CELEMICS

Your trusted partner for NGS solution

2022

CELEMICS CUSTOMER PUBLICATIONS

Past Client Cases with Summaries

Celemics provides results that can be trusted by customers.

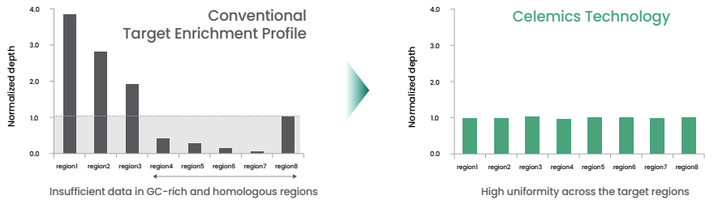
Targeted Sequencing Solution

At Celemics, we support our customers through target hybridization-based NGS services and products individually designed and manufactured by experienced researchers and technicians. We have established a robust system for customized design panels and developed a variety of kits according to our customer's needs.

All Ready-to-use kits are completely validated and provide industry leading market performance. Our research team has designed and manufactured over a thousand customized panels, and promises to offer products and services of the highest quality to our customers.

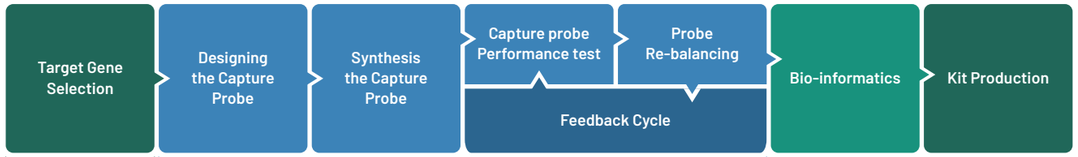
Probe Design Technology

Market Need and Celemics' Solution



Panel Manufacturing Process

Market Need and Celemics' Solution



With our development experience and know-how from designing over 1,000 customized panels, we provide fully optimized custom target enrichment panels for our customers.

High Compatibility
Illumina, Ion Torrent, Pacific Bioscience, MGISeq

Provides Pre-performance validation data
Customers can check the panel performance before receiving the product.

High Uniformity and Coverage by Re-balancing technology
Generate high quality data / High sensitivity analysis

BTSeq™ - Barcode Targeted Sequencing

Celemics has developed sample preparation techniques and bioinformatics software enabling cost-effective workflow. BTSeq™ provides highly accurate results with short turnaround time (TAT) by effectively correcting sequencing error and generating consensus sequences through Celemics' proprietary techniques.

BTSeq™ (Barcode Tagged Sequencing)

High Accuracy Achieved by NGS-Based BTSeq™ Sequencing Service

Wide Range of DNA Sizes
No limitation of DNA size : 200 bp - 20 kb or longer
Plasmid sequencing with large insert DNA

NGS-based, High Sequencing Accuracy
NGS-based high sequencing quality
Digitized sequencing results

No Limitation of Origin
Sequencing samples of various species
Virus, Bacteriophage, Mycobiome, etc.

Fast TAT, No Need for Primer Walking
NGS-based result, within 24 hours after sample arrival
No need of repetitive primer synthesis
No need of repetitive Sanger sequencing cycles

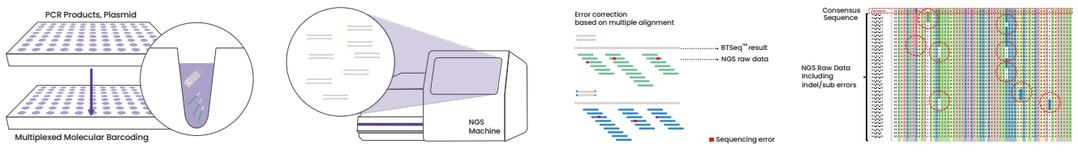
Cost-effective
Unparalleled cost-effectiveness compared to Sanger
Only sequencing primer information required, eliminating the need of sequencing primer synthesis

No Need of High Concentration Sample
Compatible with unpurified PCR products
Low-amount sample requirements as little as 10 ng/μl

BTSeq™ Service Process

High Accuracy Achieved by NGS-Based BTSeq™ Sequencing Service

Sample Preparation → NGS Analysis → Data Processing → Statistical & Bioinformatics Analysis



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VIRUS & BACTERIA

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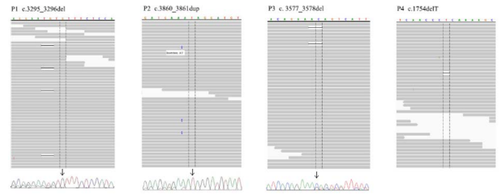
Oncology
Solid, Somatic / Germline

1. BMC Med Genomics. 2019 Jul

CANCER | SOMATIC | GERMLINE | FFPE | WGS

Next-generation sequencing with comprehensive bioinformatics analysis facilitates somatic mosaic APC gene mutation detection in patients with familial adenomatous polyposis

Cancer Type	Colorectal Cancer
Sample	28 Patients with familial adenomatous polyposis
Study purpose	Analyzing peripheral blood samples from patients with unexplained FAP using NGS to estimate the frequency of somatic mosaic mutations in the APC gene.
Main data	Visual verification of variants with Integrative Genomic Viewer (IGV) and sequencing chromatogram with secondary confirmation test results.



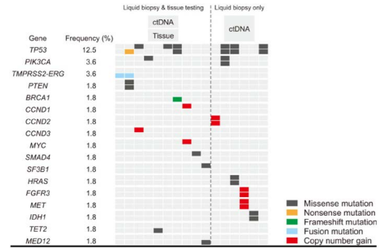
Conclusion	The NGS with an adequate combination of bioinformatics tools is effective to detect low level somatic variants in a single assay.

2. Inverstig Clin Urol. 2021 Mar

CANCER | SOMATIC | GERMLINE | CTDNA | CUSTOMIZED PANEL

Genomic mutation profiling using liquid biopsy in Korean patients with prostate cancer: Circulating tumor DNA mutation predicts the development of castration resistance

Cancer Type	Prostate Cancer (ctDNA)
Sample	Plasma samples from 56 prostate cancer patients
Study purpose	To investigate germline and somatic mutation profiles in Korean patients with prostate cancer using liquid biopsy and solid tissue testing
Main data	Somatic mutations detected by liquid biopsy and solid cancer tissue testing in 56 patients with prostate cancer.



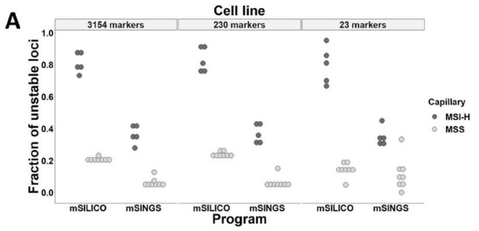
Conclusion	Korean patients with prostate cancer showed a relatively low germline mutation rate compared to other ethnicities. The ctDNA mutations detected by liquid biopsy can predict the development of castration resistance in patients with mHSPC.

3. PLoS One. 2021 Feb

CANCER | SOMATIC | GERMLINE | MSI/TMB | CUSTOMIZED PANEL

Targeted next-generation sequencing-based detection of microsatellite instability in colorectal carcinomas

Cancer Type	Colorectal Cancer
Sample	13 CRC cell lines, 84 fresh and 119 formalin-fixed CRC tissues
Study purpose	Developing a computational method and panel markers to assess microsatellite instability (MSI) using a targeted next-generation sequencing (NGS) platform
Main data	Comparison of the performances of mSILICO and mSINGS in the detection of microsatellite instability.



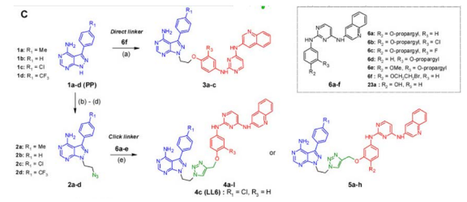
Conclusion	We developed a new computational method and microsatellite marker panels for the determination of MSI that does not require paired normal tissues.

4. Theranostics. 2021 Jan

CANCER | SOMATIC | CUSTOMIZED PANEL

Development of the phenylpyrazolo [3, 4-d] pyrimidine-based, insulin-like growth factor receptor/Src/AXL-targeting small molecule kinase inhibitor

Cancer Type	Lung Cancer
Sample	Human lung cancer cell lines
Study purpose	The development of novel multitarget anticancer drugs that block IGF-1R, Src, and AXL is urgently needed.
Main data	Synthesis of LL6 and determination of its cellular targets.



Conclusion	Our results show the potential of LL6 as a novel IGF-1R/Src/AXL-targeting small molecule kinase inhibitor, providing a new avenue for anticancer therapies.

References

1. BMC Med Genomics. 2019 Jul 3;12(1):103. doi: 10.1186/s12920-019-0553-0.
2. Investig Clin Urol. 2021 Mar;62(2):224-232. doi: 10.4111/icu.20200406.
3. PLoS One. 2021 Feb 1;16(2):e0246356. doi: 10.1371/journal.pone.0246356.
4. Theranostics. 2021 Jan 1;11(4):1918-1936. doi: 10.7150/thno.48865.

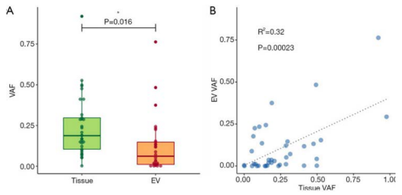
Oncology | Solid, Somatic / Germline

5. Transl Lung Cancer Res. 2021 Jan

CANCER | SOMATIC | CELEMAG CLEAN-UP BEADS

Genomic profiling of extracellular vesicle-derived DNA from bronchoalveolar lavage fluid of patients with lung adenocarcinoma

Cancer Type	Lung Cancer
Sample	20 patients with lung adenocarcinoma
Study purpose	Investigating the reliability of BALF-EV as a source for DNA of sufficient quality and at adequate quantities for use in NGS analysis for the detection of somatic mutations in EGFR-mutated lung adenocarcinoma in comparison with that of tissue DNA.
Main data	VAF of clinically significant putative somatic mutations.



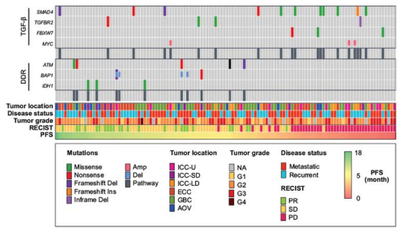
Conclusion	BALF EV DNA in patients with NSCLC can be a reliable DNA source for targeted NGS for the identification of actionable genetic alterations

6. Hepatology. 2021 Oct

CANCER | SOMATIC | CANCE MASTER

Molecular Characterization of Biliary Tract Cancer Predicts Chemotherapy and PD-1/PD-L1 Blockade Responses

Cancer Type	Biliary tract cancer (BTC)
Sample	121 advanced BTC patients
Study purpose	To identify the molecular features of treatment responses to chemotherapy and immunotherapy in BTCs.
Main data	Molecular alterations associated with systemic chemotherapy response in biliary tract cancer



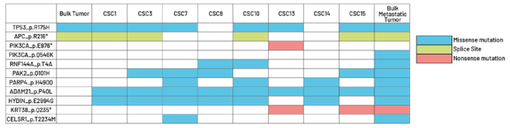
Conclusion	This study proposes predictive molecular features of chemotherapy and immunotherapy responses in advanced BTCs using clinical sequencing platforms. Our result provides an intuitive framework to guide the treatment of advanced BTCs benefiting from therapeutic agents based on the tumors' molecular features.

7. Biochem Biophys Res Commun. 2021 Jun

CANCER | SOMATIC | TOPQXSEP MAGBEAD | WGS

Phenotype-based single cell sequencing identifies diverse genetic subclones in CD133 positive cancer stem cells

Cancer Type	Colorectal Cancer
Sample	Frozen colon cancer tissues from 5 patients
Study purpose	Articulating the presence of heterogeneous subclones within CD133 positive cancer stem cells through single cell sequencing.
Main data	Mutations in single CSCs also identified in metastatic tumor tissue.



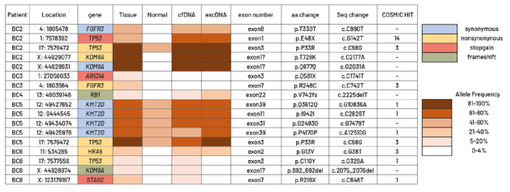
Conclusion	this study investigated heterogenous subclones of CD133-positive CSCs by novel single cell isolation method, and suggested that CSCs in primary colorectal tumors possess genetic subclones each sharing genetic profiles with subsequent liver metastatic tissue of the same patient

8. Sci Rep. 2018 Oct

CANCER | SOMATIC | CTDNA | CUSTOMIZED PANEL

Urinary Exosomal and cell-free DNA Detects Somatic Mutation and Copy Number Alteration in Urothelial Carcinoma of Bladder

Cancer Type	Urothelial bladder carcinoma (UBC)
Sample	9 tumor tissues and 9 matched blood samples and 9 urine samples
Study purpose	to assess the availability of cell-free DNA (cfDNA) and exosomal DNA (exoDNA) in urine as a source for liquid biopsy in UBC.
Main data	Somatic mutations identified in bladder cancer and genomic profiling in matched urinary cell free DNA and exosomal DNA.



Conclusion	Using cfDNA and exoDNA, we successfully identified somatic mutations and CNVs of UBC and we demonstrated that urinary exoDNA could be another source of liquid biopsy.

References

1. Transl Lung Cancer Res. 2021 Jan;10(1):104-116. doi: 10.21037/tlcr-20-888.
2. Hepatology. 2021 Oct;74(4):1914-1931. doi: 10.1002/hep.31862.
3. Biochem Biophys Res Commun. 2021 Jun 18;558:209-215. doi: 10.1016/j.bbrc.2020.09.005.
4. Sci Rep. 2018 Oct 2;8(1):14707. doi: 10.1038/s41598-018-32900-6.

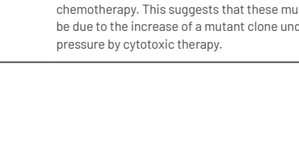
Oncology | Solid, Somatic / Germline

9. Commun Biol. 2020 Apr

CANCER | SOMATIC | CUSTOMIZED PANEL

Single-cell analysis of a mutant library generated using CRISPR-guided deaminase in human melanoma cells

Cancer Type	Melanoma
Sample	BE3-blasticidin fragment inserted piggyBac-BE3-GFP plasmid
Study purpose	We demonstrate a previously unreported method combining CRISPR RNA-guided deaminase and CROP-Seq technology that enables the introduction of SNVs in multiple genes and screening of the impact on function in addition to analyses of perturbations in single cells.
Main data	Introduction and functional screening of multiple mutations using population analysis



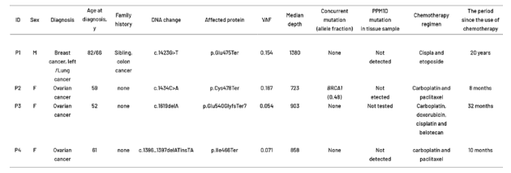
Conclusion	According to our simulation, our system could cover 36,211 missense mutations and 3,491 nonsense mutations among the mutations listed in the CGC7. This indicates that a large proportion of known cancer-related mutations could be generated and examined using our system.

10. PLoS One. 2019 Jun

CANCER | SOMATIC | FFPE | CUSTOMIZED PANEL

Somatic mosaic truncating mutations of PPM1D in blood can result from expansion of a mutant clone under selective pressure of chemotherapy

Cancer Type	Breast and Ovarian cancer
Sample	Peripheral Blood samples from 1,195 patients, including 719 patients with breast cancer and 240 with ovarian cancer
Study purpose	To identify whether the PPM1D mutation predisposes patients to such cancers or if it results from the cancer and therapy, somatic PPM1D mutations in association with previous cancer and chemotherapy need to be explored.
Main data	Characteristics of PPM1D truncating mutation carriers.



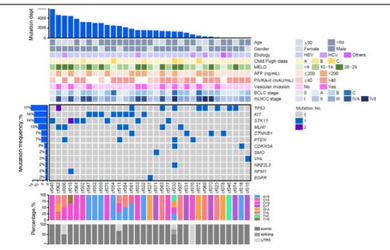
Conclusion	We investigated somatic mosaic PPM1D mutations in patients with various cancers, including breast and ovarian cancers and found that all four patients bearing the truncating mutations had a history of cisplatin-based chemotherapy. This suggests that these mutations may be due to the increase of a mutant clone under selective pressure by cytotoxic therapy.

11. Sci Rep. 2020 Oct

CANCER | SOMATIC | CTDNA | CUSTOMIZED PANEL

MLH1 single-nucleotide variant in circulating tumor DNA predicts overall survival of patients with hepatocellular carcinoma

Cancer Type	Hepatocellular carcinoma (HCC)
Sample	A total of 146 consecutive treatment-naïve patients with HCC
Study purpose	We aimed to identify novel single-nucleotide variants (SNVs) in circulating tumor DNA (ctDNA) in patients with HCC.
Main data	SNV landscape of 33 patients with HCC who tested positive for SNVs using ctDNA sequencing of 69 cancer genes.



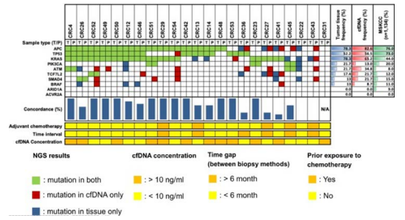
Conclusion	MLH1 SNV detection in ctDNA is feasible, and thus, ctDNA can be used to confidently detect somatic mutations in HCC tissue.

12. Cancer Res Treat. 2018 Jul

CANCER | SOMATIC | CTDNA | CUSTOMIZED PANEL

Liquid biopsy-based tumor profiling for metastatic colorectal cancer patients with ultra-deep targeted sequencing

Cancer Type	Colorectal cancer
Sample	54 patients with metastatic colorectal cancer
Study purpose	we devised a simple bioinformatics pipeline for discovering somatic mutations, which removes sequencing errors from true mutation signals during ultra-deep targeted sequencing of cfDNA from patients with cancer.
Main data	Actionable cfDNA mutations detected by ultra-deep targeted sequencing.



Conclusion	The current study showed that use of optimized somatic calling may allow detection of clinically actionable somatic mutations in plasma ctDNA.

References

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2. PLoS One. 2019 Jun 26;14(6):e0217521. doi: 10.1371/journal.pone.0217521.
3. Sci Rep. 2020 Oct 20;10(1):17862. doi: 10.1038/s41598-020-74494-y.
4. PLoS One. 2020 May 7;15(5):e0232754. doi: 10.1371/journal.pone.0232754.

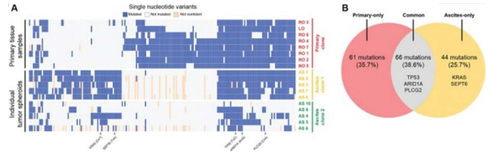
Oncology | Solid, Somatic / Germline

13. Sci Rep. 2018 Aug

CANCER | SOMATIC | TOPQXSEP MAGBEAD | WGS

Evaluating Tumor Evolution via Genomic Profiling of Individual Tumor Spheroids in a Malignant Ascites

Cancer Type	Ovarian Cancer
Sample	A 42 yr old female patient diagnosed with primary high-grade serous ovarian cancer (Grade 3, stage IIIC) presented with malignant ascites and peritoneal seeding.
Study purpose	To uncover the genetic heterogeneity of tumor cells in malignant ascites, we introduced a genetic profiling method for individual tumor spheroids which are the common form of tumor cells floating in malignant ascites.
Main data	SNV analysis based on the WES data.



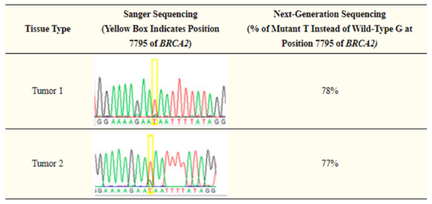
Conclusion	From the sequencing data, we discovered clonal or subclonal somatic CNAs and SNVs, based on which we constructed phylogenetic trees and inferred the evolutionary history of tumor cells in the patient. As a result, we found that the tumor cells in the malignant ascites were an independent lineage from the primary tumor.

14. Cancers. 2021 May

CANCER | SOMATIC | GERMLINE | FFPE | ONCORISK

The Combination of Single-Cell and Next-Generation Sequencing Can Reveal Mosaicism for BRCA2 Mutations and the Fine Molecular Details of Tumorigenesis

Cancer Type	Ovarian Cancer
Sample	Ovarian Cancer Patient (The patient is 66 years old, female)
Study purpose	We establish a diagnostic pipeline using high-resolution microscopy and laser microcapture microscopy to test for BRCA1/2 mutations in the tumor at the single-cell level, followed by deep next-generation sequencing of various tissues from the patient.
Main data	Summary of the results of the Sanger and next-generation sequencing on different tissues from the patient



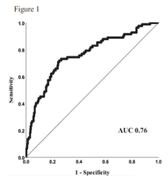
Conclusion	To show the power of our approach, we used it to compare the BRCA2 mutational status of tumor samples with several nontumorous tissues from an ovary cancer patient. We proved that the patient showed a mosaic pattern in the case of the BRCA2 c.7795G>T mutation and, based on our results, we conclude that this mutation occurred de novo, during early embryonic development.

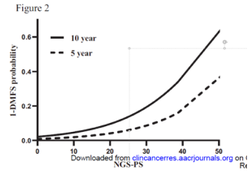
15. Clin Cancer Res. 2020 Dec

CANCER | SOMATIC | FFPE | CUSTOMIZED PANEL

Development and validation of a next-generation sequencing-based multigene assay to predict the prognosis of estrogen receptor-positive, HER2-negative breast cancer

Cancer Type	Breast Cancer
Sample	250 and 93 archived breast cancer samples with a known recurrence score in the training and verification sets. The assay was validated in 413 independent samples with long-term follow-up data on distant metastasis.
Study purpose	This study aimed to develop and validate an NGS-based multigene assay to predict the distant recurrence risk.
Main data	Receiver operating characteristic curve of NGS-Prognostic Score classified for distant recurrence and Probability of distant recurrence at 5 and 10 years based on NGS-Prognostic Scores.





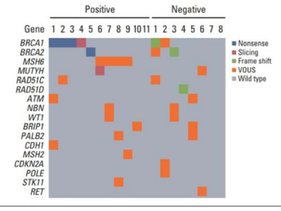
Conclusion	The newly developed and validated NGS-based multigene assay can predict the distant recurrence risk in ER-positive, HER2-negative breast cancer.

16. Cancer Res Treat. 2018 Jul

CANCER | SOMATIC | ONCORISK

Comparison of Clinical Features and Outcomes in Epithelial Ovarian Cancer according to Tumorigenicity in Patient-Derived Xenograft Models

Cancer Type	Epithelial ovarian cancer (EOC)
Sample	88 EOC patients who underwent primary or interval debulking surgery.
Study purpose	To evaluate whether tumorigenicity was associated with the clinical features and outcomes of EOC patients.
Main data	Comparison of germline mutation spectra relative to tumorigenicity using a 35-multigene panel next-generation sequencing assay. VOUS, variants of unknown significance.



Conclusion	Tumorigenicity in a xenograft model was a strong prognostic factor and was associated with more aggressive tumors in EOC patients.

References

1. Sci Rep. 2018 Aug 24;8(1):12724. doi: 10.1038/s41598-018-31097-y.
2. Cancers. 2021 May 13;13(10):2354. doi: 10.3390/cancers13102354.
3. Clin Cancer Res. 2020 Dec 15;26(24):6513-6522. doi: 10.1158/1078-0432.CCR-20-2107.
4. Cancer Res Treat. 2018 Jul;50(3):956-963. doi: 10.4143/crt.2017.181

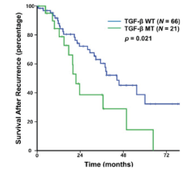
Oncology | Solid, Somatic / Germline

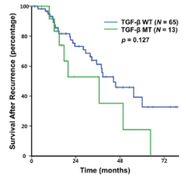
17. BMC Cancer. 2019 May

CANCER | SOMATIC | FFPE | CUSTOMIZED PANEL

Association of pathway mutation with survival after recurrence in colorectal cancer patients treated with adjuvant fluoropyrimidine and oxaliplatin chemotherapy

Cancer Type	Colorectal cancer (CRC)
Sample	Of the 516 patients with stage III or high-risk stage II CRC patients treated with surgery and adjuvant chemotherapy, 87 who had distant recurrence were included in the present study.
Study purpose	The purpose of this study was to assess the association between pathway mutations and survival after recurrence.
Main data	TGF-β pathway mutation and survival after recurrence / TGF-β pathway mutation and survival after recurrence in Non-MAC patients.





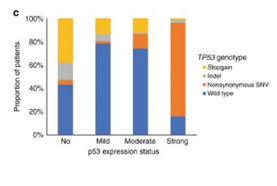
Conclusion	Mutation in genes within TGF-β pathway may have negative prognostic role for SAR in CRC. Other pathway mutations were not associated with SAR.

18. Br J Cancer. 2019 Apr

CANCER | SOMATIC | MSI/TMB | CUSTOMIZED PANEL

p53 expression status is associated with cancer-specific survival in stage III and high-risk stage II colorectal cancer patients treated with oxaliplatin-based adjuvant chemotherapy

Cancer Type	Colorectal cancer (CRC)
Sample	We analysed CRCs (N = 621) for the presence of TP53 alterations and for p53 expression, using targeted resequencing and immunohistochemistry.
Study purpose	We attempted to elucidate whether p53 expression or TP53 mutation status was associated with cancer-specific survival in adjuvant FOLFOX-treated patients with stage III or high-risk stage II colorectal cancer.
Main data	Correlation between p53 expression and TP53 genotype



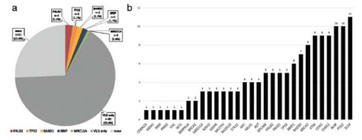
Conclusion	p53-mild expression status was found to be an independent prognostic marker in adjuvant FOLFOX-treated patients with stage III and high-risk stage II CRC.

19. BMC Cancer. 2018 Jan

CANCER | GERMLINE | ONCORISK

Variants of cancer susceptibility genes in Korean BRCA1/2 mutation-negative patients with high risk for hereditary breast cancer

Cancer Type	Breast Cancer
Sample	120 patients who were negative for BRCA1/2 mutations, but had been diagnosed with breast cancer
Study purpose	Evaluating the incidence and spectrum of pathogenic and likely pathogenic variants of cancer susceptibility genes in BRCA1/2 mutation-negative Korean patients with a high risk for hereditary breast cancer using a comprehensive multigene panel that included 35 cancer susceptibility genes.
Main data	Percentage of patients with pathogenic or likely pathogenic mutations corresponding with each gene and number of patients with variants of uncertain significance (VUS) for each gene



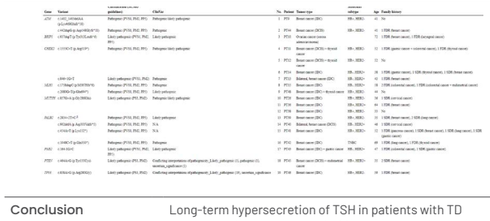
Conclusion	These combined results demonstrate that multigene panels offer an alternative strategy for identifying veiled pathogenic and likely pathogenic mutations in breast cancer susceptibility genes.

20. Cancer Sci. 2020 Oct

CANCER | GERMLINE | CUSTOMIZED PANEL

Exon splicing analysis of intronic variants in multigene cancer panel testing for hereditary breast/ovarian cancer

Cancer Type	Pan-Cancer
Sample	700 patients who were suspected of a familial predisposition to cancer
Study purpose	We employed a comprehensive multigene panel that included 23 known or suspected cancer susceptibility genes to test Korean patients suspected of HBOC.
Main data	Characteristics of BRCA 1/2-variant-negative patients with pathogenic/likely pathogenic variants in other cancer-associated genes



Conclusion	Long-term hypersecretion of TSH in patients with TD may induce the development of thyroid cancer through direct stimulation as a growth factor and indirect changes in thyroid tissue that result in a precancerous fibrotic condition.

References

1. BMC Cancer. 2019 May 6;19(1):421. doi: 10.1186/s12885-019-5650-0.
2. Br J Cancer. 2019 Apr;120(8):797-805. doi: 10.1038/s41416-019-0429-2.
3. BMC Cancer. 2018 Jan 16;18(1):83. doi: 10.1186/s12885-017-3940-y.
4. Cancer Sci. 2020 Oct;111(10):3912-3925. doi: 10.1111/cas.14600.

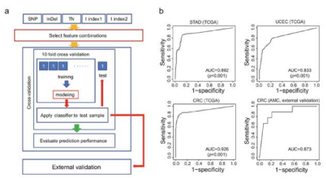
Oncology | Solid, Somatic / Germline

21. NPJ Genom Med. 2020 Jan

CANCER | SOMATIC | MSI/TMB | CUSTOMIZED PANEL

Spontaneous mutations in the single TTN gene represent high tumor mutation burden

Cancer Type	Pan-Cancer
Sample	Whole-exome sequencing (WES) data from the pan-cancer cohort (n = 10,224) of TCGA, and targeted sequencing (tNGS) and TTN gene sequencing from 24 colorectal cancer samples (AMC cohort)
Study purpose	we examined if mutation status within a single gene could be representative of TMB as assessed by larger-scale sequencing such as WES or tNGS.
Main data	Prediction model construction using TTN-TMB and association between immunostimulatory signature and mutation.



Conclusion	We demonstrated that mutation count in a single gene, TTN, can be used to estimate TMB.

22. Clin Chim Acta. 2021 Oct

CANCER | GERMLINE | CUSTOMIZED PANEL

Evaluation of a hybridization capture-based hereditary cancer panel for the ion semiconductor-based next-generation sequencing system

Cancer Type	Hereditary cancer
Sample	31 samples that harbored gene variants of a hereditary cancer predisposition (HCP) panel and NA12878 reference material
Study purpose	We compared the analytic performance of Illumina's NextSeq and Ion S5 XL using a hybridization capture-based target enrichment method.
Main data	Sequencing run statistics and Analytical performance of next-generation sequencing (NGS) compared with Sanger sequencing and high-confidence calls of NA12878 reference materials

Parameter	Ion S5 XL	Illumina NextSeq 550Dx
Mapped Reads	1,933,120	962,134
Mean Read Length	167 bp	245 bp
On-target reads, %	82.3%	56.8%
Average base coverage depth	1,774x	324x
Target base coverage at 30x, %	100	100

Sequencer/variant caller	False positives, n	False negatives, n	True positives, n	True negatives, n	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Accuracy, % (95% CI)
S5 XL/ Torrent variant caller	0	2	66	83,055	97.06 (89.79-99.64)	100	100.00 (99.99-100.00)
Illumina NextSeq 550Dx/GATK	0	1	67	83,055	98.53 (92.08-99.86)	100	100.00 (99.99-100.00)

GATK, genome analysis toolkit; CI, confidence interval. *High-quality variants of NA12878 from Get-RM and NIST data set used to define true positive variant calls (http://www.ncbi.nlm.nih.gov/variation/tools/get-rm/) Zook et al. PMID 24477786).

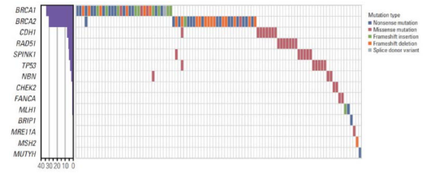
Conclusion	This study demonstrated that a hybrid capture panel kit can be successfully implemented using the ThermoFisher Scientific Ion S5 XL instrument and offers the opportunity to select a variety of hybridization-based capture panels from various manufacturers.

23. Cancer Res Treat. 2020 Jul

CANCER | GERMLINE | CUSTOMIZED PANEL

Detection of Germline Mutations in Breast Cancer Patients with Clinical Features of Hereditary Cancer Syndrome Using a Multi-Gene Panel Test

Cancer Type	Breast Cancer
Sample	496 breast cancer patients with clinical features of HBOC who underwent breast cancer surgery
Study purpose	We assessed the frequency of germline mutations using an next-generation sequencing (NGS)-based multiple-gene panel containing 64 cancer-predisposing genes in Korean breast cancer patients with clinical features of hereditary breast and ovarian cancer syndrome (HBOC).
Main data	Summary of 48 deleterious mutations in 95 patients.



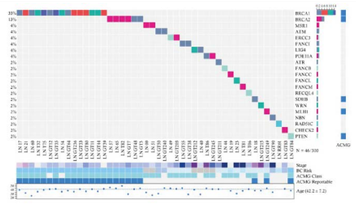
Conclusion	NGS-based multiple-gene panel testing improved the detection rates of deleterious mutations and provided a cost-effective cancer risk assessment.

24. Cancers. 2018 Sep

CANCER | GERMLINE | ONCORISK

Comprehensive Analysis of Germline Variants in Mexican Patients with Hereditary Breast and Ovarian Cancer Susceptibility

Cancer Type	Breast and Ovarian Cancer
Sample	327 patients were enrolled based on criteria established in the Genetic/Familial High-Risk Assessment: Breast and Ovarian of the National Comprehensive Cancer Network (NCCN) guidelines.
Study purpose	To determine the prevalence of pathogenic variants in cancer predisposing genes in Mexican patients
Main data	Allelic distribution of the pathogenic variants in patients with cancer.



Conclusion	Tumorigenicity in a xenograft model was a strong prognostic factor and was associated with more aggressive tumors in EOC patients.

References

1. NPJ Genom Med. 2020 Jan 14;5:33. doi: 10.1038/s41525-019-0107-6.
2. Clin Chim Acta. 2021 Oct;521:223-228. doi: 10.1016/j.cca.2021.07.018.
3. Cancer Res Treat. 2020 Jul;52(3):697-713. doi: 10.4143/crt.2019.559.
4. Cancers. 2018 Sep 27;10(10):361. doi: 10.3390/cancers10100361.

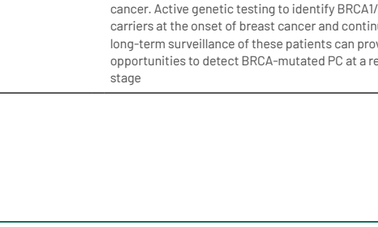
Oncology | Solid, Somatic / Germline

25. Thyroid. 2020 Nov

CANCER | GERMLINE | CUSTOMIZED PANEL

Anaplastic Thyroid Cancer Arising from Dyshormonogenetic Goiter: c.3070T>C and Novel c.7070T>C Mutation in the Thyroglobulin Gene

Cancer Type	Thyroid cancer
Sample	46-year-old woman with congenital thyroid dyshormonogenesis (TD) who had two germline thyroglobulin (TG) gene mutation
Study purpose	Describing a patient with TD caused by a TG gene mutation who developed anaplastic thyroid cancer, along with two siblings who had an identical TG gene mutation.
Main data	Family pedigree and DNA sequence analysis of two heterozygous TG gene mutations in the three sisters.



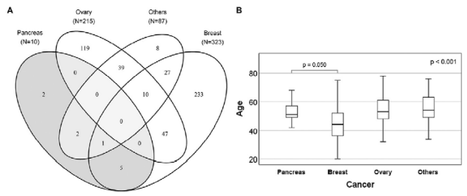
Conclusion	Long-term hypersecretion of TSH in patients with TD may induce the development of thyroid cancer through direct stimulation as a growth factor and indirect changes in thyroid tissue that result in a precancerous fibrotic condition.

26. Pancreatology. 2021 Apr

CANCER | GERMLINE | CUSTOMIZED PANEL

Biologic behavior of resected BRCA-mutated pancreatic cancer: Comparison with sporadic pancreatic cancer and other BRCA-related cancers

Cancer Type	Pancreatic cancer (PC)
Sample	493 patients who had pathogenic BRCA1/2 mutations were enrolled in the study
Study purpose	We investigated the oncologic characteristics of resected PC with BRCA mutation to suggest management strategies.
Main data	Distribution of the cancers for BRCA1/2 mutation carriers (N ¼ 493) and their onset age.



Conclusion	BRCA-mutated PC occurs later than BRCA-mutated breast cancer. Active genetic testing to identify BRCA1/2 mutation carriers at the onset of breast cancer and continuous long-term surveillance of these patients can provide opportunities to detect BRCA-mutated PC at a resectable stage

References

1. Thyroid. 2020 Nov;30(11):1676-1680. doi: 10.1089/thy.2020.0248.
2. Pancreatology. 2021 Apr;21(3):544-549. doi: 10.1016/j.pan.2021.02.007.

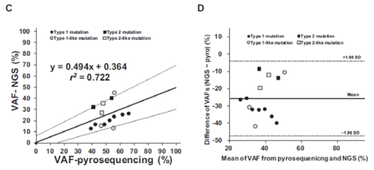
Oncology
Blood Cancer

27. Clin Chim Acta. 2018 Aug

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Pyrosequencing-based quantitative measurement of CALR mutation allele burdens and their clinical implications in patients with myeloproliferative neoplasms

Cancer Type	Myeloproliferative neoplasms (MPNs)
Sample	24 patients who had been diagnosed with MPN from 1997 to 2016 without JAK2 or MPL mutations.
Study purpose	We developed a pyrosequencing-based method for the quantification of CALR mutations and compared the results using Sanger sequencing, fragment length analysis (FLA), digital-droplet PCR (ddPCR), and next-generation sequencing (NGS).
Main data	Linear regression plots and Bland-Altman bias plots of the variant allele frequencies (VAFs) of CALR mutations between results measured by pyrosequencing and next generation sequencing (NGS)



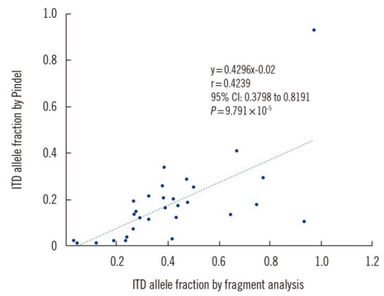
Conclusion	Pyrosequencing was a useful rapid sequencing method to determine the burden of CALR mutations.

28. Ann Lab Med. 2019 May

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

FLT3 Internal Tandem Duplication in Patients With Acute Myeloid Leukemia Is Readily Detectable in a Single Next-Generation Sequencing Assay Using the Pindel Algorithm

Cancer Type	Acute myeloid leukemia (AML)
Sample	Bone marrow aspirates of 229 patients
Study purpose	To determine whether FLT3 ITD mutations could be accurately identified from targeted multigene NGS data
Main data	Correlation of the ITD mutant allele fraction between fragment analysis and the Pindel (0.2.0) algorithm for patients harboring FLT3 ITD mutation.



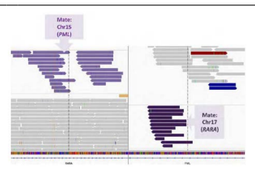
Conclusion	The Pindel algorithm was highly effective in detecting FLT3 ITD mutations in the NGS assessment of AML patients and was superior to GATK MuTect2.

29. PLoS One. 2019 Mar

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Targeted next generation sequencing can serve as an alternative to conventional tests in myeloid neoplasms

Cancer Type	Myeloid neoplasms
Sample	129 patients (95 were diagnosed with Acute myeloid leukemia, 31 were diagnosed with Myeloproliferative neoplasms, and three were diagnosed with Myelodysplastic syndrome)
Study purpose	We have designed a comprehensive next-generation sequencing assay to detect somatic mutations, translocations, and germline mutations in a single assay and have evaluated its clinical utility in patients with myeloid neoplasms.
Main data	With capture probes targeting intronic breakpoints, DNA sequencing could detect recurrent translocations



Conclusion	We demonstrated that NGS testing, as a single assay, can be a good supplement for a number of conventional molecular and cytogenetic tests through careful probe design and comprehensive bioinformatics analyses.

30. Ann Lab Med. 2021 May

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

A Case of Acute Myeloid Leukemia With inv(16)(p13.1q22):CBFB-MYH11 Presenting With Faggot Cells

Cancer Type	Acute Myeloid Leukemia (AML)
Sample	65-year-old woman
Study purpose	Unlike in other AMLs, in acute promyelocytic leukemia (APL), bleeding is the most common cause of early death. Thus, prompt treatment of patients with APL is necessary, and a presumptive APL diagnosis should be made
Main data	Characteristics of four AML cases with inv(16)(p13.1q22) with faggot cells

	Present case	Jerez et al. [4]	Garrastazu-Sánchez et al. [5]	Kim et al. [6]
Sex/age (yr)	F/65	M/32	M/36	M/12
Underlying disease	DM, colon adenoma	HIV infection, Hodgkin lymphoma	None	None
Initial CBC	WBC count 9.4 × 10^9/L Hb 95 g/L Platelet count 37 × 10^9/L	WBC count 67.4 × 10^9/L Hb 85 g/L Platelet count 10 × 10^9/L	WBC count 22.0 × 10^9/L Hb 98 g/L Platelet count 42 × 10^9/L	WBC count 20.85 × 10^9/L Hb 106 g/L Platelet count 55 × 10^9/L
Cytogenetic study	47,XX,inv(16)(p13.1q22),+22[17]/46,XX[3]	47,XY,+8,inv(16)(p13q22)[20]	inv(16) and hyperdiploidy of 52 chromosomes	47,XY,inv(16)(p13.1q22),+22[20]
Molecular study (rearrangement/variant)	*CBFB-MYH11 KIT* (p.Asp816Val)	*CBFB-MYH11*	*CBFB-MYH11 KIT* (p.Asp816Val)	*KIT* (p.Asp815Tyr)
Disease course	CR after induction CTx	CR after induction CTx	CR after induction CTx	Died two days after remission

Conclusion	We report a rare AML case with inv(16)(p13.1q22); CBFB-MYH11, resembling APL due to faggot cell presence.

References

1. Clin Chim Acta. 2018 Aug;483:183-191. doi: 10.1016/j.cca.2018.05.001.
2. Ann Lab Med. 2019 May;39(3):327-329. doi: 10.3343/alm.2019.39.3.327.
3. PLoS One. 2019 Mar 6;14(3):e0212228. doi: 10.1371/journal.pone.0212228.
4. Ann Lab Med. 2021 May 1;41(3):333-335. doi: 10.3343/alm.2021.41.3.333.

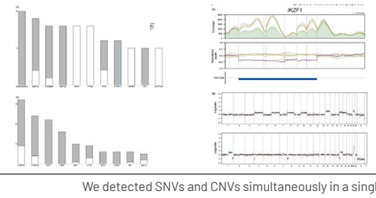
Oncology
Blood Cancer

31. Leuk Lymphoma. 2019 Dec

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Clinical utility of targeted NGS panel with comprehensive bioinformatics analysis for patients with acute lymphoblastic leukemia

Cancer Type	Acute lymphoblastic leukemia (ALL)
Sample	Bone marrow aspirates from 100 Patients with lymphoblastic leukemia
Study purpose	We have designed a comprehensive next-generation sequencing (NGS) assay to detect somatic mutations, translocations, and copy number changes and have evaluated its clinical utility in patients with ALL
Main data	The frequency of single nucleotide variations and copy number variations identified more than five patients. Visualization of genetic copy number analysis showing IKZF1 exon 4–7 deletion and chromosomal copy number analysis



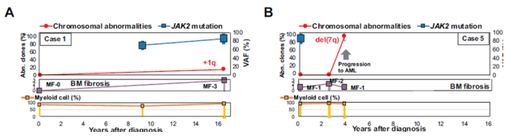
Conclusion	We detected SNVs and CNVs simultaneously in a single assay, which could provide an alternative or supplement for several conventional tests and simplify the testing processes.

32. Blood Cells Mol Dis. 2019 Jul

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Cytogenetic evolution in myeloproliferative neoplasms with different molecular abnormalities

Cancer Type	Myeloproliferative neoplasms (MPNs)
Sample	Bone marrow aspirate samples or peripheral blood of 21 patients.
Study purpose	we studied the changes in chromosomal abnormalities in MPN patients during long-term follow-up and investigated the correlation of the molecular and hematologic characteristics of the disease.
Main data	The percentage of metaphases with chromosomal abnormalities and the variant allele frequencies (VAFs) of JAK2 or CALR mutations are plotted according to years after diagnosis for 12 patients (A–L) for whom mutation burden data were available and cytogenetic abnormalities were detected.



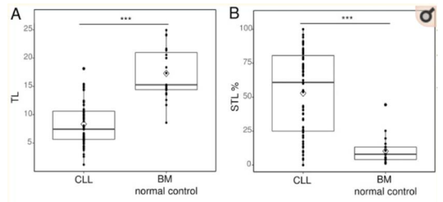
Conclusion	For many MPN patients, cytogenetic abnormalities clonally evolved during disease progression and were associated with the molecular characteristics.

33. PLoS One. 2019 Jul

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Telomere length and its correlation with gene mutations in chronic lymphocytic leukemia in a Korean population

Cancer Type	Chronic lymphocytic leukemia (CLL)
Sample	110 patients (41 females and 69 males) diagnosed with CLL
Study purpose	To investigate the prognostic significance of telomere length and its correlation with cytogenetic aberrations and somatic mutations
Main data	The TL and shortest TL% (STL%) of CLL patients



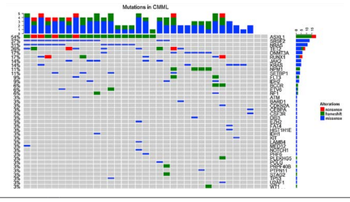
Conclusion	TL was attrited in CLL, and attrited telomeres were correlated with adverse survival and other well-known adverse prognostic factors.

34. Leuk Res. 2019 Sep

CANCER | BLOOD CANCER | CUSTOMIZED PANEL

Targeted sequencing aids in identifying clonality in chronic myelomonocytic leukemia

Cancer Type	Chronic myelomonocytic leukemia (CMML)
Sample	41 samples from 35 patients with CMML (BM aspirate).
Study purpose	Because genomic analysis of CMML has not been reported in Korean patients, we characterized molecular and cytogenetic abnormalities in patients with CMML.
Main data	Distribution of mutations in chronic myelomonocytic leukemia



Conclusion	We examined the demographic features and genetic profiles of Korean patients with CMML patients, revealing clonality by targeted sequencing and/or cytogenetics in most patients and showing some differences in genetic profiles compared to in Caucasians.

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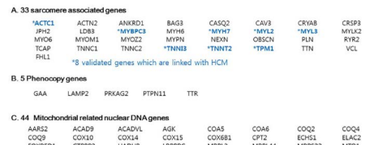
Inherited Diseases

36. Mitochondrion. 2020 Jul

INHERITED DISEASE | MITOCHONDRIA | CUSTOMIZED PANEL

Differential contributions of sarcomere and mitochondria-related multigene variants to the endophenotype of hypertrophic cardiomyopathy

Sample	432 patients (194 (45%) with apical hypertrophic cardiomyopathy)
Study purpose	We investigated phenotype-based clinical and genetic characteristics of hypertrophic cardiomyopathy patients using comprehensive genetic tests and rare variant association analysis.
Main data	Eighty-two nuclear genes were included in a comprehensive hypertrophic cardiomyopathy (HCM)-specific panel



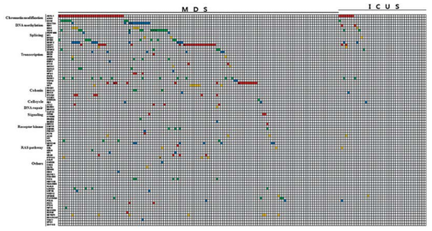
Conclusion	Our results provide a clue towards explaining the difference between the prevalence and phenotype of apical HCM in Asian populations, and a foundation for genetics-based approaches that may enable individualized risk stratification for HCM patients.

37. Leuk Lymphoma. 2019 Mar

INHERITED DISEASE | CUSTOMIZED PANEL

ASXL1 is a molecular predictor in idiopathic cytopenia of undetermined significance

Sample	40 patients with idiopathic cytopenia of undetermined significance (ICUS) and 128 patients with myelodysplastic syndrome (MDS)
Study purpose	We investigated the mutational profiles and clinical implications of genetic mutations in patients with ICUS using the targeted sequencing panel containing 88 genes.
Main data	Eighty-two nuclear genes were included in a comprehensive hypertrophic cardiomyopathy (HCM)-specific panel



Conclusion	The ASXL1 mutation which is frequently detected in elderly patients is a molecular predictor for pancytopenia and survival in patients with ICUS.

38. Exp Clin Endocrinol Diabetes. 2021 Jun

INHERITED DISEASE | CUSTOMIZED PANEL

Functional Characteristics of Novel FGFR1 Mutations in Patients with Isolated Gonadotropin-Releasing Hormone Deficiency

Sample	8 patients (from 7 families) with FGFR1 mutations identified by targeted gene panel sequencing or whole exome sequencing (WES)
Study purpose	This study was performed to investigate clinical phenotypes and functional characteristics of FGFR1 mutations in patients with Isolated gonadotropin-releasing hormone (GnRH) deficiency (IGD)
Main data	FGFR1 mutations in the studied patients.

Family No.	Subject No.	Nucleotide change	Amino acid change	Intron/Exon	Domain	ACMG/AMP guideline
1	1	c.265C>T	p.Q89 *	3	D1 loop	Likely pathogenic
2	2	c.551dup	p.N185Kfs * 16	5	D1 loop	Likely pathogenic
3	3	c.630T>A	p.Y210 *	6	D2 loop	Likely pathogenic
3	4	c.630T>A	p.Y210 *	6	D2 loop	Likely pathogenic
4	5	c.1015T>C	p.Y339H	8	D3 loop	Likely pathogenic
5	6	c.2042G>T	p.S681I	15	Tyrosine kinase domain	Uncertain significance
6	7	c.1663 + 2T>G	Splice site	12	Tyrosine kinase domain	Uncertain significance
7	8	c.1855-1G>A	Splice site	13	Tyrosine kinase domain	Uncertain significance

Conclusion	This study identified seven loss-of-function mutations in FGFR1 which showed different degrees of impairment in vitro. These results expand the known phenotypic spectrum of FGFR1 mutations and suggest a broader biologic role of FGFR1 in reproduction.

39. Am J Clin Pathol. 2021 Jun

INHERITED DISEASE | CUSTOMIZED PANEL

Ultradeep Sequencing Analysis of Paroxysmal Nocturnal Hemoglobinuria Clones Detected by Flow Cytometry: PIG Mutation in Small PNH Clones

Sample	89 specimens from 63 patients whose paroxysmal nocturnal hemoglobinuria (PNH) clone size was ≥0.1% by flow cytometry (FCM)
Study purpose	We aimed to determine whether small PNH clones detected by FCM harbor PIG gene mutations with quantitative correlation.
Main data	Ultradeep Targeted Sequencing and PNH FCM Results of 27 Patients Who Harbored PIG Gene Mutation.

ID	Sex	Dx	PNH-related Sx*	Gene	Accession Number	Nucleotide Change	Protein Change	Total Depth	VAF, %	RBC Clone Size (FCM), %	Granulocyte Clone Size (FCM), %
P-02	F	Classic PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.1188 + 1G>A		1,616	1.86	0.75	2.60
				PIGA	NM_002641.3	c.*985C>T		4,321	0.74		
P-03	F	AA-PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.356G>A	p.Arg119Gln	1,671	1.20	0.59	0.05
P-06	M	Classic PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.1266dupT	p.Thr423Hfs	543	87.40	84.31	99.68
P-07	M	AA-PNH	Mesenteric vein thrombosis	*PIGA*	NM_002641.3	c.469C>G	p.Ser163Arg	1,770	53.22	16.22	63.3
				PIGA	NM_002641.3	c.1322delT	p.Phe441Tfs	1,471	1.09		
P-08	F	AA-PNH	None	*PIGA*	NM_002641.3	c.635delC	p.Pro212Tfs	3,613	2.22	0.9	4.57
P-09	F	Classic PNH	Hemolytic anemia, IMA thrombosis	*PIGA*	NM_002641.3	c.1067C>G	p.Ser164Arg	3,861	61.74	72.88	99.55
				PIGA	NM_002641.3	c.491C>T	p.Ser164Leu	3,638	6.66		
				PIGA	NM_002641.3	c.471delT	p.Phe157fs	3,590	0.78		
P-10	F	AA-PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.635delC	p.Pro212fs	3,580	66.88	74.25	99.83
P-11	F	MDS-PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.1260C>T	p.Cys420Cys	3,692	0.72	0.2	0.05
				NR_033836.1	n.173 + 6C>T			4,752	0.68		
P-12	M	AA-PNH	None	*PIGA*	NM_002641.3	c.*704delA		2,262	0.57	0.11	0.04
P-14	M	Classic PNH	Hemolytic anemia	*PIGM*	NM_1451072	c.459_462delGGTC	p.Val154fs	4,947	84.50	44.4	93.45
				PIGA	NM_002641.3	c.517delG	p.Val173fs	2,235	0.63		
P-15	F	AA-PNH	None	*PIGA*	NM_002641.3	c.947delT	p.Met316Ifs	2,534	4.50	2.72	20.63
P-17	M	Classic PNH	Hemolytic anemia	*PIGA*	NM_002641.3	c.1183_1186 + 2delGAAA/GGT	p.Glu395_Lys396del	869	33.49	36.49	79.86
				PIGA	NM_002641.3	c.262A>G	p.Lys88Glu	2,070	14.11		
				PIGA	NM_002641.3	c.1003G>A	p.Gly335Arg	1,002	4.29		
				PIGA	NM_002641.3	c.110T>G	p.Met37Arg	1,907	1.78		

Conclusion	Our results showed that in small PNH clones PIG gene mutations were present in only a small portion without significant correlation to VAF or the presence or absence of a PIG mutation.

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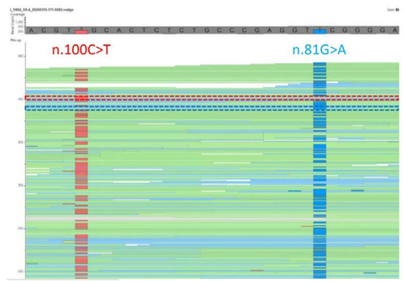
Inherited Diseases

40. Sci Rep. 2018 Aug

INHERITED DISEASE | CUSTOMIZED PANEL

Metaphyseal Dysplasia Without Hypotrichosis Caused by RNA Component of Mitochondrial RNA-Processing Endo-ribonuclease (RMRP) Gene Variants: The First Case in Korea

Sample	A girl aged five years and 10 months
Study purpose	Reporting the first case in Korea of a girl with compound heterozygous RNA-processing endoribonuclease (RMRP) variants, n.81G > A and n.100C > T, that were diagnosed as Metaphyseal dysplasia without hypotrichosis (MDWH).
Main data	Integrated genome browser snapshot of the RNA component of mitochondrial RMRP gene variants.



41. Genes. 2021 May

INHERITED DISEASE | CUSTOMIZED PANEL

Genetic Confirmation and Identification of Novel Variants for Glanzmann Thrombasthenia and Other Inherited Platelet Function Disorders: A Study by the Korean Pediatric Hematology Oncology Group (KPHOG)

Sample	: Blood samples from 11 Korean inherited platelet function disorders (IPFD) patients
Study purpose	This study aimed to perform genetic confirmation and differential diagnosis of Korean Inherited platelet function disorders (IPFDs) using next-generation sequencing (NGS).
Main data	Laboratory results and identified genetic variants in Korean patients with Glanzmann thrombasthenia and other inherited platelet function disorders.

ID	Plt (×10⁴/L)	PFA-100, EPI (sec) (Reference)	PFA-100, ADP (sec) (Reference)	Light Transmission Aggregometry	Flow Cytometry	Gene	Genetic Variants	Classification
1	427	265 (80–180)	220 (50–110)	NA	Decreased CD41 expression	*ITGB3*	c.1913+5G>T c.1421G>T (p.Gly484Val)	PV LPV
2	491	166 (80–180)	174 (50–110)	NA	NA	*ITGB3*	c.1913+5G>T [Hm]	PV
3	347	229 (80–180)	234 (50–110)	NA	NA	*ITGA2B*	c.2975del (p.Glu992Qfs*5*) c.2333A>C (p.Gln778Pro)	LPV PV
4	193	NA	NA	Decreased response to ADP, COL, EPI, normal response to R1S	NA	*ITGB3*	c.1913+5G>T [Hm]	PV
5	313	>300 (81–192)	157 (81–110)	NA	Complete deficiency of CD61/CD41a expression in platelet	*ITGB3*	c.917A>C (p.His306Pro) c.1913+5G>T	PV PV
6	234	244 (82–182)	239 (82–109)	Decreased response to ADP, COL, EPI, normal response to R2S	NA	*ITGB3*	c.1913+5G>T [Hm]	PV
7	218	NA	NA	Decreased response to ADP, COL, EPI, normal response to R2S	Decreased CD41 expression	*ITGA2B*	c.257T>C (p.Leu86Pro) c.2333A>C (p.Gln778Pro)	LPV LPV
8	392	223 (81–192)	240 (81–110)	NA	Decreased CD41 expression	*ITGA2B*	c.1750C> T (p.Arg584*) c.1184delT (p.Glu397Sfs*)	PV LPV
9	309	234 (82–182)	212 (82–109)	Decreased response to ADP, COL, EPI, normal response to R2S	Decreased CD41 expression	*ITGA2B*	c.2390del (p.Gly797Valfs*29) c.2333A>C (p.Gln778Pro)	PV PV
10	269	NA	NA	Decreased response to ADP, COL, EPI, normal response to R2S	Decreased CD41 expression	*ITGB3*	c.1913+5G>T c.1595G>T (p.Cys532Phe)	LPV LPV
11	442	>300 (82–182)	>300 (82–109)	Decreased response to ADP, COL, EPI, normal response to R2S	NA	*RASGRF2*	c.1479dup (p.Arg493Alafs*54) c.813+1G>A	LPV LPV

Conclusion	We demonstrated the successful application of NGS for the accurate and differential diagnosis of heterogeneous IPFDs.

42. Genes. 2021 May

INHERITED DISEASE | CUSTOMIZED PANEL

Clinical and Genetic Characteristics of Korean Congenital Stationary Night Blindness Patients

Sample	19 Korean patients with congenital stationary night blindness (CSNB)
Study purpose	we described the specific details of each case in this paper and were therefore able to comprehend the overall characteristics and causative gene mutations in Korean CSNB patients.
Main data	Pathogenic or likely pathogenic mutations identified in 19 patients with congenital stationary night blindness.

No.	Gene	Transcript	Nucleotide Change	Amino Acid Change	Zygosity	Segregation	CADD	EXTRINSIC	Splice Aid	MAF (Gnomad)	Domain	Novel Variant	
1	*GNAT1*	NM_000172	c.1544delG	p.(Leu648Cysfs*15)	Hemi	-	-	0.887	-	0.248580	-	Novel	
			c.1031-1G>A		Hemi	-	32	0.147	0.96	Not found	-	Novel	
2	*GNAT2*	NM_000173.4	c.775C>A	p.(Arg259Ser)	Hemi	-	24.5	0.884	-	10.253338	α subunit of G protein	Novel	
			c.328C>T	p.(Arg110*)	Hemi	-	38	0.897	-	1.249130	-		
3	*TRPM1*	NM_002420.4	c.3794delA	p.(Asn1265Ilefs*42)	Hemi	-	26.8	0.991	-	Not found	-	Lee et al. [10]	
4	*NYX*	NM_022567.2	c.182_183insT	p.(Cys61Valfs*53)	Hemi	Maternal	32	0.981	-	Not found	Leucine-rich repeat	Novel	
5	*NYX*	NM_022567.2	c.38-1_38delGCinsTT		Hemi	Maternal	14.18	-	-	Not found	-	ClinVar [11]	
6	*CACNA1F*	NM_005183.2	exon13~21 delexon		Hemi	-	-	-	-	Not found	-	Novel	
7	*CACNA1F*	NM_005183.2	c.1301C>T	p.(Ala1434Val)	Hemi	Maternal	17.47	0.143	0.80	Not found	-	Hove et al. [10]	
8	*CACNA1F*	NM_005183.2	c.2171_2179delins17	p.(Gly724Glufs*61)	Hemi	Maternal	27.3	0.999	-	Not found	Ion transport	Novel	
9	*CACNA1F*	NM_005183.2	c.1910+1G>A		Hemi	-	24.9	0.978	0.95	Not found	Ion transport	Novel	
10	*CACNA1F*	NM_005183.2	c.4049G>A	p.(Gly1351Asp)	Hemi	-	27.2	0.987	-	Not found	Voltage-dependent calcium channel	Kim et al. [11]	
11	*CACNA1F*	NM_005183.3	c.1624del	p.(Phe1158Serfs*23)	Hemi	Maternal	35.4	0.940	-	Not found	-	Ren et al. [17]	
12	*CACNA1F*	NM_005183.2	c.3914C>T	p.(Arg1372*)	Hemi	-	32.6	0.312	-	Not found	-	Zito et al. [10]	
13	*CACNA1F*	NM_005183.2	c.4042-1G>T		Hemi	Maternal	34	0.993	0.98	Not found	Voltage-dependent calcium channel	Novel	
14	*CACNA1F*	NM_005183.2	c.1910+1G>A		Hemi	-	24.9	0.978	0.95	Not found	Ion transport	Novel	
15	*CACNA1F*	NM_005183.2	c.5479C>T	p.(Arg1827*)	Hemi	Maternal	36	0.202	-	1.193192	-	Weiz et al. [10]	
16	*CACNA1F*	NM_005183.2	c.2578+1G>A		Hemi	-	34	0.993	0.88	1.82948	-	Wang et al. [10]	
17	*CACNA1F*	NM_005183.2	c.828G>A	p.(Gly276Arg)	Hemi	-	28.2	0.974	-	Not found	Ion transport	Sun et al. [11]	
18	*CACNA1F*	NM_005183.2	c.2705T>A	p.(Leu902Gln)	Hemi	Maternal	25.3	0.958	-	Not found	Ion transport	Novel	
19	*CACNA1F*	NM_005183.2	c.2707-1G>C		Hemi	-	33	0.994	0.99	Not found	Ion transport	Novel	

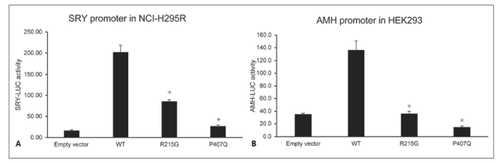
Conclusion	This is the first Korean CSNB case series on the genotype–phenotype correlation. The Riggs and complete types of TPRM1 gene mutations presented good visual acuity, whereas the incomplete and complete types of NYX gene mutations were frequently associated with poor visual acuity and nystagmus

43. Sex Dev. 2019

INHERITED DISEASE | CUSTOMIZED PANEL

Molecular Characteristics of Sequence Variants in GATA4 in Patients with 46, XY Disorders of Sex Development without Cardiac Defects

Sample	49 consecutive patients with 46,XY disorder of sex development (DSD)
Study purpose	The present study thus aimed to characterize 2 patients presenting with 46,XY DSD without congenital heart defects (CHDs) to better understand the phenotypic variability and functional characteristics of GATA4 variants.
Main data	Transcriptional activity of the 2 identified GATA variants towards the AMH (A) and SRY (B) promoters.



Conclusion	Mutations in GATA4 are a rare cause of 46,XY DSD without heart anomalies and that GATA4 mutations in patients with 46,XY DSD may not be associated with CHDs

References

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Inherited Diseases

44. Neurosurgery. 2020 Aug

INHERITED DISEASE | CUSTOMIZED PANEL

Molecular Diagnosis of Craniosynostosis Using Targeted Next-Generation Sequencing

Sample	110 unrelated Korean patients with craniosynostosis (CRS), including 40 syndromic and 70 non-syndromic cases.
Study purpose	To investigate the genomic landscape of CRS in a Korean cohort and also to establish a practical diagnostic workflow by applying targeted panel sequencing.
Main data	Integrated genome browser snapshot of the RNA component of mitochondrial RMRP gene variants.

TABLE 2. Identified Pathogenic Variants and Final Diagnosis

Gene (transcript)	Proband	Sex	Age	Sequence change	Amino acid change	Genetic mode	Allele frequency	Origin of variant	CRS	Other clinical features	Final diagnosis (after genetic testing)
FGFR3 (NM_000142.4)	P203	F	8m	c.749C>G	p.P250R	AD	NR	De novo	LC	Facial asymmetry	Muenke syndrome
	P076	F	5m	c.749C>G	p.P250R	AD	NR	NA	RC	Facial asymmetry, anal duplication, neonatal seizure	Muenke syndrome
	P100	F	10m	c.749C>G	p.P250R	AD	NR	NA	BC	Facial asymmetry	Muenke syndrome
	P104	F	11	c.749C>G	p.P250R	AD	NR	NA	RC	Facial asymmetry	Muenke syndrome
FGFR2 (NM_000141.4)	P109	F	5	c.958A>G	p.T320A	AD	NR	De novo	P	Exophthalmos, low-set ears	Crouzon syndrome
	P064	M	3	c.1021G>C	p.G341R	AD	NR	NA	RC, BL, M	Exophthalmos, Low-set ears, Both tri-angular face	Crouzon syndrome
	P092	M	10m	c.1024T>G	p.C342G	AD	NR	De novo	S, BC	Exophthalmos, large thumbs and toes, hearing impairment	Pfeiffer syndrome
TWIST1 (NM_000474.3)	P027	F	6	c.396_406dup	p.I33_I36dup	AD	NR	Maternal inherited	BC	Maternal history of CRS	Saethre–Chotzen syndrome
	P097	F	7	c.397_408dup	p.I33_I36dup	AD	NR	NA	BC	Facial asymmetry	Saethre–Chotzen syndrome
	P004	F	4	c.401C>G	p.P134R	AD	NR	De novo	BC	Sunken midface, frontal bossing, nasolacrimal duct obstruction	Saethre–Chotzen syndrome
	P114	F	7	c.466A>G	p.I156V	AD	NR	NA	RC	Chiari malformation, tongue-tie	Saethre–Chotzen syndrome
	P025	F	7	c.467T>C	p.I156T	AD	NR	NA	BC	Cleft uvula, ventricular septal defect, hearing impairment	Saethre–Chotzen syndrome
TCF12 (NM_207037.1)	P039	F	2	c.339G>C	p.E113D	AD	NR	NA	RC	Facial asymmetry	TCF12-related CRS
	P058	F	10	c.627delT	p.S210VfsTer35	AD	NR	De novo	RC	Low set ears, preauricular fistula, high palate, short 5th fingers, Leg-length asymmetry	TCF12-related CRS
	P068	M	3	c.1468-7A>G	splicing variant	AD	NR	NA	RC	Hypospadias	TCF12-related CRS
	P052	F	8	c.979C>T	p.P327S	AD	13×10^{-4}	NA	LC	Choledochal cyst	TCF12-related CRS

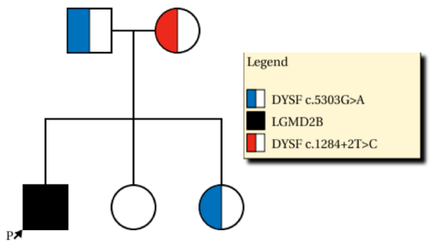
Conclusion	The present study shows the wide genomic landscape of CRS, revealing various genetic factors for CRS pathogenesis.

45. Diagnostics. 2020 Jul

INHERITED DISEASE | CUSTOMIZED PANEL

Incidental Severe Fatty Degeneration of the Erector Spinae in a Patient with L5–S1 Disc Extrusion Diagnosed with Limb-Girdle Muscular Dystrophy R2 Dysferin-Related

Sample	A 35-year-old male presented with right leg pain for 2 weeks without a previous history of limb weakness.
Study purpose	Case Report
Main data	Family pedigree diagnosed with compound heterozygous DYSF (dysferlin gene) variants.



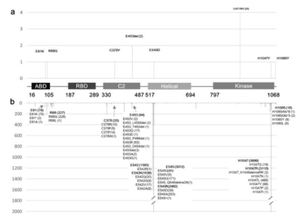
Conclusion	In the current study, we described a case with incidental severe fatty degeneration of the erector spinae who presented with L5–S1 disc extrusion and eventually was diagnosed with LGMD R2 dysferin-related.

46. Orphanet J Rare Dis. 2020 Aug

INHERITED DISEASE | CUSTOMIZED PANEL

Detailed analysis of phenotypes and genotypes in megalencephaly-capillary malformation-polymicrogyria syndrome caused by somatic mosaicism of PIK3CA mutations

Sample	12 patients from 12 families who satisfied the clinical Megalencephaly-capillary malformation-polymicrogyria syndrome (MCAP) criteria and were confirmed genetically to have PIK3CA pathogenic variants.
Study purpose	We report on the clinical and molecular genetic characteristics of 12 Korean patients confirmed as having MCAP.
Main data	Distribution of PIK3CA variants identified in this study and cancers.



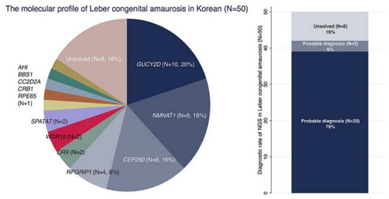
Conclusion	Using high-depth NGS panel sequencing, allele frequencies of mosaicisms even lower than 10% were detected successfully.

47. Mol Vis. 2020 Feb

INHERITED DISEASE | CUSTOMIZED PANEL

Copy number variations and multiallelic variants in Korean patients with Leber congenital amaurosis

Sample	50 patients (27 patients (54%) were male, and 11 (22%) showed systemic features)
Study purpose	We comprehensively evaluated the mutational spectrum of Leber congenital amaurosis (LCA) and investigated the molecular diagnostic rate and genotype-phenotype correlation in a Korean cohort.
Main data	Molecular diagnosis of Leber congenital amaurosis in Korean patients.



Conclusion	Mutations in GUCY2D, NMNAT1, and CEP290 appeared to be the major genetic causes of LCA in Korean patients. The overall molecular pickup rate of LCA was 84%. We also found that 4% of patients had multiple molecular diagnoses in two different disease loci, and 6% of patients were surgically or medically actionable.

References

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Inherited Diseases

48. Atherosclerosis. 2015 Nov

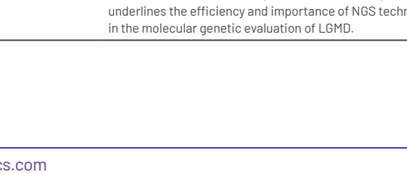
INHERITED DISEASE | CUSTOMIZED PANEL

Clinical features of familial hypercholesterolemia in Korea: Predictors of pathogenic mutations and coronary artery disease e A study supported by the Korean Society of Lipidology and Atherosclerosis

Sample	97 patients with low-density lipoprotein-cholesterol >190 mg/dL and xanthoma or familial hypercholesterolemia (FH)-compatible family history
Study purpose	The aim of this study was to determine the clinical features and the best diagnostic approach in Korean FH patients.
Main data	Prediction of putative pathogenic mutations according to four sets of clinical diagnostic criteria for FM.

Criteria	Type	Mutation rate (%)	Sensitivity	Specificity
Simon Broome Register	Definite	7/19 (37)	0.23	0.82
	Definite + possible	29/81 (36)	0.94	0.21
Dutch Lipid Clinic Network	Definite	8/27 (30)	0.26	0.97
	Definite + probable	31/90 (34)	1.00	0.03
MEDPED	Definite + probable + possible	31/96 (32)	1.00	0.02
	Total cholesterol	12/16 (75)	0.39	0.94
	LDL-cholesterol	14/21 (67)	0.45	0.89
Japanese		23/59 (39)	0.74	0.45

MEDPED: Make Early Diagnosis to Prevent Early Deaths.



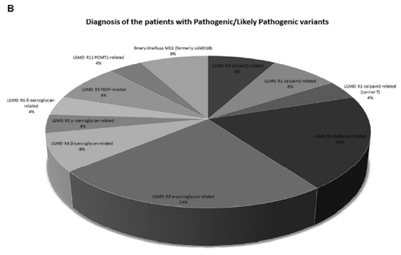
Conclusion	An LDL-C level of 225 mg/dL was suggested as the best threshold for predicting carriers

49. Ann Hum Genet. 2019 Sep

INHERITED DISEASE | CUSTOMIZED PANEL

Impact of next-generation sequencing panels in the evaluation of limb-girdle muscular dystrophies

Sample	74 patients suspected of Limb-girdle muscular dystrophy (LGMD)
Study purpose	We have evaluated the diagnostic rates of our custom NGS gene panel and investigated variant frequencies associated with LGMD subtypes in Turkey. The association between genotype and LGMD phenotypes was also analyzed.
Main data	Diagnosis of the patients with pathogenic/likely pathogenic variants.



Conclusion	We have achieved a 33.8% diagnosis rate in our 74-patient cohorts by using custom target capture LGMD gene panel. This ratio is consistent with previous literature reports and underlines the efficiency and importance of NGS technology in the molecular genetic evaluation of LGMD.

50. Exp Clin Endocrinol Diabetes. 2019 Sep

INHERITED DISEASE | CUSTOMIZED PANEL

Targeted Gene Panel Sequencing for Molecular Diagnosis of Kallmann Syndrome and Normosmic Idiopathic Hypogonadotropic Hypogonadism

Sample	28 patients with Isolated gonadotropin-releasing hormone (GnRH) deficiency (IGD) from 27 independent families.
Study purpose	This study was performed to establish the genetic etiology of IGD using a targeted gene panel sequencing of 69 known human IGD genes.
Main data	Molecular genetic findings in patients harboring pathogenic or likely pathogenic variants

Subject	Sex	Age at presentation (years)	Phenotype	Sequence variants			Interpretation
				Gene	Nucleotide change	Amino acid change	
1	M	14	Kallmann syndrome, hearing defect	*CHD7*	c.5405-7G>A	Splice site	Pathogenic
2	M	21	Kallmann syndrome	*PROKR2*	c.533G>C	p.W178S	Pathogenic
3	M	16	Kallmann syndrome, hearing defect	*CHD7*	c.118C>T	p.Q40 *	Pathogenic
4	F	19	nIHH, primary amenorrhea	*FGFR1*	c.1015T>C	p.Y339H	Likely pathogenic
5	M	20	Kallmann syndrome	*FGFR1*	c.551dup	p.N185Kfs * 16	Likely pathogenic
6	M	16	nIHH	*ANOS1*	c.1260del	p.Q421Kfs * 61	Likely pathogenic
7	M	18	nIHH	*SOX3*	c.699_719del	p.A234_A240del	Likely pathogenic
8	M	20	nIHH	*TACR3*	c.527_533del/ c.527_533del	p.M176Tfs * 14/ p.M176Tfs * 14	Pathogenic
9	M	16	nIHH				
10	M	18	nIHH, finger syndactyly	*FGFR1*	c.1855-1G>A	Splice site	Likely pathogenic
11	M	7	Anosmia, micropenis, cryptorchidism	*FGFR1*	c.1663+2T>G	Splice site	Likely pathogenic

F, female; M, male; nIHH, normosmic idiopathic hypogonadotropic hypogonadism

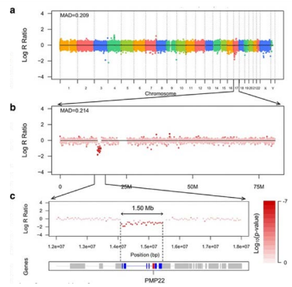
Conclusion	We achieved a genetic diagnosis in 10 families (37 %) and detected variant of uncertain significance (VUS) in two patients (7.4 %). In addition, novel pathogenic or likely pathogenic variants were identified in eight probands in ANOS1, CHD7, FGFR1, TACR3, and SOX3.

51. Orphanet J Rare Dis. 2018 Mar

INHERITED DISEASE | CUSTOMIZED PANEL

Frequency of hereditary neuropathy with liability to pressure palsies (HNPP) due to 17p11.2 deletion in a Korean newborn population

Sample	Capillary or cord blood samples from 11,885 neonates
Study purpose	A total of 11,885 neonates were evaluated for constitutional chromosomal abnormalities using the NGS-based CNV analysis.
Main data	Combined log R ratio (LRR) plots of the 17p11.2 copy number variation (CNV) regions.



Conclusion	Our data suggest that PMP22 Del HNPP might not be uncommon at least in the Korean population.

References

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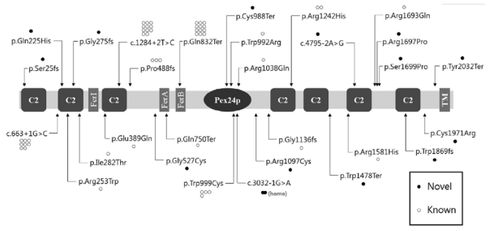
Inherited Diseases

52. Neuromuscul Disord. 2015 Jun

INHERITED DISEASE | CUSTOMIZED PANEL

Targeted next-generation sequencing for the genetic diagnosis of dysferlinopathy

Sample	41 patients with dysferlinopathy (24 males/17 females)
Study purpose	We applied and validated a targeted NGS based sequencing method for mutation detection in patients with dysferlinopathy, which was confirmed by immunohistochemical (IHC) staining and/or western blot analysis of skeletal muscles.
Main data	Distribution of pathogenic variants discovered in the DYSF gene.



Conclusion	this study demonstrates that the high-throughput mutation screening method based on hybrid capture and NGS is highly accurate and efficient for the genetic diagnosis of dysferlinopathy and provides supportive evidence for the incorporation of the DYSF gene into multi-gene NGS panel tests for muscular dystrophy.

53. Mutat Res. 2015 Jul

INHERITED DISEASE | CUSTOMIZED PANEL

Cytogenetic heterogeneity and their serial dynamic changes during acquisition of cytogenetic aberrations in cultured mesenchymal stem cells

Sample	Human adipose tissue-derived mesenchymal stem cells
Study purpose	we aimed to investigate whether such a minority of cells can expand over time or if they ultimately disappear during MSC passaging
Main data	Variant allele frequency in human umbilical cord blood-derived mesenchymal stem cells.

Gene	cDNA change	Amino acid substitution
NOTCH1	c.T4319C	p.I1440T
MLH1	c.A68G	p.E23G
GNAS	c.G1148A	p.R383Q
TP53	c.A733C	p.T245P

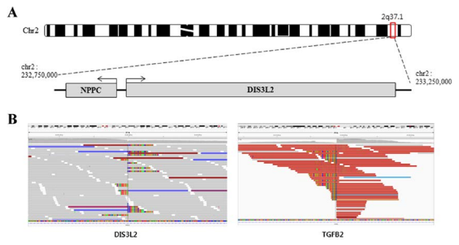
Conclusion	We tracked cytogenetic heterogeneity using G-banding and interphase FISH analyses during the cancerous transformation of MSCs. Heterogeneity among clones with distinct chromosomal aberrations dynamically changed over time, similar to what is observed in cancer stem cells. We conclude that to accurately evaluate of the tumorigenic potential of MSCs, interphase FISH analyses should be used in combination with conventional cytogenetics.

54. Am J Med Genet A. 2015 May

INHERITED DISEASE | CUSTOMIZED PANEL

Skeletal overgrowth syndrome caused by overexpression of C-type natriuretic peptide in a girl with balanced chromosomal translocation, t(1;2)(q41;q37.1)

Sample	A girl (Case Report)
Study purpose	We present a fourth case of chromosomal translocation on 2q37.1, whose recipient site interrupted the TGFB2 gene, resulting in the combined phenotypes of CNP overproduction and Loeys–Dietz syndrome (LDS) type IV (MIM 614816).
Main data	Schematic diagram of the targeted region for the next-generation sequencing and Scheme of soft-clipped reads of the breakpoint between the DIS3L2 and TGFB2 sequences



Conclusion	We have identified a balanced chromosomal translocation between 1q41 and 2q37.1

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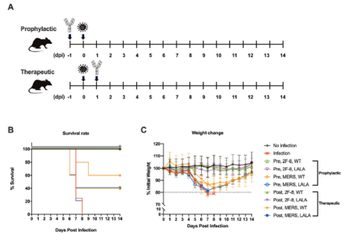
Virus & Bacteria

55. Biochem Biophys Res Commun. 2021 Mar

VIRUS | ZIKA VIRUS | TRUEREPERTOIRE

Neutralization of Zika virus by E protein domain III-Specific human monoclonal antibody

Sample	ZIKV envelope domain III-specific neutralizing antibodies (nAbs) from two convalescent patients with ZIKV infection.
Study purpose	The discovery that ZIKV infection in infants and adults is associated with neurological complications showed that countermeasures against ZIKV infection are needed
Main data	In vivo prophylactic and therapeutic efficacy of 2F-8 antibody against ZIKV infection



Conclusion	2F-8, a potent anti-ZIKV DIII-specific mAb isolated from ZIKV-infected patients, potently neutralized Asian and American strains of ZIKV in vitro.

56. Microbiol Resour Announc. 2021 Jan

VIRUS | SARS-COV-2 | WGS

Genome Sequences of Two GH Clade SARS-CoV-2 Strains Isolated from Patients with COVID-19 in South Korea

Sample	2 patients with COVID-19 who were hospitalized in Severance Hospital, Yonsei University
Study purpose	Reporting the genome sequences of two GH clade severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strains isolated from nasopharyngeal swabs from patients with coronavirus disease 2019 (COVID-19) in South Korea.
Main data	Nucleotide and amino acid changes in the YS006 and YS008 strains, in comparison to the reference strain

Nucleotide position	Nucleotide in strain (clade):			Gene name[b]	Amino acid change[c]
	Hu-1 (L)[a]	YS006 (GH)	YS008 (GH)		
241	C	T	T	5′ UTR	
1059	C	T	T	nsp2	T85I
3037	C	T	T	nsp3	
11916	C	T	T	nsp7	S25L
14408	C	T	T	nsp12	P323L
16650	C	T	T	nsp13	
20675	A	T	T	nsp16	Q6L
23403	A	G	G	Spike	D614G
25563	G	T	T	ORF3a	Q57H
26261	C	C	T	E	S6L[d]
29179	G	T	T	N	
29779	G	T	T	3′ UTR	

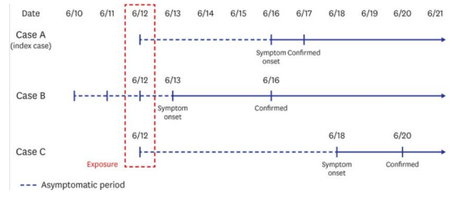
Conclusion	These strains had two mutations in the untranslated regions and seven nonsynonymous substitutions in open reading frames, compared with Wuhan/Hu-1/2019, showing 99.96% sequence identity.

57. J Korean Med Sci. 2020 Nov

VIRUS | SARS-COV-2 | WGS

Evidence of Long-Distance Droplet Transmission of SARS-CoV-2 by Direct Air Flow in a Restaurant in Korea

Sample	The epidemiological investigation was implemented based on personal interviews and data collection on closed-circuit television images, and cell phone location data. Nasopharyngeal specimens of cases and close contacts were collected
Study purpose	The transmission mode of severe acute respiratory syndrome coronavirus 2 is primarily known as droplet transmission. However, a recent argument has emerged about the possibility of airborne transmission. On June 17, there was a coronavirus disease 2019 (COVID-19) outbreak in Korea associated with long distance droplet transmission.
Main data	The asymptomatic period and symptom onset of all three coronavirus disease 2019 cases.



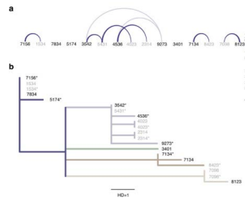
Conclusion	Droplet transmission can occur at a distance greater than 2 m if there is direct air flow from an infected person.

58. Sci Rep. 2021 Mar

VIRUS | SARS-COV-2 | WGS

Genomic Investigation of the Coronavirus Disease 2019 Outbreak in the Republic of Korea

Sample	Nasopharyngeal and oropharyngeal (NP/OP) swabs and sputum were used for SARS-CoV-2 RNA isolation
Study purpose	We evaluated the accuracy of genomic investigation by directly comparing South Korea's comprehensive contact tracing data with the genomic associations among severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) whole genome sequences.
Main data	Contact tracing record arc diagram (a) and maximum likelihood tree (b) of initial 15 cases prior to a church outbreak in South Korea.



Conclusion	Our genomic investigation of the COVID-19 outbreak in South Korea was highly consistent with our comprehensive and rigorous contact tracing records.

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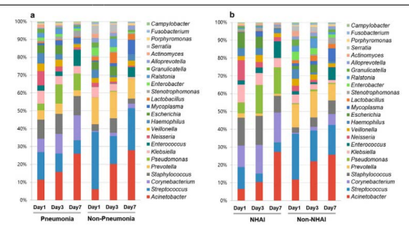
Virus & Bacteria

59. J Transl Med. 2020 Dec

BACTERIA XSEP MAGBEAD

Respiratory microbiome proles differ by recent hospitalization and nursing home residence in patients on mechanical ventilation

Sample	180 endotracheal aspirates (ETAs) from 60 mechanically ventilated intensive care unit (ICU) patients
Study purpose	Redefining nursing-home- and hospital-associated infections (NHAI) group by revising existing Healthcare-associated pneumonia (HCAP) risk factors.
Main data	Relative abundance of bacterial communities in the endotracheal aspirates of the study participants over time.



Conclusion	In this prospective observational cohort study of mechanically ventilated patients, the loss of diversity and dysbiosis of the respiratory microbiome were more profound in patients with than without risk factors for NHAI, which were in turn positively associated with the presence of Corynebacterium, and negatively associated with that of Granulicatella, Streptococcus, Staphylococcus and Veillonella.

References

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Others

60. Biomolecules. 2020 Mar

OTHERS TRUEREPERTOIRE

A High-Throughput Single-Clone Phage Fluorescence Microwell Immunoassay and Laser-Driven Clonal Retrieval System

- We describe a high-throughput single-clonal screening system comprised of fluorescence immunoassays as well as a laser-driven clonal DNA retrieval system using microchip technology. The use of a single-clone-level approach in combination with an elaborate sample retrieval method enabled high-throughput sample retrieval with minimal amplification bias and sample cross-contamination.
- The efficiency of this system was tested by using a single-chain variable fragment (scFv) library displayed on phages with a complexity of 5.21 × 105, harboring random mutations at five amino acid residues. Without biopanning, we could screen 78 antigen-reactive (AR) scFv sequences with mutations, restricted to the randomized residues when 70,000 clones were screened in parallel. We believe that the result is superior, or at least equivalent, to the conventional biopanning and screening procedure.

61. Genes Genomics. 2019 May

OTHERS

Enzymatic construction of shRNA library from oligonucleotide library

- We develop a new method that efficiently constructs a shRNA library at low cost, using treatments with several enzymes and an oligonucleotide library.
- The library of shRNA expression cassettes, which were cloned into a lentiviral plasmid, was produced through several enzymatic reactions, starting from a library of 20,000 different short oligonucleotides produced by microarray-based oligonucleotide synthesis.
- The NGS sequence analysis of the library shows that 99.8% of them (19,956 from 20,000 sequences) were contained in the library: 63.2% of them represent the correct sequences and the rest showed one or two base pair differences from the expected sequences.

62. Nat Commun. 2019 Feb

OTHERS

Barcode-free next-generation sequencing error validation for ultra-rare variant detection

- NGS has limitations in detecting rare-frequency variants (< 1%) because of high sequencing errors (> 0.1~1%). NGS errors could be filtered out using molecular barcodes, by comparing read replicates among those with the same barcodes. Accordingly, these barcoding methods require redundant reads of non-target sequences, resulting in high sequencing cost.
- We present a cost-effective NGS error validation method in a barcode-free manner. By physically extracting and individually amplifying the DNA clones of erroneous reads, we distinguish true variants of frequency > 0.003% from the systematic NGS error and selectively validate NGS error after NGS. We achieve a PCR-induced error rate of 2.5×10-6 per base per doubling event, using 10 times less sequencing reads compared to those from previous studies.

63. Nat Biotechnol. 2018 Mar

OTHERS

Deep learning improves prediction of CRISPR-Cpf1 guide RNA activity

- We present two algorithms to predict the activity of AsCpf1 guide RNAs.
- Indel frequencies for 15,000 target sequences were used in a deep-learning framework based on a convolutional neural network to train Seq-deepCpf1. We then incorporated chromatin accessibility information to create the better-performing DeepCpf1 algorithm for cell lines for which such information is available and show that both algorithms outperform previous machine learning algorithms on our own and published data sets.

64. Nucleic Acids Res. 2018 May

OTHERS

High-throughput construction of multiple cas9 gene variants via assembly of high-depth tiled and sequence-verified oligonucleotides

- We introduce the concept of high-depth tiled oligo design to successfully utilize megacloned oligos for gene synthesis.
- Using acquired oligos from a single round of the megacloning process, we assembled 72 of 81 target Cas9-coding gene variants. We further validated 62 of these cas9 constructs, and deposited the plasmids to Add gene for subsequent functional characterization by the scientific community.
- This study demonstrates the utility of using sequence-verified oligos for DNA assembly and provides a practical and reliable optimized method for high-throughput gene synthesis.

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