSeq 3000 System, HiSeq 4000 System, HiSeq X Ten System

Analysis

BaseSpace® Sequence Hub, BaseSpace Correlation Engine, BaseSpace Cohort Analyzer

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Whole-genome sequencing

Large-scale whole-genome sequencing of the Icelandic population

Findings

- Researchers discovered 20 million SNPs and 1.5 million insertions-deletions (indels) in 2,636 Icelanders. Data revealed an excess of homozygosity and rare protein-coding variants in the Icelandic population.
- 61.6% of variants with a minor allele frequency of < 0.1% were found to be loss of function, 46.4% were moderate impact, 37.5% were low impact, and 36.0% were other categories.
- An association was found between a recessive frameshift mutation in MYL4 and early onset atrial fibrillation, multiple mutations in ABCB4 associated with the risk of liver disease, and an intronic variant in GNAS associated with increased thyroid-stimulating hormone levels when inherited maternally.

Method

The authors performed whole-genome sequencing on 2,636 Icelanders to provide a comprehensive understanding of the Icelandic population. Data served as the basis to impute the associations between variants in sequence and phenotype.

Source

Gudbjartsson DF, Helgason H, Gudjonsson SA, et al. Large-scale whole-genome sequencing of the Icelandic population. *Nat Genet.* 2015;47:435-444.

Supporting publications

Yano K, Yamamoto E, Aya K, et al. Genome-wide association study using whole-genome sequencing rapidly identifies new genes influencing agronomic traits in rice. *Nat Genet.* 2016;48(8):927-934.

Goldmann JM, Wong WS, Pinelli M, et al. Parent-of-origin-specific signatures of de novo mutations. *Nat Genet.* 2016;48(8):935-939.

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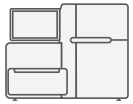
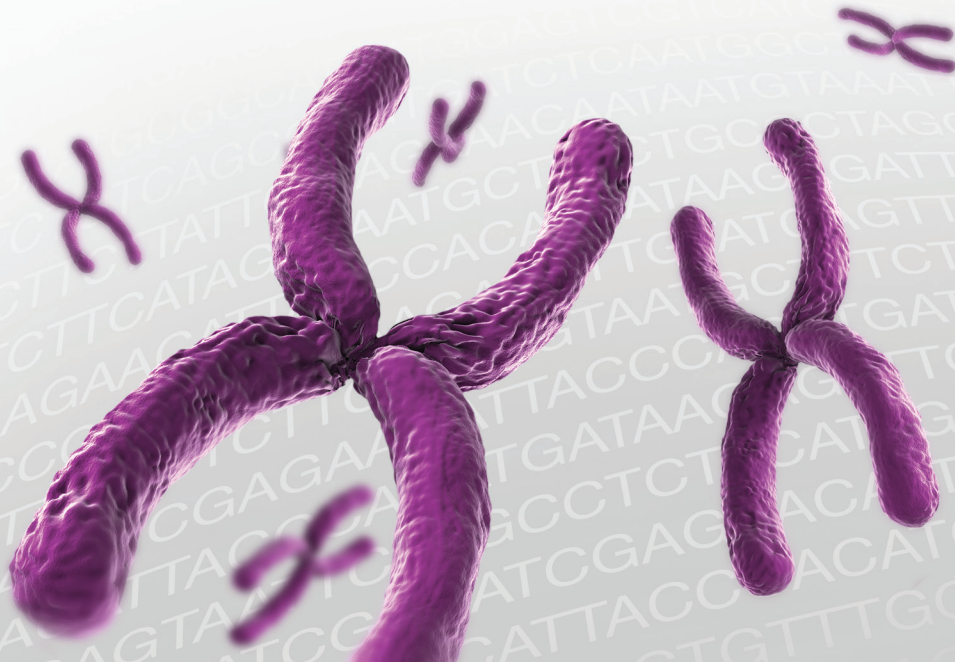
Recommended Illumina workflow

Library prep
TruSeq® DNA PCR-Free Library Prep Kit,
TruSeq Nano DNA Library Prep Kit



Sequencing
HiSeq® 2500 System, HiSeq 3000 System,
HiSeq 4000 System, HiSeq X System

Analysis
VariantStudio Software, BaseSpace® Variant Interpreter,
Whole Genome Sequencing BaseSpace® App



Whole-transcriptome sequencing

Comprehensive RNA profiling of villous trophoblast and decidua basalis in pregnancies complicated by preterm birth following intra-amniotic infection

Findings

- Researchers identified 128 unique long transcripts and 7 mature microRNAs that were differentially expressed between pregnancies complicated by intra-amniotic infection(IAI)-induced preterm birth (PTB).
- A transcriptional signature consistent with acute inflammation in the villous trophoblast (VT) was identified, highlighting novel signaling pathways involved in IAI, suggesting putative therapeutic targets and potential biomarkers associated with IAI-induced PTB.

Method

RNA sequencing was performed on 15 paired placental VT and decidua basalis (DB) specimens. Fifteen samples included 5 cases of spontaneous PTB in the setting of amniocentesis-proven IAI and histological chorioamnionitis, 5 cases of spontaneous idiopathic PTB, and 5 cases of physiologic term pregnancy.

Source

Ackerman WE IV, Buhimschi IA, Eidem HR, et al. Comprehensive RNA profiling of villous trophoblast and decidua basalis in pregnancies complicated by preterm birth following intra-amniotic infection. *Placenta.* 2016;44:23-33.

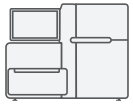
Supporting publications

Atianand MK, Hu W, Satpathy AT, et al. A long noncoding RNA lincRNA-EPS acts as a transcriptional brake to restrain inflammation. *Cell*. 2016;165:1672-1685.

McCullen MV, Li H, Cam M, Sen SK, McVicar DW, Anderson SK. *Genes Immun*. 2016;17(6):349-357.

Recommended Illumina workflow

Library prep
TruSeq® Stranded Total RNA Library Prep Kit,
TruSeq Stranded mRNA Library Prep Kit



Sequencing
HiSeq® 2500 System, HiSeq 3000 System,
HiSeq 4000 System

Analysis
RNA-Seq Alignment BaseSpace® App,
Cufflinks Assembly & DE BaseSpace App

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Single-cell sequencing

G&T-Seq: parallel sequencing of single-cell genomes and transcriptomes

Findings

- Researchers discovered cellular properties that could not have been inferred by the use of DNA or RNA sequencing alone.

Method

The authors developed a method called genome and transcriptome sequencing (G&T-Seq). The protocol enables the separation and sequencing of genomic DNA and full-length mRNA from single cells. Single cells were isolated and lysed. RNA was captured using biotinylated oligo (dT) capture primers and separated from DNA using streptavidin-coated magnetic beads. The Smart-seq2 method was used to amplify captured RNA on the bead, and the MDA method was used to amplify DNA.

Source

Wu J, Huang B, Chen H, et al. G&T-seq: parallel sequencing of single-cell genomes and transcriptomes. *Nat Methods.* 2015;12:519-522.

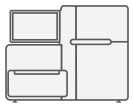
Supporting publications

Wu J., Huang B., Chen H., et al. The landscape of accessible chromatin in mammalian preimplantation embryos. *Nature.* 2016;534(7609):652-657.

Tasic B, Menon V, Nguyen T, et al. Adult mouse cortical cell taxonomy revealed by single cell transcriptomics. *Nat Neurosci.* 2016;19:335-346.

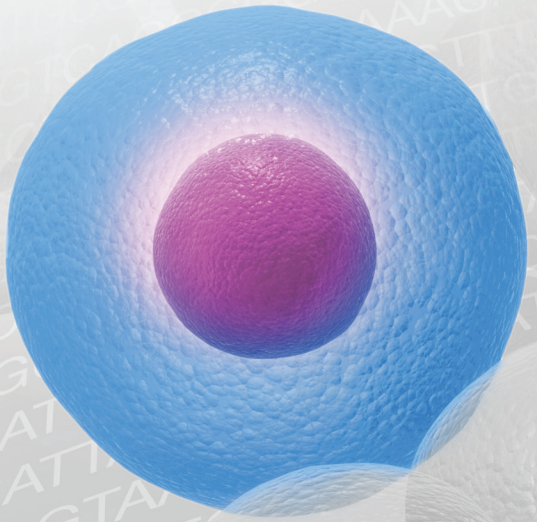
Recommended Illumina workflow

Library prep
Single-cell suspension,
Nextera® XT DNA Library Prep Kit



Sequencing
HiSeq® 2500 System, HiSeq 3000 System,
HiSeq 4000 System

Analysis
BaseSpace® Sequence Hub



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