KSBi-BIML 2026

Bioinformatics & Machine Learning(BIML) Workshop for Life Scientists

생명정보학 & 머신러닝 워크샵 (온라인)

Cancer multi-omics data analysis based on AI

홍동완 _ 이노원

KSBI KOREAN SOCIETY FOR BIOINFORMATICS | 한국생명정보학회

본 강의 자료는 한국생명정보학회가 주관하는 BIML 2026 워크샵을 목적으로
제작된 것으로 해당 목적 이외의 다른 용도로 사용할 수 없음을 분명하게 알립니다.

이를 다른 사람과 공유하거나 복제, 배포, 전송할 수 없으며 만약 이러한 사항을 위반할 경우
발생하는 **모든 법적 책임은 행위자 본인에게 있음**을 알립니다.

KSBi-BIML 2026

Bioinformatics & Machine Learning (BIML) Workshop for Life Scientists

한국생명정보학회가 주최하는 BIML-2026 동계 Bioinformatics &Machine Learning 교육 워크숍에 여러분을 초대합니다.

BIML 워크숍은 생명정보학 연구자들이 최신 AI바이오 분야의 인공지능 기반 분석 기술과 바이오 데이터 분석 기법을 이론과 실습을 통해 체계적으로 배울 수 있는 전문 교육 프로그램입니다. 2015년에 시작된 BIML 워크숍은 올해로 12년 차를 맞이하며, 국내 생명정보학 분야의 최초이자 최고 수준의 교육 프로그램으로 자리 잡았습니다. 이번 워크숍은 크게 인공지능바이오(AI바이오) 분야와 디지털바이오 분야, 두 분야로 구성됩니다.

AI바이오 분야에서는 생명정보 분석에 폭넓게 응용되고 있는 다양한 인공지능 기반 자료 모델링 기법을 다룰 예정입니다. 특히, 인공지능 심층학습을 활용한 단백질 구조 예측, 유전체 분석, 신약 개발에 대한 이론 및 실습 강의가 진행됩니다.

또한 디지털바이오 분야에서는 단일세포오믹스, 공간오믹스, 멀티오믹스, 메타오믹스에 대한 강의도 마련되어 있어, 연구자들의 분석 역량 강화에 실질적인 도움을 줄 것으로 기대됩니다.

또한 2024년부터 추가된 의료정보 자료 분석을 다루는 강의를 올해도 지속해서 운영하고자 합니다. 이는 최근 의료정보 자료 분석에 관한 연구 수요 증가를 반영한 것으로, 관련 연구를 수행하는 의과학자 및 의료정보 연구자들에게 유용한 지침을 제공할 것입니다.

또한, 올해도 생명정보학 기술의 다양화에 발맞춰 온라인 강좌를 대폭 확대했습니다. 올해는 무료 강좌 10개를 포함한 총 40개 이상의 강좌가 개설되며, 연구 주제에 맞는 강좌 추천과 강연료 할인 혜택도 제공합니다.

BIML-2026는 국내 주요 연구 중심 대학의 전임 교수 및 각 분야 최고 전문가들의 강의로 구성되어 있으며, 기초 이론부터 최신 연구 동향까지 아우르는 심도 있는 교육의 장이 될 것으로 확신합니다.

여러분의 많은 관심과 참여를 기대합니다!

2026년 2월

한국생명정보학회장 류 성 호

강의개요

Cancer multi-omics data analysis based on AI

암 멀티 오믹스 데이터는 전 세계적으로 지속적이고 엄청난 양으로 증가하고 있으나 분석 및 분석 결과의 해석을 최적화하기에는 구조가 상당히 이질적이고 복잡하며, 데이터의 크기 또한 방대하여 상당한 어려움을 겪고 있다.

본 강의에서는 암 멀티 오믹스 데이터를 효과적이고 빠르게 처리하기 위해 인공지능 기법을 활용하여 분석/해석할 수 있는 방법을 강의한다. 암 멀티 오믹스로부터 생성된 돌연변이 및 유전자 발현 등 데이터 특징에 따른 인공지능 활용 방법에 대해 이해를 한다. 특히, AlphaFold2를 활용하여 3차원 단백질 구조를 예측할 수 있는 응용 사례를 보이고, 3차원 단백질 예측 구조에 대해 특화된 자동화 평가 방법을 제안한다. 수강생의 인공지능 활용 범위를 고도화하며 인공지능 빅 데이터 시대에 필요한 생물정보학자의 역량을 갖추는 것을 목표로 한다.

강의는 다음의 내용을 포함한다:

- Multi-omics 데이터를 활용한 인공지능
- 암 유전자 돌연변이/유전자 발현/단백질 발현 데이터를 활용한 인공지능 응용
- Alphafold2를 이용한 단백질 3차원 구조 예측
- 구조 예측 결과의 평가 및 해석

* 참고강의교재: 담당교수 강의 노트

* 교육생준비물: 노트북 (메모리 8GB 이상, 디스크 여유공간 30GB 이상, 온라인 접속)

* 강의 난이도: 초급

* 강의: 홍 동 완 교수 (가톨릭대학교 의과대학)

Curriculum Vitae

Speaker Name: Dongwan Hong, Ph.D.

▶ **Personal Info**

Name	Dongwan Hong
Title	Professor
Affiliation	Catholic University of Korea, College of Medicine

▶ **Contact Information**

Address	222 Banpodae-ro, Soecho-gu, Seoul 06591, Republic of Korea
Email	dwhong@catholic.ac.kr

Research Interest

Cancer genomics, Big data, and Artificial Intelligence

Educational Experience

2002-2007	Ph.D. Dept. of Computer Engineering, Hallym University
1992-1996	B.S. Dept. of Computer Science Hallym University

Professional Experience

2020-present	Professor, Catholic University of Korea, College of Medicine
2011-2022	Chief Researcher, National Cancer Center of Korea
2008-2011	Senior Researcher, Seoul National University, Medical Research Institute
2003-2007	Assistant Professor, Dept. of Multimedia, Sonngok University

Selected Publications (5 maximum)

1. Park et. al., Clonal dynamics in early human embryogenesis inferred from somatic mutations, 597, 393-397, Nature, 2021.
2. Kim et. al., FIREVAT: finding reliable variants without artifacts in human cancer samples using etiologically relevant, Genome Medicine, 11(1):81, 2019.
3. Park et. al., Tracing Oncogene Rearrangements in the Mutational History of Lung Adenocarcinoma, CELL, 177, 1842-1857, 2019
4. Yang et. al., RhoGAP domain-containing fusions and PPAPDC1A fusions are recurrent and prognostic in diffuse gastric cancer, NATURE COMMUNICATIONS, 9(1):4439~4439, 2018.
5. Lee el. al., Mutalisk: a web-based somatic MUTation AnaLyIS toolKit for genomic, transcriptional and epigenomic signatures, Nucleic Acids Research, 46(W1):W102~W108, 2018

KSBi-BIML 2023
(Cancer multi-omics data analysis based on AI)

Prof. Dongwan Hong, Ph.D.
(dwhong@catholic.ac.kr, http://honglab.catholic.ac.kr)
Catholic University of Korea, College of Medicine

본 강의 자료는 한국생명정보학회가 주관하는 KSBi-BIML 2023 워크샵 온라인 수업을 목적으로 제작된것으로 해당 목적 이외의 다른 용도로 사용할 수 없음을 분명하게 알립니다. 수업 목적으로 배포 및 전송 받은 경우에도 이를 다른 사람과 공유하거나 복제, 배포, 전송할 수 없습니다.

만약 이러한 사항을 위반할 경우 발생하는 모든 법적 책임은 전적으로 불법 행위자 본인에게 있음을 경고합니다.

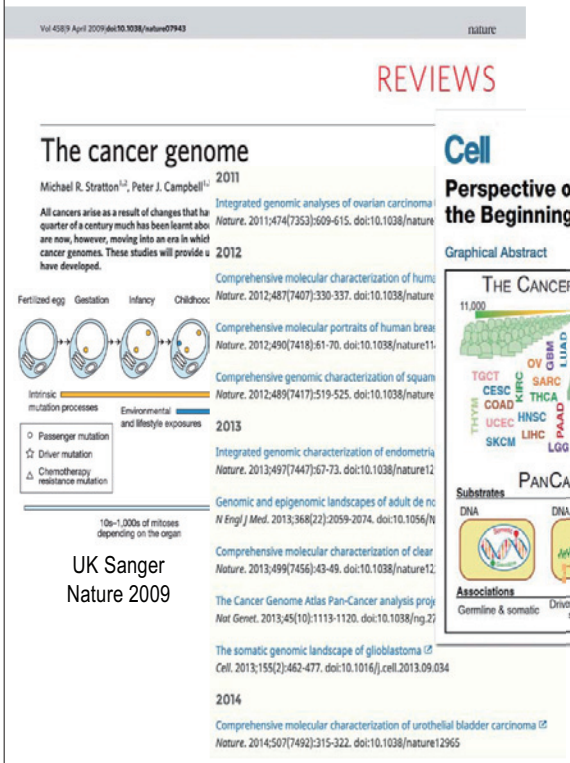
2

Overview

- **Part I: Cancer Genome Analysis**
  - Mutational Signature Analysis: Mutalisk
- **Part II: Artificial Intelligence Study using Cancer Big Data**
  - Use AlphaFold

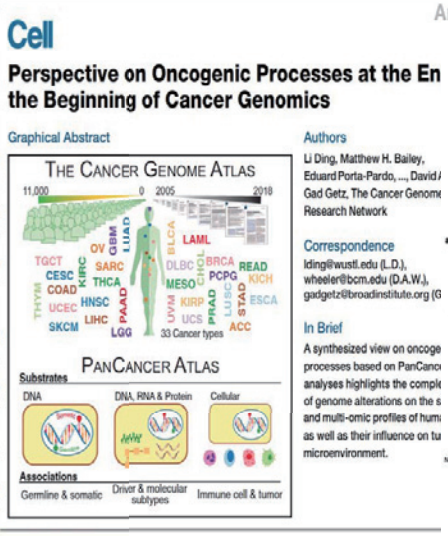
SBi 한국생명정보학회 Korean Society for Bioinformatics

The History of Cancer Genomics



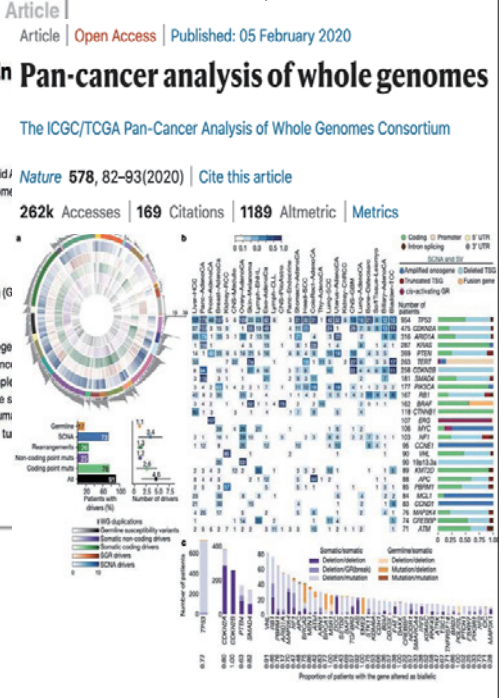
UK Sanger
Nature 2009

TCGA Research Network Publication



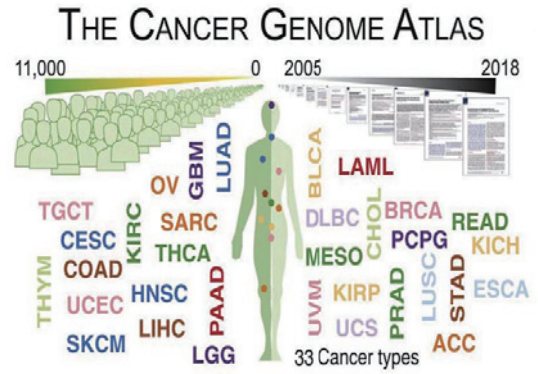
Ding et al., Cell 2018

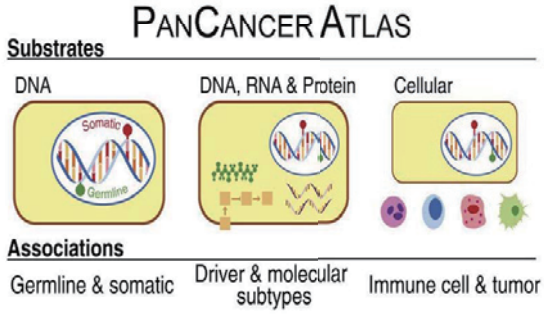
~2,700 PanCan WGS



Nature, 2020

Cancer Big Project





Li Ding et. al., Cell 2018

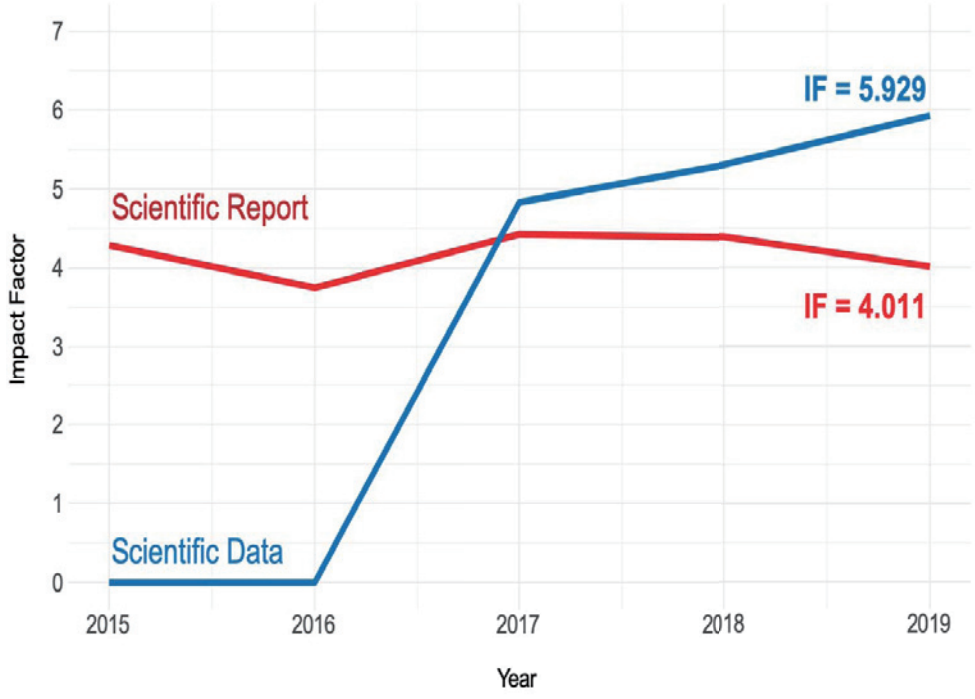
F-22 Raptor stealth fighters

- TCGA project was finished with advancements in cancer genomics
  - Systemized large-scale genomics-based cancer research (33 types / 11,000 tumors)

HISTORY OF CANCER TREATMENT MODALITIES

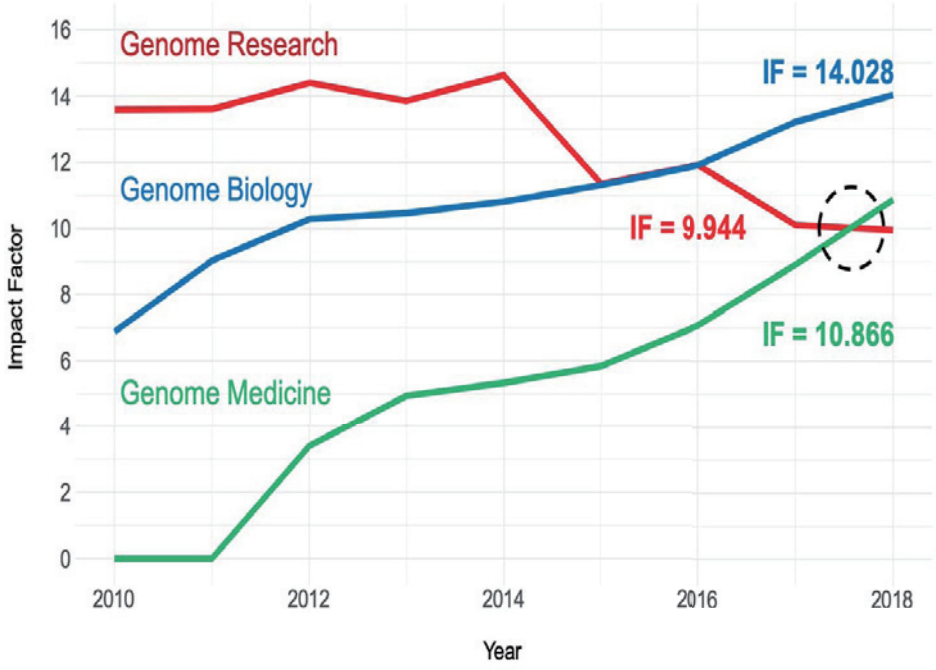
	SURGERY	RADIATION	CHEMO-THERAPY	TARGETED DRUGS	IMMUNO-THERAPY
APPROACH	Cut out accessible tumor cells to stop growth and prevent their spread	Use highly concentrated X-rays or radioactive isotopes to kill cancerous cells	Use cytotoxic drugs to kill or inhibit cancer cells	Interfere with a mechanism required for, or that supports tumor growth	Support the immune system's innate ability to recognize and eliminate tumor cells
SINCE	1800s	early 1900s	late 1940s	2000s	2010s
LIMITATIONS	Many inaccessible tumors ineligible; limited effectiveness if tumor has already begun to spread	Limited effectiveness if tumor has already begun to spread; potentially dangerous for tumors near vital organs	High toxicity and often does not destroy the whole tumor, leading to high rates of recurrence	Limited tumor types eligible; high efficiency but short durability driving high rates of recurrence	Applicable to all tumors at all stages of disease including metastatic tumors; responses are highly durable; potential for lower toxicity profiles; synergistic with other treatments

Trend 1. Data are More Impactful Than Individual Reports



Report < **Data**

Trend 2. Medicine Outweighs Research



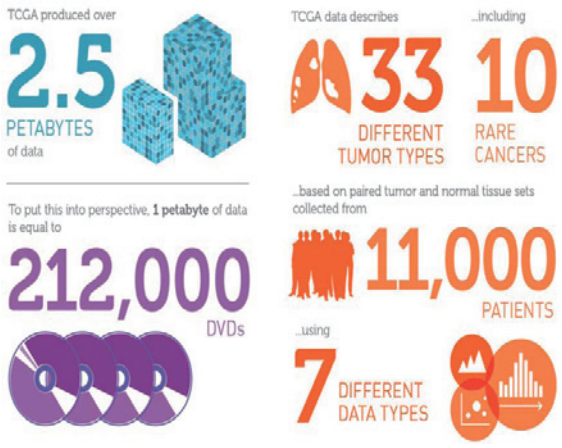
Research < **Medicine**

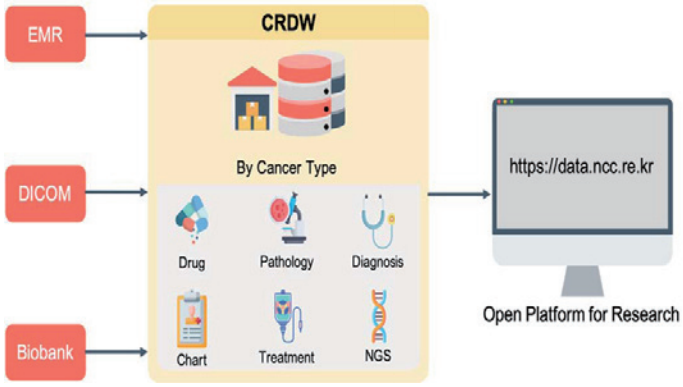
Clinical Genomic Big Data

12,500,000 patients

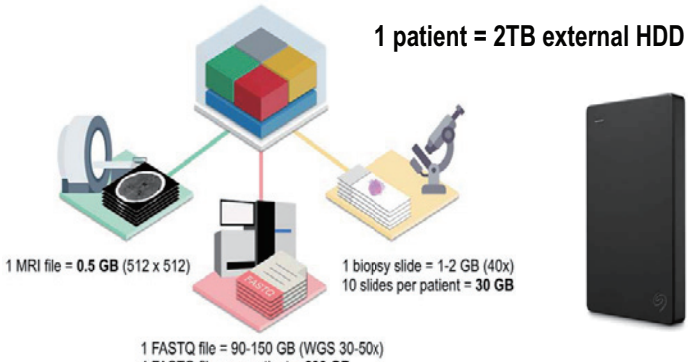
500 PB (2012) -> 25,000 PB (2020)

Exa -> Zeta -> Yotta





1 patient = 2TB external HDD



TCGA Research Network

ICGC Mutational Signatures Working Group

With which methods?

ICGC ARGO

- For SBS, DBS and indel signatures, should we:
  - stick to the original ICGC PCAWG pipelines **SigProfiler** (Sanger) and **SigAnalyzer** (Broad)
  - test other methods (**>25 published tools** including EMu, SomaticSignatures, Palimpsest, **Mutalisk**, BayesNMF…). For review: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0221235
  - Choose one approach or combine several?

- For SV signatures:
  - not sure the PCAWG method can be easily reproduced (**ClusterSV** available to generate footprints but extracting signatures from that is not obvious)
  - alternatives include **Palimpsest** or **Signal**

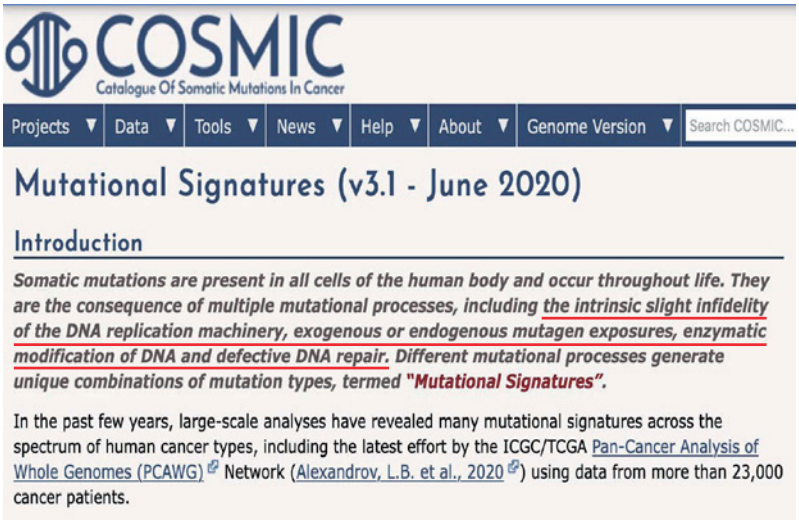
- For signatures of repair deficiencies:
  - Mismatch repair deficiency -> **MSIsensor**, **MSIseq**, **MOSAIC**…
  - Homologous recombination defects –> **Signature 3**, **HRDetect**, **SigMA**, combined **HRD scores**…

Participants: Alvin Ng (Sanger), Dongwan Hong, Paz Polak (Broad;NY), Eric Letouzé (Paris genome center)

mutalisk
MUTATION ANALYSIS TOOLKIT

a web-based somatic MUTation AnaLyIS toolKit for genomic, transcriptional and epigenomic signatures

Nucleic Acids Research (2018)



C>A

C>T

https://cancer.sanger.ac.uk/cosmic/signatures

Signature-based websites

As the number of mutational signatures and variant classes considered has increased, the need for a curated census of signatures has become apparent. Here, we deliver such a resource by providing a comprehensive overview of the key information known, suspected or widely discussed in the scientific literature for each of the identified mutational signatures on a dedicated website.

This summary includes the mutational profile, proposed aetiology and tissue distribution of each signature, as well as potential associations with other mutational signatures and how the signature has changed during iterations of analysis.

Currently, three different variant classes are considered, resulting in the following sets of mutational signatures.

Single Base Substitution (SBS) Signatures | **Doublet Base Substitution (DBS) Signatures**

Small Insertion and Deletion (ID) Signatures

Versions

Mutational signatures version 3 was released as part of COSMIC release v89 (May 2019) and updated to version 3.1 in COSMIC release v91 (June 2020). The version 3.1 update expands and improves upon the version 2 signatures (March 2015) that were part of earlier COSMIC releases and can still be consulted.

Mutational Signatures Version 2

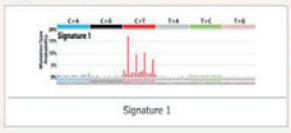
Bioinformatic tools

The current set of mutational signatures has been extracted using SigProfiler, a compilation of publicly available bioinformatic tools addressing all the steps needed for signature identification. SigProfiler functionalities include mutation matrix generation from raw data and signature extraction, among others.

SigProfiler Bioinformatic Tools

Mutational Signature v2

Signature 1



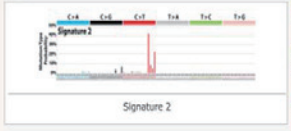
Cancer types: Signature 1 has been found in all cancer types and in most cancer samples.

Proposed aetiology: Signature 1 is the result of an endogenous mutational process initiated by spontaneous deamination of 5-methylcytosine.

Additional mutational features: Signature 1 is associated with small numbers of small insertions and deletions in most tissue types.

Comments: The number of Signature 1 mutations correlates with age of cancer diagnosis.

Signature 2



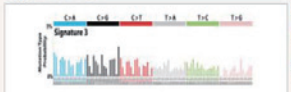
Cancer types: Signature 2 has been found in 22 cancer types, but most commonly in cervical and bladder cancers. In most of these 22 cancer types, Signature 2 is present in at least 10% of samples.

Proposed aetiology: Signature 2 has been attributed to activity of the AID/APOBEC family of cytidine deaminases. On the basis of similarities in the sequence context of cytosine mutations caused by APOBEC enzymes in experimental systems, a role for APOBEC1, APOBEC3A and/or APOBEC3B in human cancer appears more likely than for other members of the family.

Additional mutational features: Transcriptional strand bias of mutations has been observed in exons, but is not present or is weaker in introns.

Comments: Signature 2 is usually found in the same samples as Signature 13. It has been proposed that activation of AID/APOBEC cytidine deaminases is due to viral infection, retrotransposon jumping or to tissue inflammation. Currently, there is limited evidence to support these hypotheses. A germline deletion polymorphism involving APOBEC3A and APOBEC3B is associated with the presence of large numbers of Signature 2 and 13 mutations and with predisposition to breast cancer. Mutations of similar patterns to Signatures 2 and 13 are commonly found in the phenomenon of local hypermutation present in some cancers, known as kataegis, potentially implicating AID/APOBEC enzymes in this process as well.

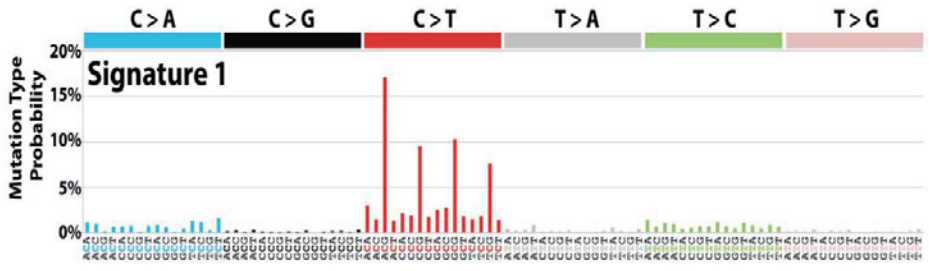
Signature 3



Cancer types: Signature 3 has been found in breast, ovarian, and pancreatic cancers.

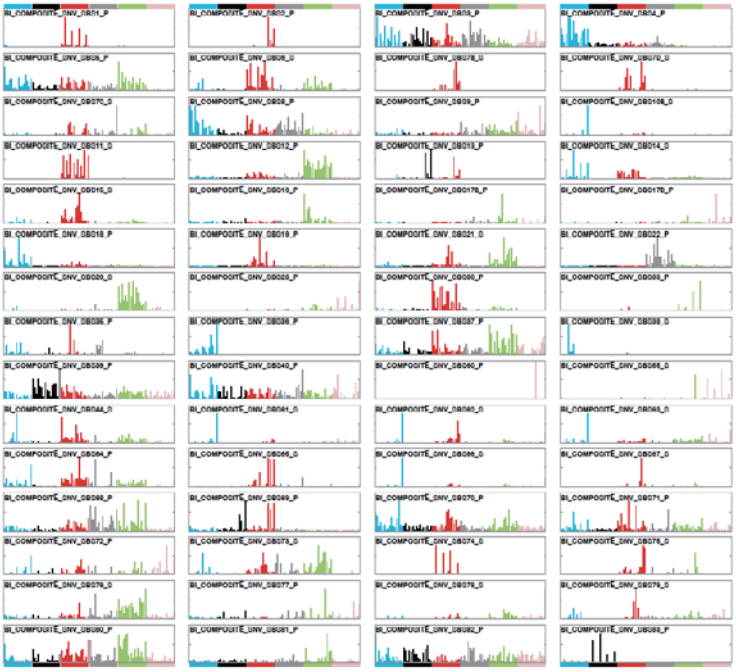
Proposed aetiology: Signature 3 is associated with failure of DNA double-strand break-repair by homologous recombination.

Additional mutational features: Signature 3 associates strongly with elevated numbers of large (longer than 3bp) insertions and deletions with overlapping microhomology at breakpoint junctions.



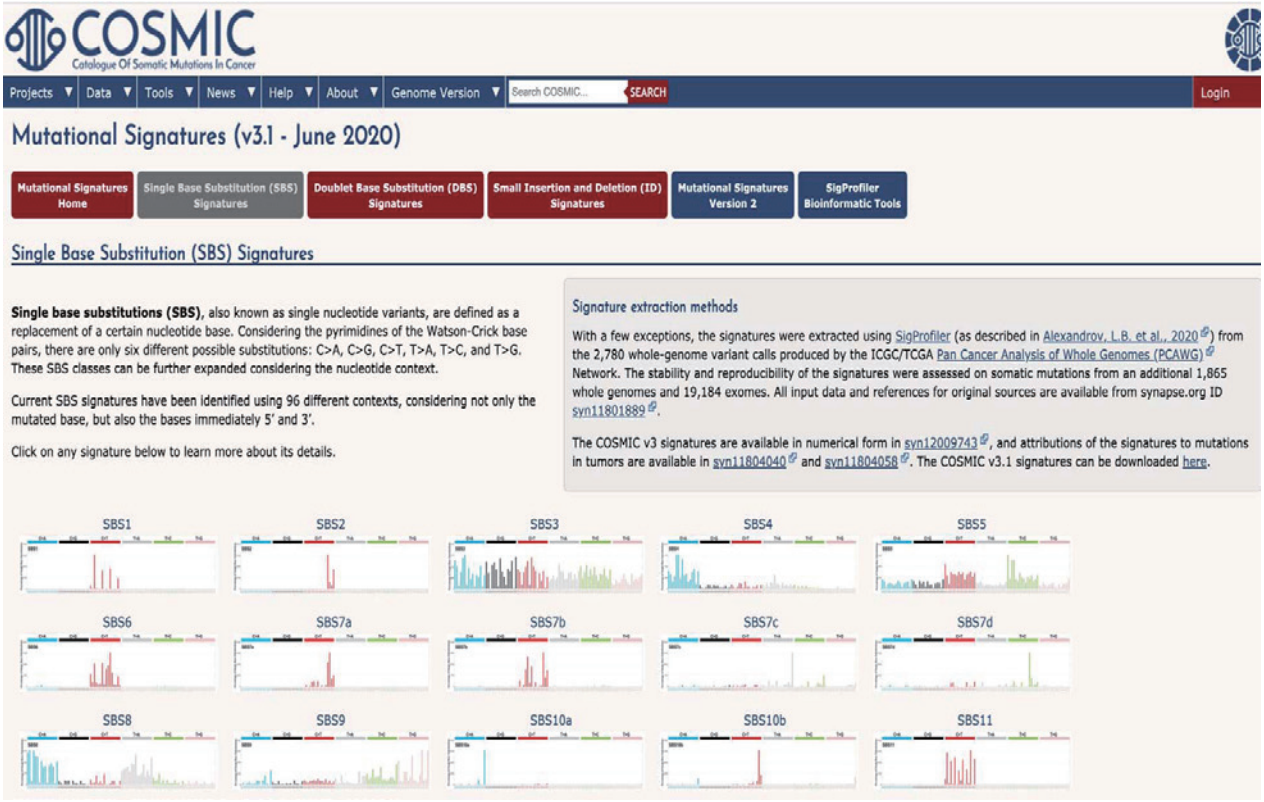
Mutational Signature (v3 – May 2019)

- Single Base Substitution (SBS): 65 signatures (18 possible sequencing artifacts)
- Double Base Substitution (DBS): 11 signatures
- Small Insertion and Deletion Substitution (ID): 17 signatures



13

Mutational Signature v3.1

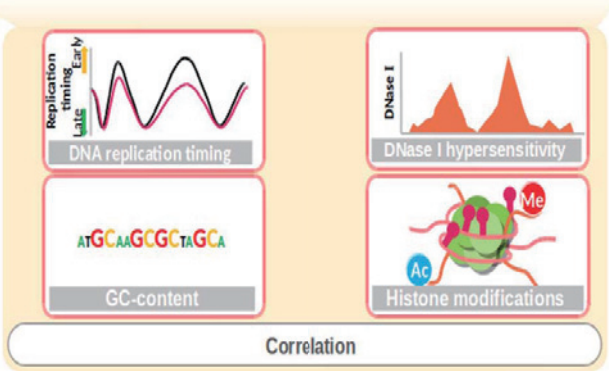


If there are 3,000 mutations
we'd expect a random dispersion of mutations (approx. 1 mutation/Mb)

Human genome ≈ 3,000-megabase (Mb)

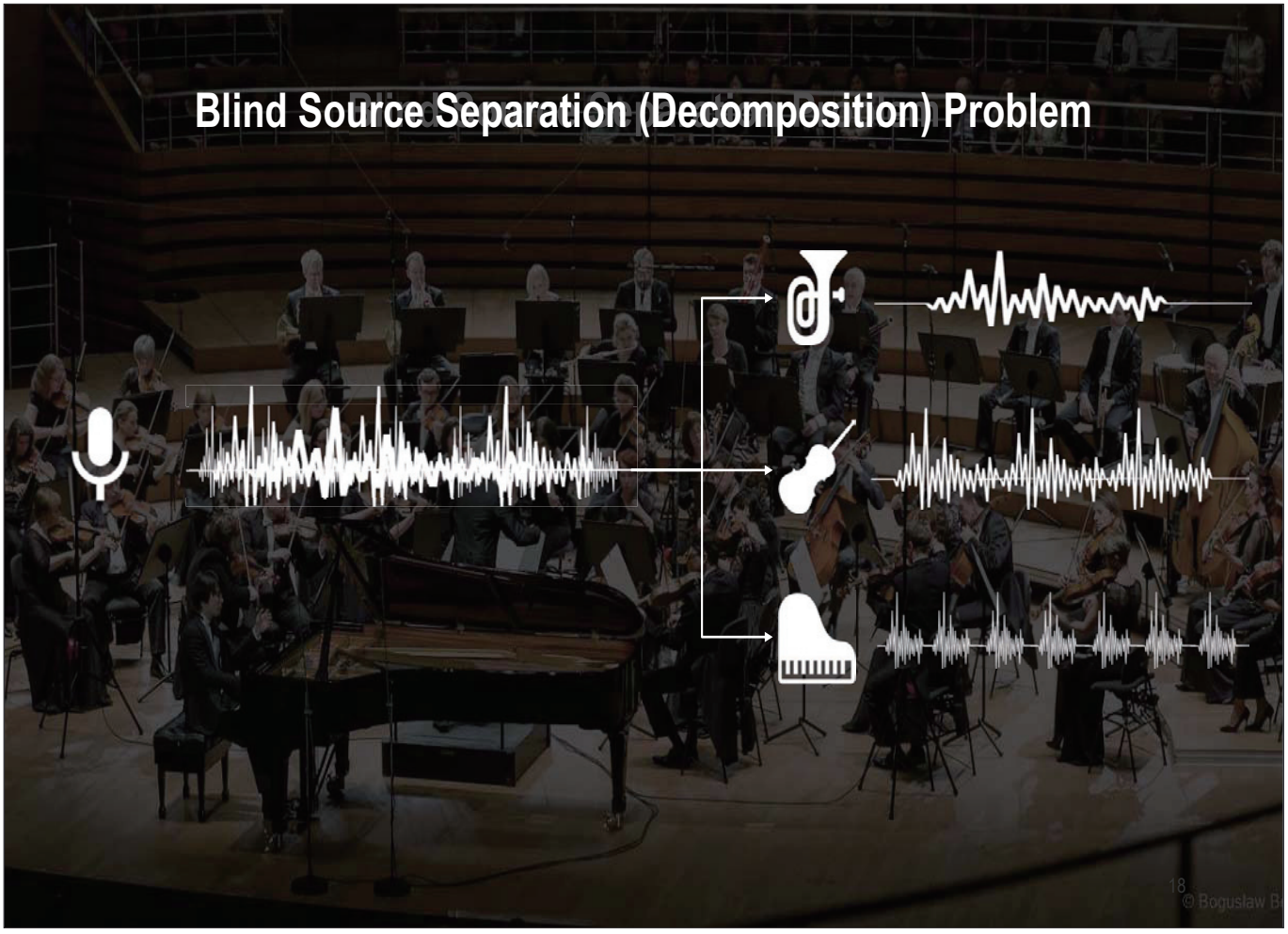
15

However, in reality, we observe uneven distribution of mutations
in genome due to favored contexts



16


© Bogusław B

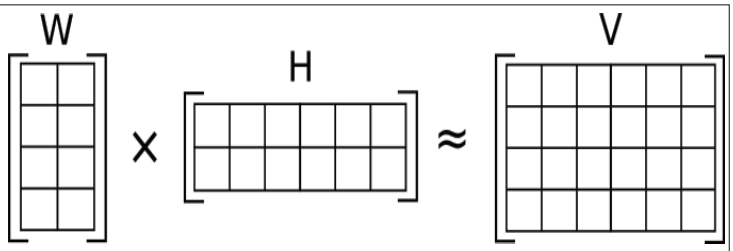

Blind Source Separation (Decomposition) Problem
18
© Bogusław B

WIKIPEDIA
The Free Encyclopedia

Article Talk

Non-negative matrix factorization

From Wikipedia, the free encyclopedia



History [edit]

In chemometrics non-negative matrix factorization has a long history under the name "self modeling curve resolution".[10] In this framework the vectors in the right matrix are continuous curves rather than discrete vectors. Also early work on non-negative matrix factorizations was performed by a Finnish group of researchers in the 1990s under the name *positive matrix factorization*.[11][12][13] It became more widely known as *non-negative matrix factorization* after Lee and Seung investigated the properties of the algorithm and published some simple and useful algorithms for two types of factorizations.[14][15]

Background [edit]

Let matrix $\mathbf{V}$ be the product of the matrices $\mathbf{W}$ and $\mathbf{H}$,

$$\mathbf{V} = \mathbf{WH}.$$

Matrix multiplication can be implemented as computing the column vectors of $\mathbf{V}$ as linear combinations of the column vectors in $\mathbf{W}$ using coefficients supplied by columns of $\mathbf{H}$. That is, each column of $\mathbf{V}$ can be computed as follows:

$$\mathbf{v}_i = \mathbf{W}\mathbf{h}_i,$$

where $\mathbf{v}_i$ is the i-th column vector of the product matrix $\mathbf{V}$ and $\mathbf{h}_i$ is the i-th column vector of the matrix $\mathbf{H}$.

When multiplying matrices, the dimensions of the factor matrices may be significantly lower than those of the product matrix and it is this property that forms the basis of NMF. NMF generates factors with significantly reduced dimensions compared to the original matrix. For example, if $\mathbf{V}$ is an $m \times n$ matrix, $\mathbf{W}$ is an $m \times p$ matrix, and $\mathbf{H}$ is a $p \times n$ matrix then p can be significantly less than both m and n.

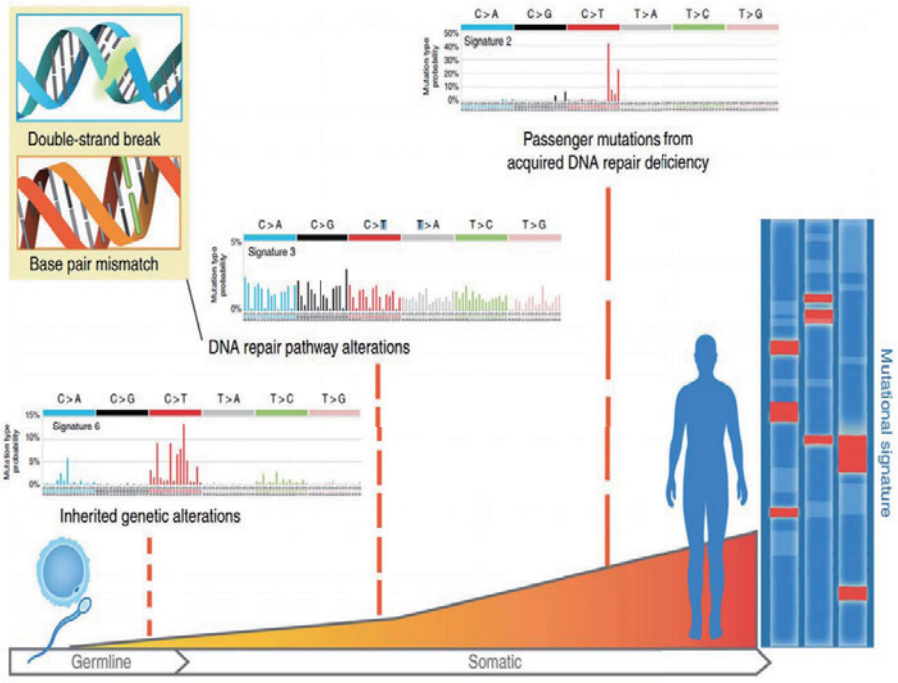
Here is an example based on a text-mining application:

- Let the input matrix (the matrix to be factored) be $\mathbf{V}$ with 10000 rows and 500 columns where words are in rows and documents are in columns. That is, we have 500 documents indexed by 10000 words. It follows that a column vector $\mathbf{v}$ in $\mathbf{V}$ represents a document.
- Assume we ask the algorithm to find 10 features in order to generate a *features matrix* $\mathbf{W}$ with 10000 rows and 10 columns and a *coefficients matrix* $\mathbf{H}$ with 10 rows and 500 columns.
- The product of $\mathbf{W}$ and $\mathbf{H}$ is a matrix with 10000 rows and 500 columns, the same shape as the input matrix $\mathbf{V}$ and, if the factorization worked, it is a reasonable approximation to the input matrix $\mathbf{V}$.
- From the treatment of matrix multiplication above it follows that each column in the product matrix $\mathbf{WH}$ is a linear combination of the 10 column vectors in the features matrix $\mathbf{W}$ with coefficients supplied by the coefficients matrix $\mathbf{H}$.

This last point is the basis of NMF because we can consider each original document in our example as being built from a small set of hidden features. NMF generates these features.

It is useful to think of each feature (column vector) in the features matrix $\mathbf{W}$ as a document archetype comprising a set of words where each word's cell value defines the word's rank in the feature: The higher a word's cell value the higher the word's rank in the feature. A column in the coefficients matrix $\mathbf{H}$ represents an original document with a cell value defining the document's rank for a feature. We can now reconstruct a document (column vector) from our input matrix by a linear combination of our features (column vectors in $\mathbf{W}$) where each feature is weighted by the feature's cell value from the document's column in $\mathbf{H}$.

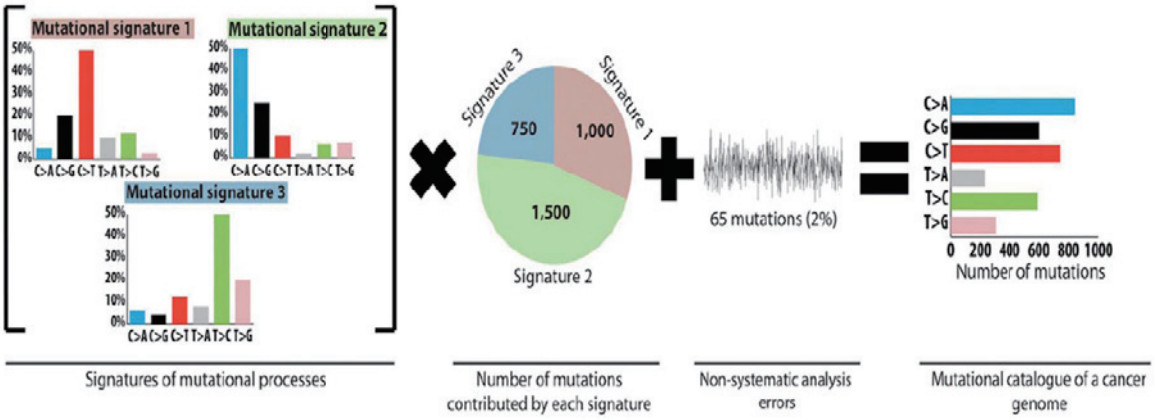
Mutations accumulated over lifetime can be decomposed



Jennifer Ma et al., *Nat Comm* 2017

20

Mutational signature decomposition



Alexandrov et al., *Cell* 2013

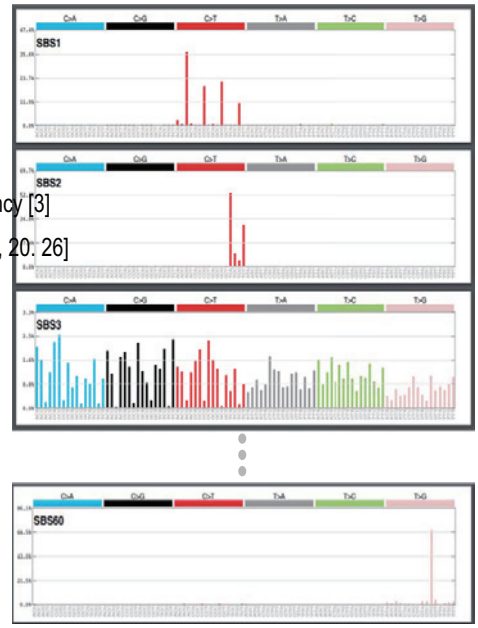
Mutational signatures

30 Catalogue of Somatic Mutations in Cancer (COSMIC) signatures

- Age [1, 5]
- APOBEC activity [2, 13]
- Homologous recombination deficiency [3]
- Defective DNA mismatch repair [15, 20, 26]
- Tobacco smoking/chewing [4, 29]
- Ultraviolet light exposure [7]
- *POLE* mutations [10]
- Exposure to aristolochic acid [22]
- Alkylating agent temozolomide [11]
- Aflatoxin [24]

Alexandrov et al., *Nature* 2013

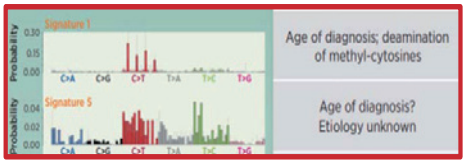
65 PanCancer Analysis of Whole Genomes (PCAWG) signatures

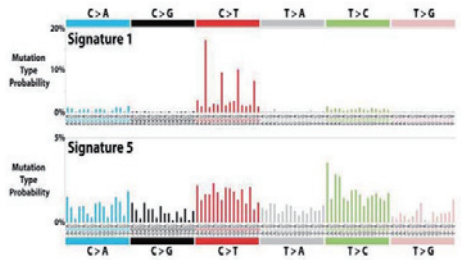


Campbell et al., *bioRxiv* 2017

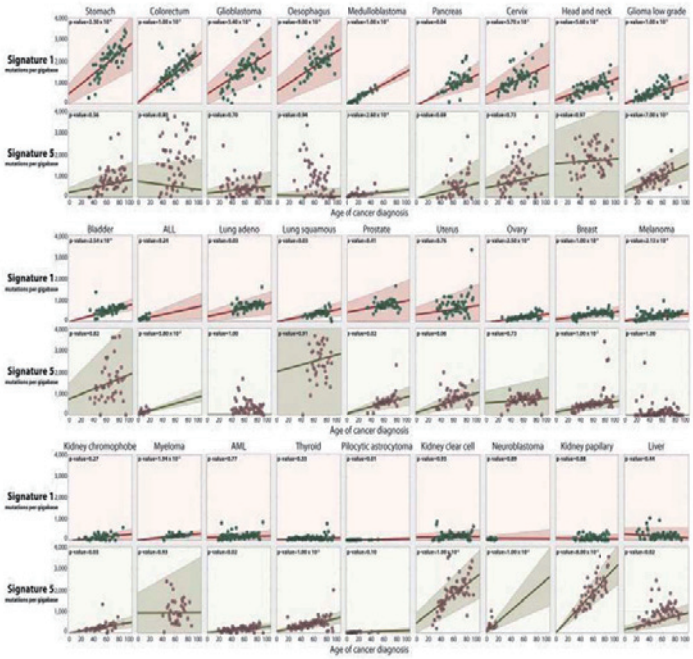
Clock-like mutational signatures

Nik-Zainal et al., *Clinical Cancer Research* 2017





Signature 1 and 5 is positively correlated to the age of patients



Alexandrov, Ludmil B., et al. *Nat Gen* 2015

Mutational signatures are clinically relevant

A	Associations	Prevalence in breast cancer	Presence in other cancer types
Signature 1	Age of diagnosis; deamination of methyl-cytosines	Common >75% of samples	Reported in nearly all other tumor types
Signature 5	Age of diagnosis? Etiology unknown	Common >75% of samples	Reported to be in many other tumor types, but not consistently
Signature 8	Increased in HR deficiency and late in cancer evolution but present at lower levels in many tumors	Common >60% of samples	Many tumor types
Signature 3	Homologous recombinational repair deficiency	Common >20% of samples	Many tumor types
Signature 2	APOBEC cytidine deaminases	Common >75% of samples	More than half of all tumor types examined so far
Signature 13	APOBEC cytidine deaminases	Common >75% of samples	Many tumor types
Signature 6	Mismatch repair deficiency	Rare <10% of samples	Adrenocortical, colon, uterine, ovarian, pancreas
Signature 20	Mismatch repair deficiency	Rare <5% of samples	Gastric
Signature 26	Mismatch repair deficiency	Rare <5% of samples	Cervical, gastric, uterine

Nik-Zainal et al., *Clinical Cancer Research* 2017

"... **mutational signatures [3, 6, 20, 26]** are a direct pathophysiologic readout of the abrogation of a DNA repair gene/pathway and could be used as a **biomarker** to report **DNA repair/deficiency** in a tumor."

nature medicine

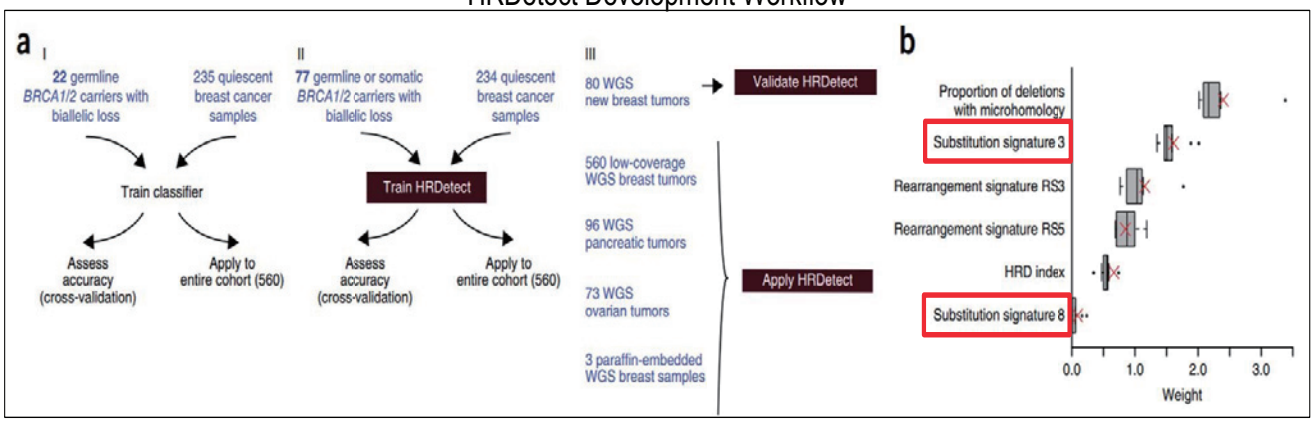
ANALYSIS

HRDetect is a predictor of *BRCA1* and *BRCA2* deficiency based on mutational signatures

Helen Davies[1,32], Dominik Glodzik[1,32], Sandro Morganella[1], Lucy R Yates[1,2], Johan Staaf[3], Xueqing Zou[1], Manasa Ramakrishna[1,4], Sancha Martin[1], Sandrine Boyault[5], Anieta M Sieuwerts[6], Peter T Simpson[7], Tari A King[8], Keiran Raine[1], Jorunn E Eyfjord[9], Gu Kong[10], Åke Borg[3], Ewan Birney[11], Hendrik G Stunnenberg[12], Marc J van de Vijver[13], Anne-Lise Borresen-Dale[14,15], John W M Martens[6], Paul N Span[16,17], Sunil R Lakhani[7,18], Anne Vincent-Salomon[19,20], Christos Sotiriou[21], Andrew Tutt[22,23], Alastair M Thompson[24], Steven Van Laere[25,26], Andrea L Richardson[27,28], Alain Viari[29,30], Peter J Campbell[1], Michael R Stratton[1] & Serena Nik-Zainal[1,31]

Mutational signature #3 (homologous recombination defect)

HRDetect Development Workflow

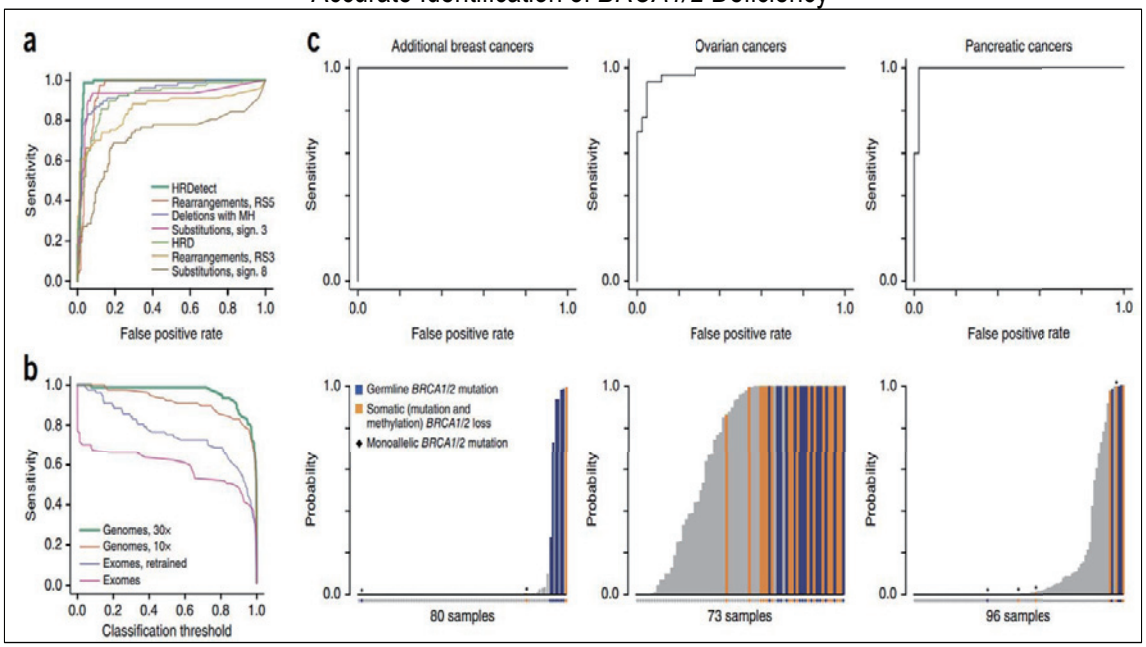


Helen Davies et al., *Nature Medicine* 2017

25

Mutational signature #3 (homologous recombination defect)

Accurate Identification of *BRCA1/2* Deficiency

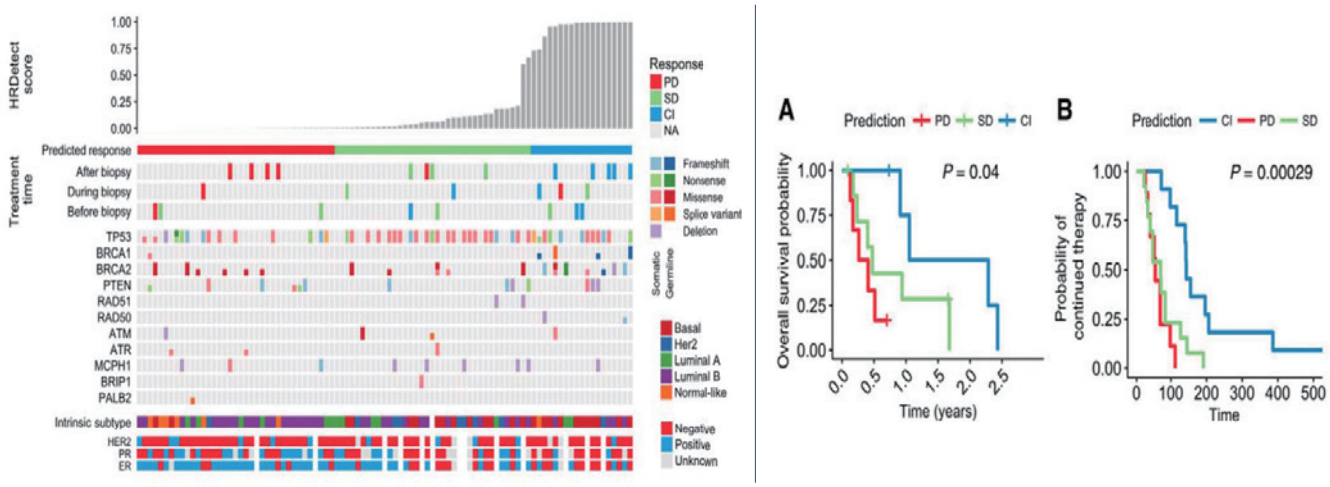


Helen Davies et al., *Nature Medicine* 2017

26

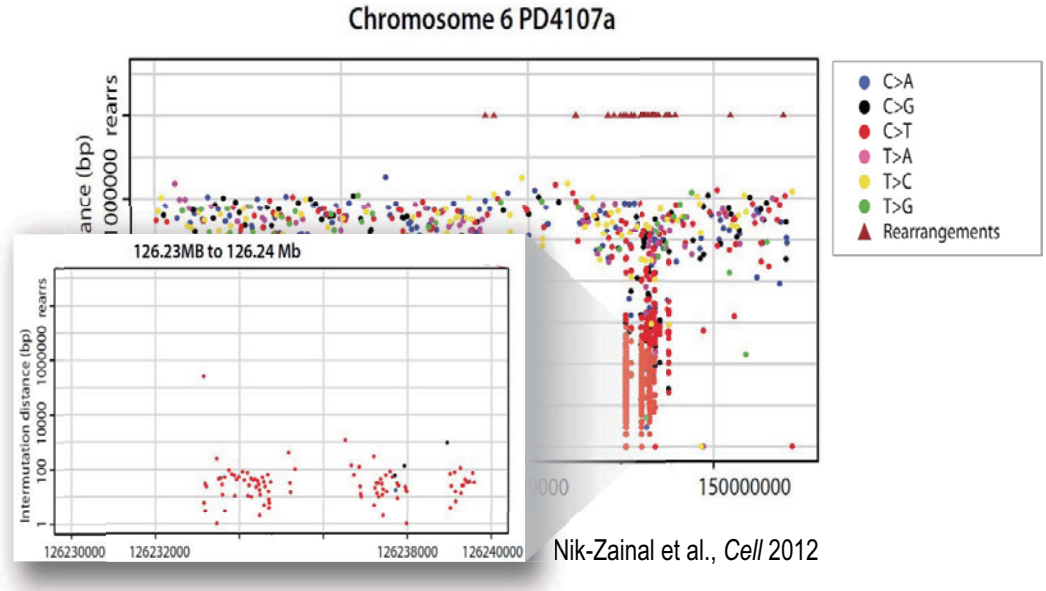
Mutational signature #3 (homologous recombination defect)

Homologous Recombination Deficiency and Platinum-Based Therapy Outcomes in Advanced Breast Cancer



Eric Y. Zhao et al., *Clinical Cancer Research* 2017

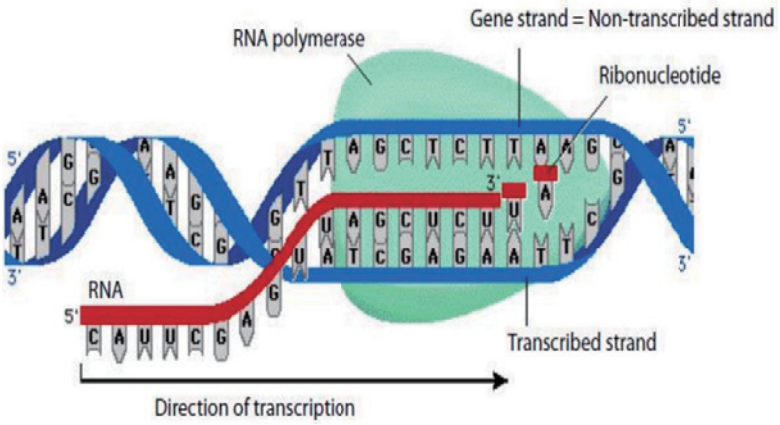
Localized hypermutations (kataegis)



Nik-Zainal et al., *Cell* 2012

- There are clusters of mutations with short distances between mutations (kataegis)
- Kataegis is co-localized with rearrangements that have features of chromothripsis

Transcriptional strand bias



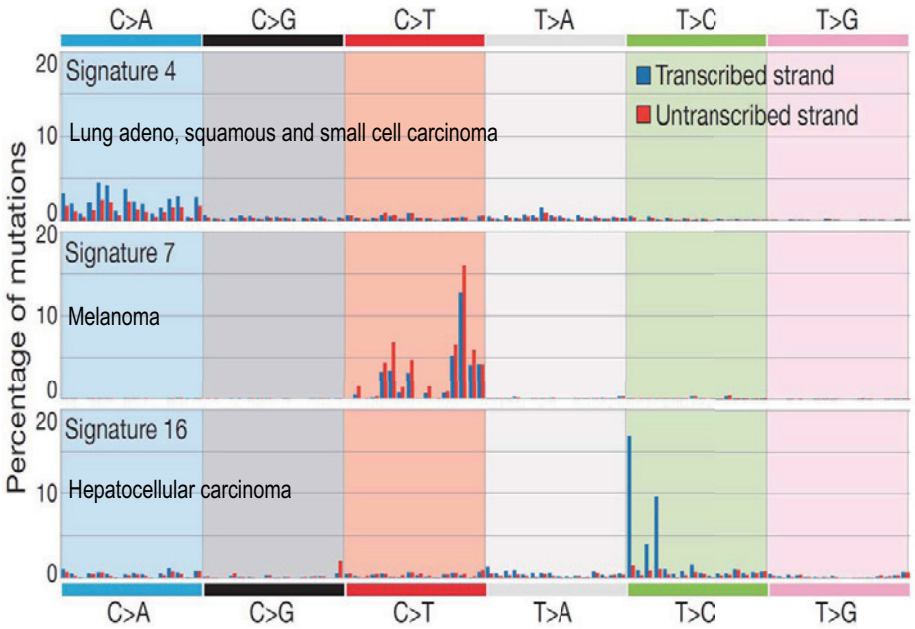
ftp://ftp.sanger.ac.uk/pub/resources/theses/snz/chapter6.pdf

Cause of transcriptional strand bias is transcription-coupled repair (TCR) of nucleotide excision repair (NER); DNA damage is repaired more efficiently on the transcribed strand

29

Somatic mutation rates are biased by transcriptional strand

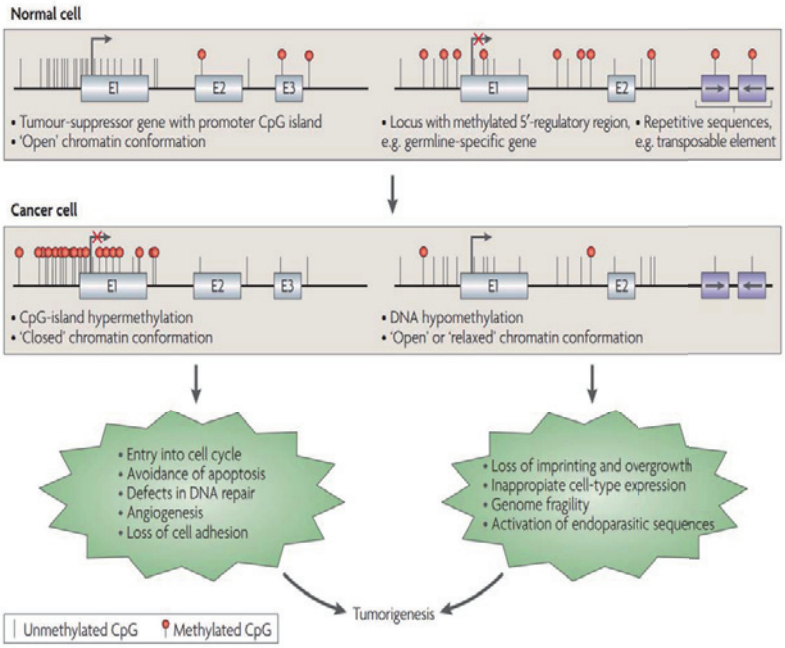
Fewer mutations accumulate on the transcribed strand



Alexandrov et al., *Nature* 2013

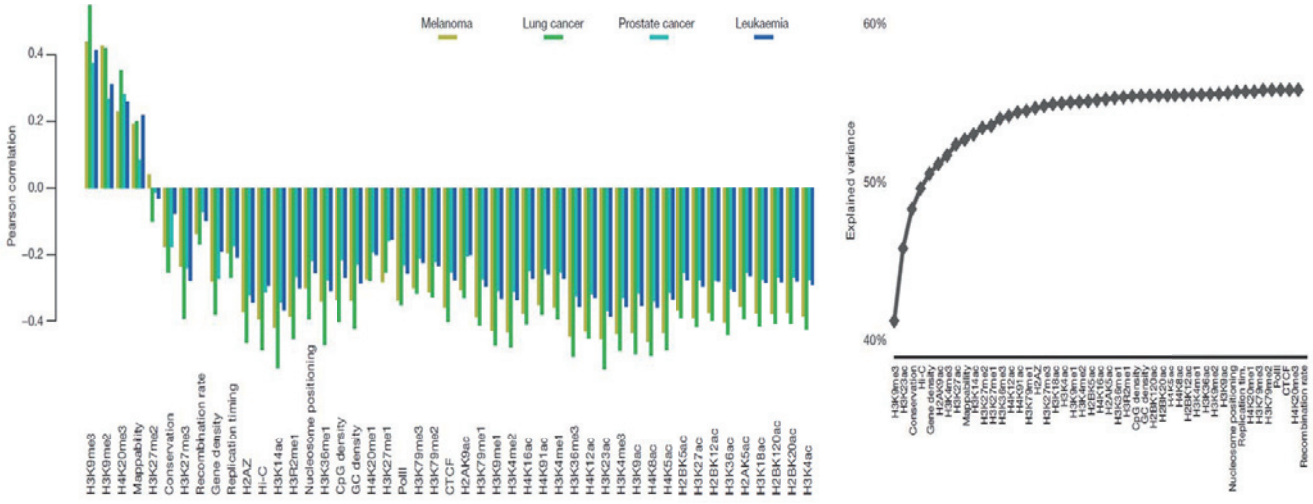
30

Cancer and epigenomics



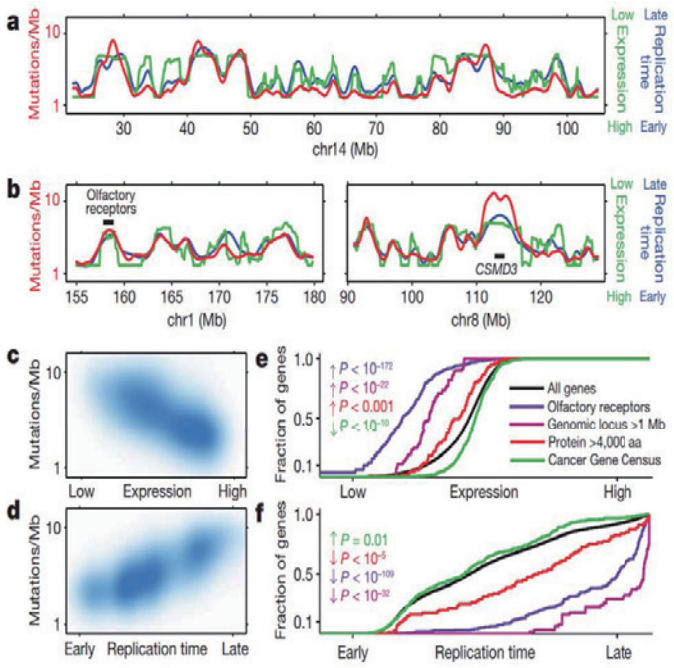
Esteller, *Nature Reviews Genetics* 2007

Mutation rates are correlated with genomic/epigenomic modifications



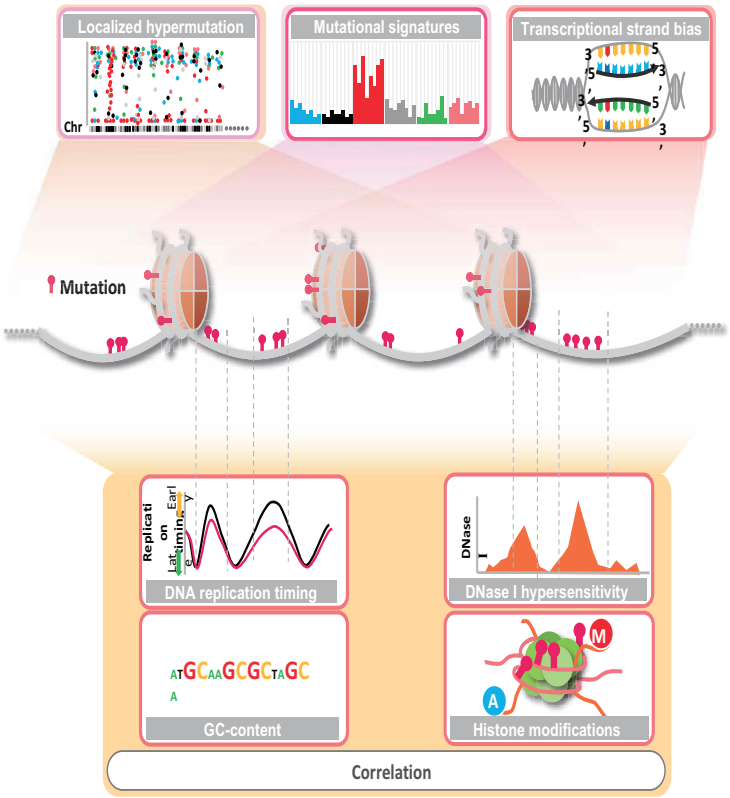
Schuster-Bockler and Lehner, *Nature* 2012

Mutation rates also vary with DNA replication timing



Lawrence et al., *Nature* 2013

Putting them altogether to better understand mutations operative in cancer



Existing mutational signature decomposition tools

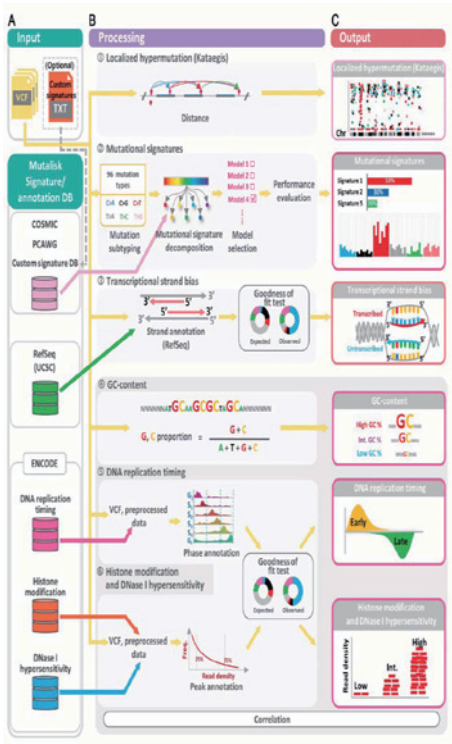
Tool	Graphical user interface available?	Batch analysis possible?	Results downloadable?
WTSI (Alexandrov et al., Cell 2013)	No	Yes	Yes
deconstructSigs (Rosenthal et al., Genome Biology 2016)	No	Yes	Yes
MutaGene (Goncearenco et al., Nucleic Acids Research 2017)	Yes	No	No

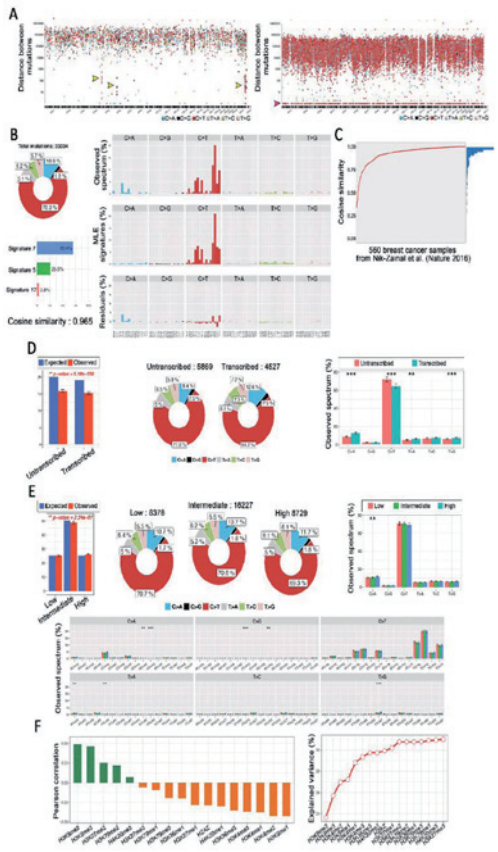
35

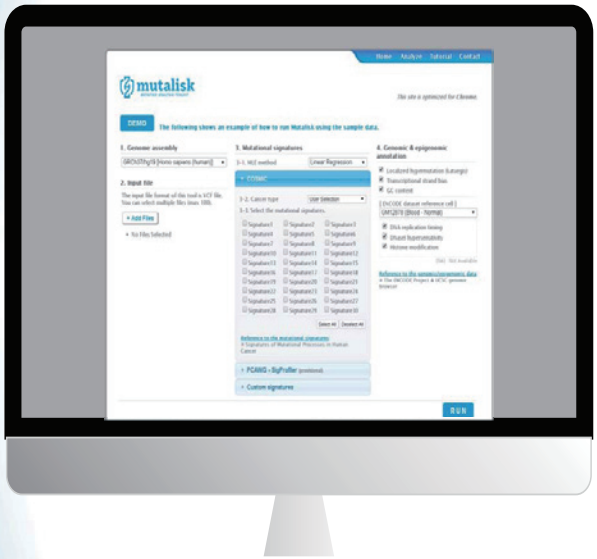
Mutalisk: a web-based somatic MUTation AnaLysIS toolKit for genomic, transcriptional and epigenomic signatures (Nucleic Acids Research, 2018)


Mutalisk: a web-based somatic MUTation AnaLysIS toolKit for genomic, transcriptional and epigenomic signatures

개방형 오픈 플랫폼







mutalisk
MUTATION ANALYSIS TOOLKIT

1. Identification of mutational signatures

1. Analysis of associations between various genome/epigenome regulatory elements and somatic mutation rates

Available at http://mutalisk.org/

37

Mutalisk (1) – analysis options

GRCh37/hg19, GRCh38/hg38, GRCm38/mm10, WBcel236/ce11, WS220/ce10

Multiple vcf files (max 100)

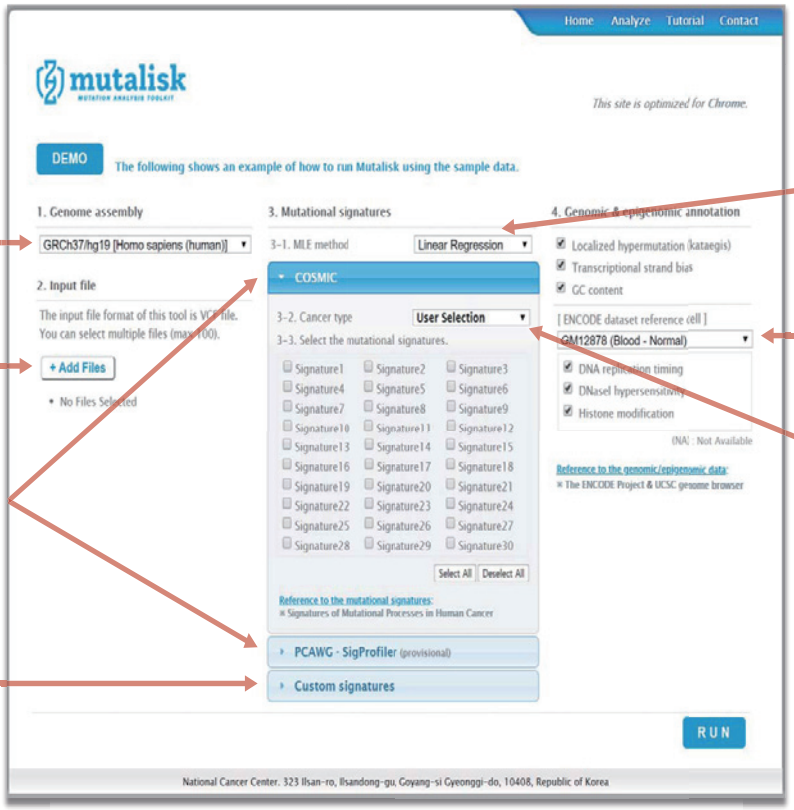
COSMIC, PCAWG (SigProfiler) signatures

User/custom signatures

Linear regression or multinomial test methods (signature decomposition)

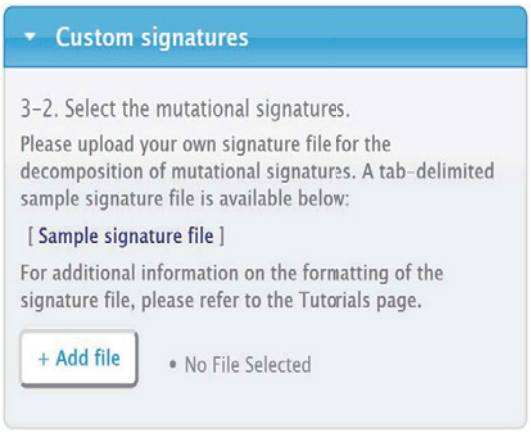
31 cell lines

42 cancer types



38

Mutalisk (1) – analysis options

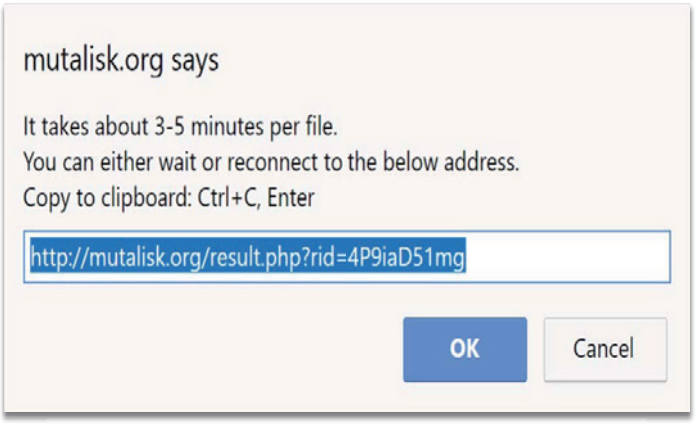


Provide a tab-delimited .txt signature file

96 mutation subtypes

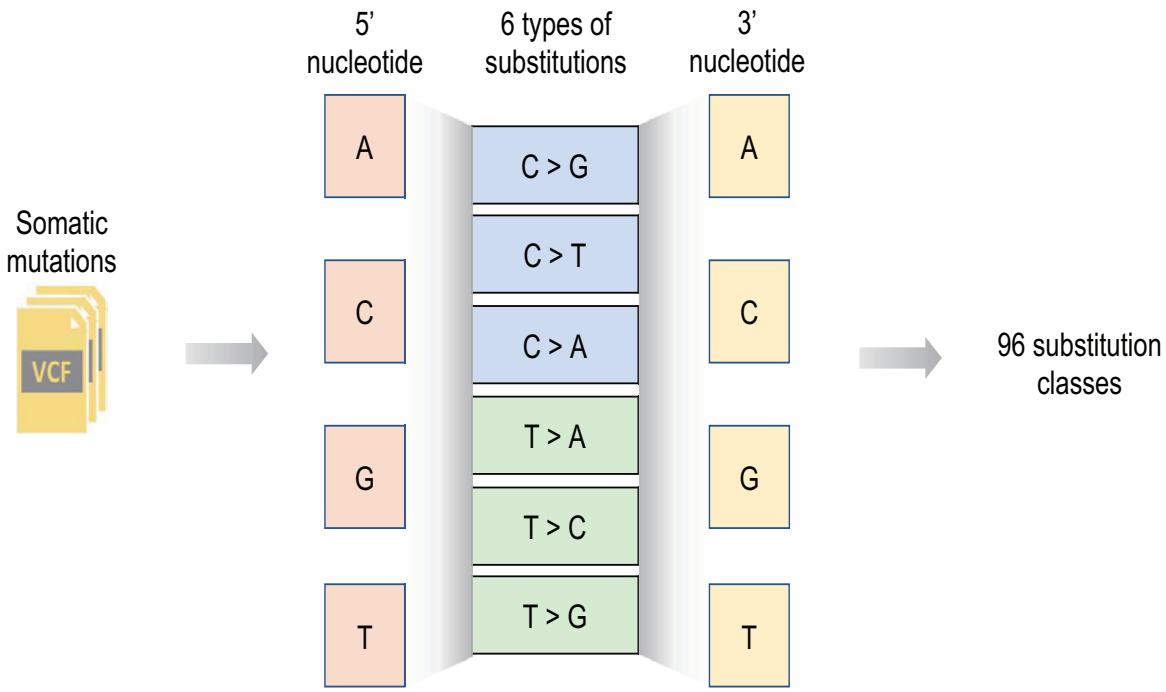
Substitution Type	Trinucleotide	Somatic Mutation Type	Signature 1	...	Signature 7
C>A	ACA	A[C>A]A	0.011098326		0.0004
C>A	ACC	A[C>A]C	0.009149341		0.0005
C>A	ACG	A[C>A]G	0.00149007		0
C>A	ACT	A[C>A]T	0.006233885		0.0004
C>G	ACA	A[C>G]A	0.001801068		0
⋮					⋮
T>G	TTT	T[T>G]T	0.004030128	...	0.0014

Mutalisk (1) – analysis options



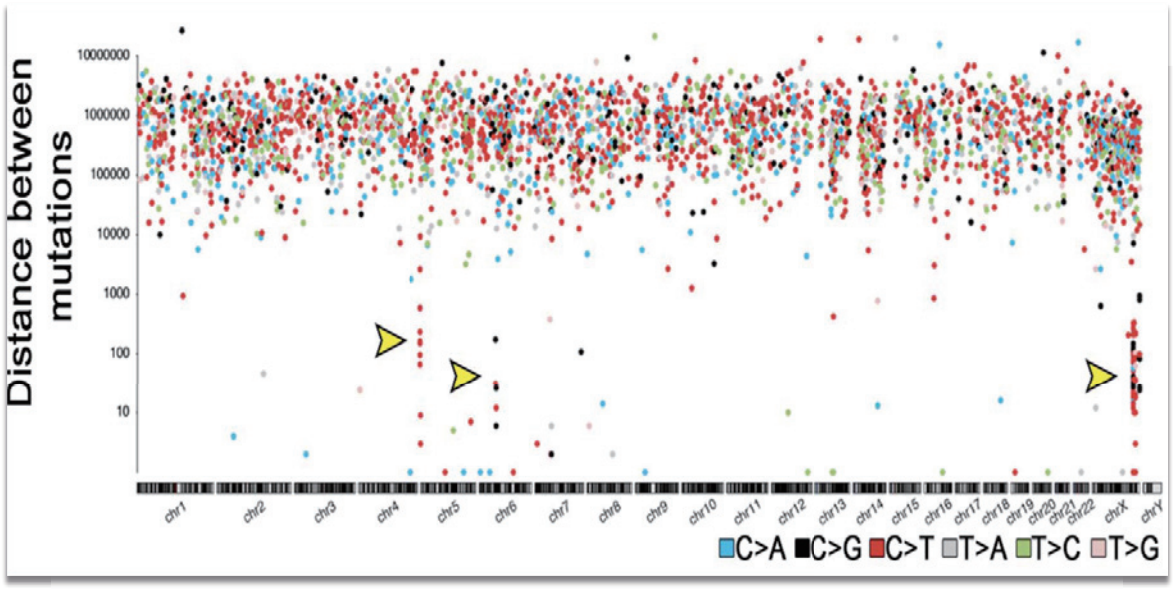
User-uploaded data are permanently deleted after 48 hours;
you may access the analysis results for 48 hours

Mutalisk (2) – preprocessing



41

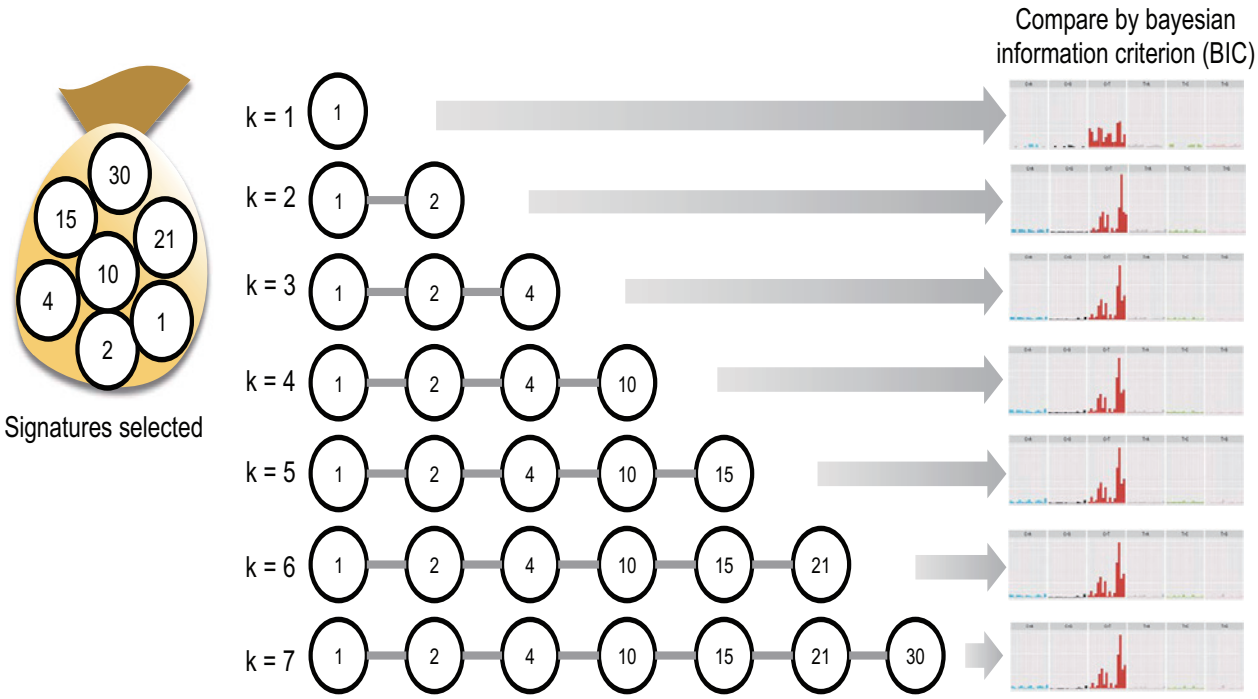
Mutalisk (3) – rainfall plot (*kataegis)*



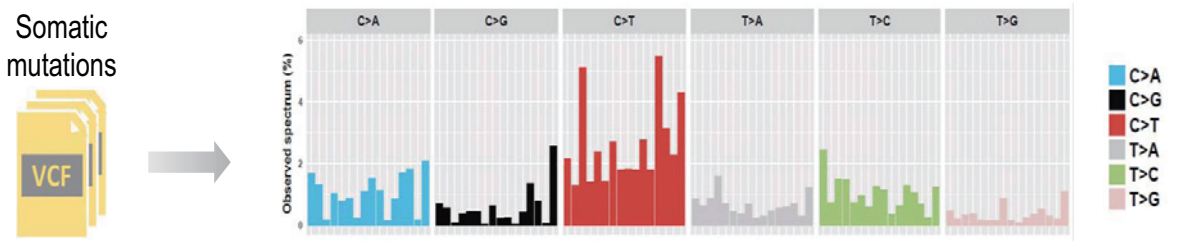
Lung cancer sample (Lee et al., *J Clin Oncol* 2017)

42

Mutalisk (4) – mutational signature identification



Mutalisk (4) – mutational signature identification



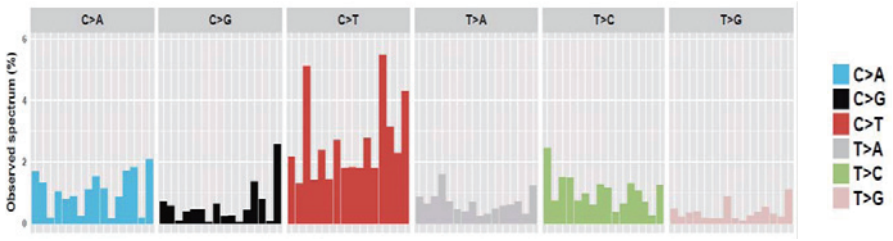
If we conjecture that there are 7 COSMIC signatures underlying the mutational profile, then

$$C(30,7) = \frac{30!}{(7!\,(30-7)!)}$$

2,035,800 different combinations of signatures

Mutalisk (4) – mutational signature identification

Somatic mutations



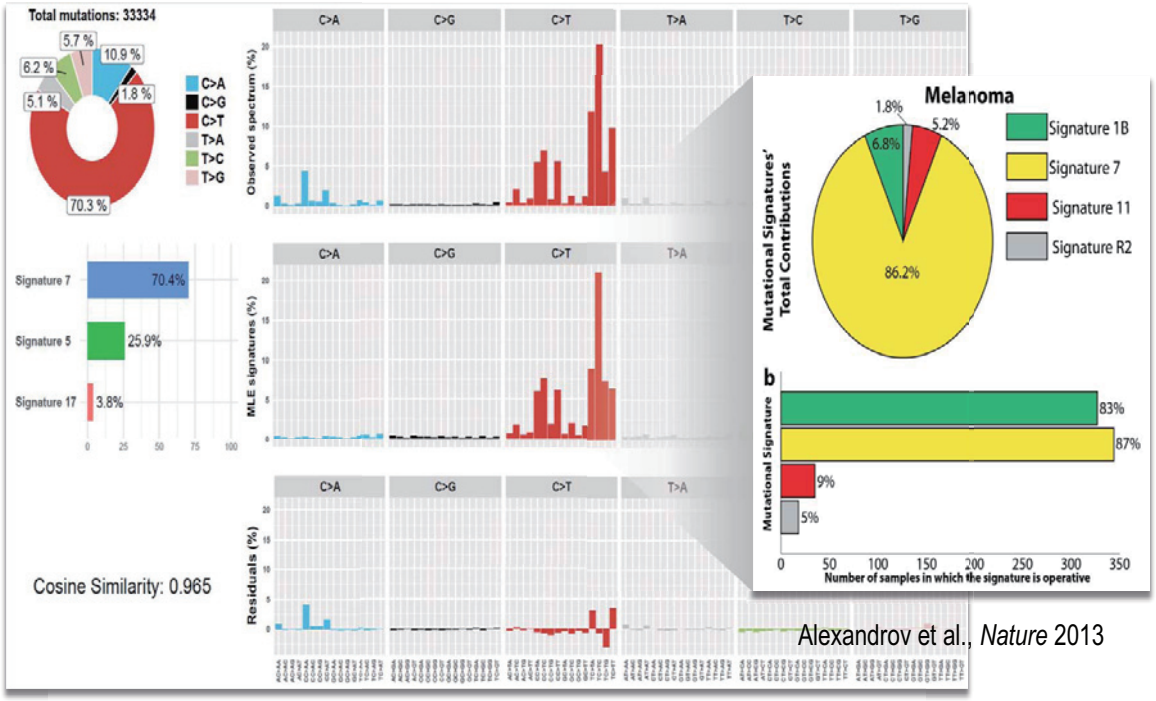
If we conjecture that there are 7 PCAWG signatures underlying the mutational profile, then

$$C(65,7) = \frac{65!}{(7!\,(65-7)!)}$$

696,190,560 different combinations of signatures

This is a computationally expensive task

Mutalisk (4) – mutational signature identification



Alexandrov et al., *Nature* 2013

Melanoma sample (Pleasance et al., *Nature* 2010)

Mutalisk (4) – mutational signature identification

Mutalisk identifies up to 7 decomposition models

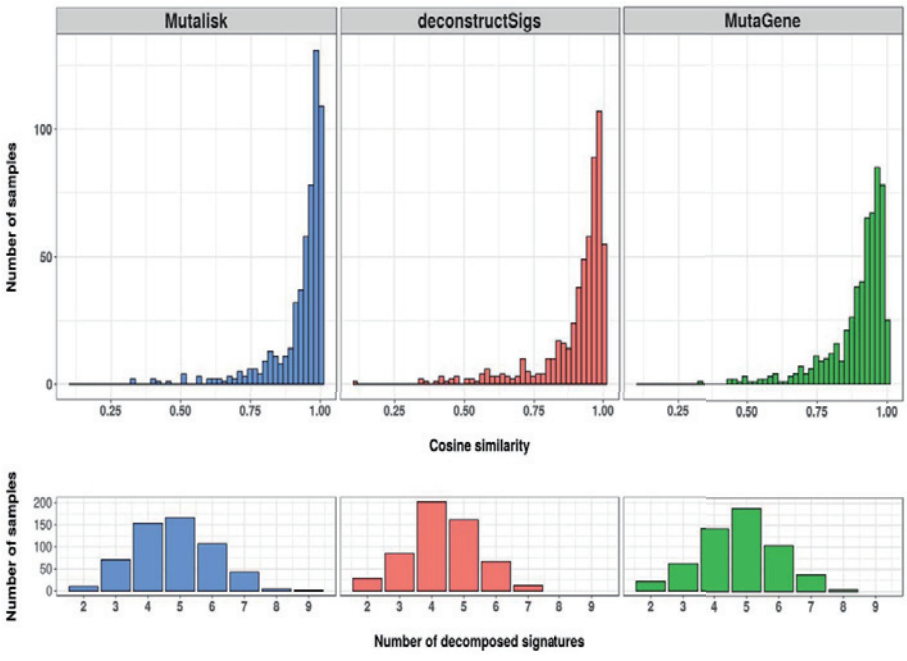
Mutational signatures

No.	Signatures	Probabilities	Cosine similarity	BIC	Confidence Interval
7	7 8 2 11 18 17 12 Our Best	0.59097 0.11749 0.10825 0.06858 0.05707 0.03374 0.02390	0.98200	222713.700	View
6	7 8 2 11 18 17	0.59163 0.14049 0.10844 0.06984 0.05328 0.03632	0.98200	222820.200	View
5	7 8 2 11 17	0.59492 0.19932 0.10851 0.06440 0.03285	0.98200	223568.700	View
3	7 8 2	0.64330 0.25263 0.10407	0.98000	224619.100	View
4	7 8 2 11	0.59826 0.22793 0.10916 0.06466	0.98100	224828.400	View
2	7 8	0.71863 0.28137	0.96800	225142.600	View
1	7	1.00000	0.78700	273566.100	View

47

Mutalisk (4) – mutational signature identification

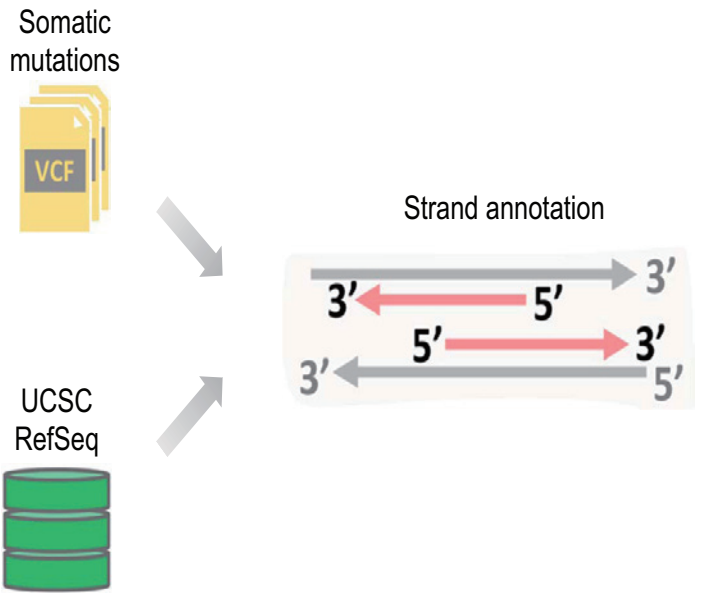
Comparison of decomposition results using 560 breast cancer samples (Nik-Zainal et al., Nature 2016)



Tool	Median cosine similarity
Mutalisk	**0.966**
deconstructSigs	0.948
MutaGene	0.931

48

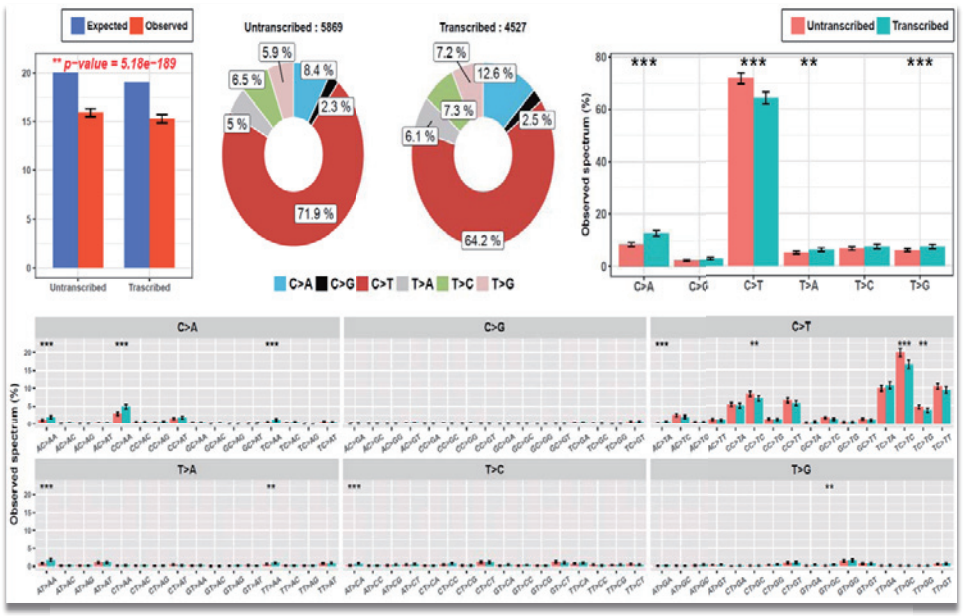
Mutalisk (5) – transcriptional strand bias analysis

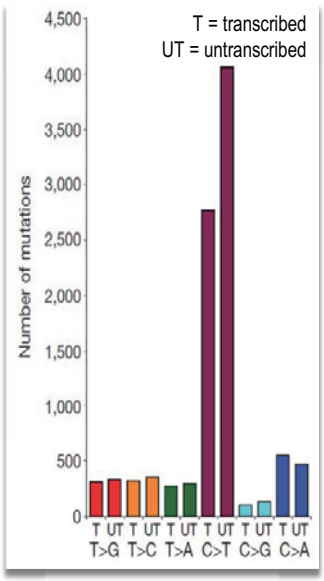


Reference genome	Transcribed strand region proportion	Untranscribed strand region proportion
CRCh37/hg19	0.19044	0.20010
GRCh38/hg38	0.18885	0.28435

49

Mutalisk (5) – transcriptional strand bias analysis



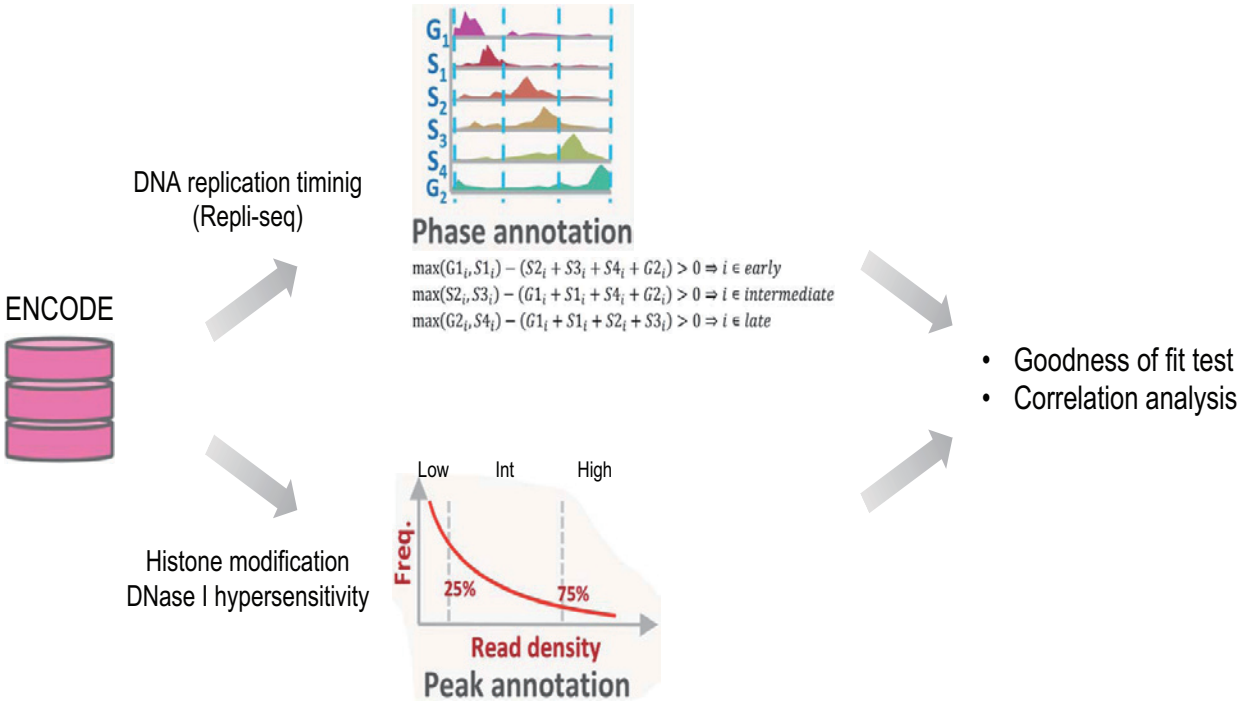


Melanoma sample (Pleasance et al., *Nature* 2010)

Pleasance et al., *Nature* 2010

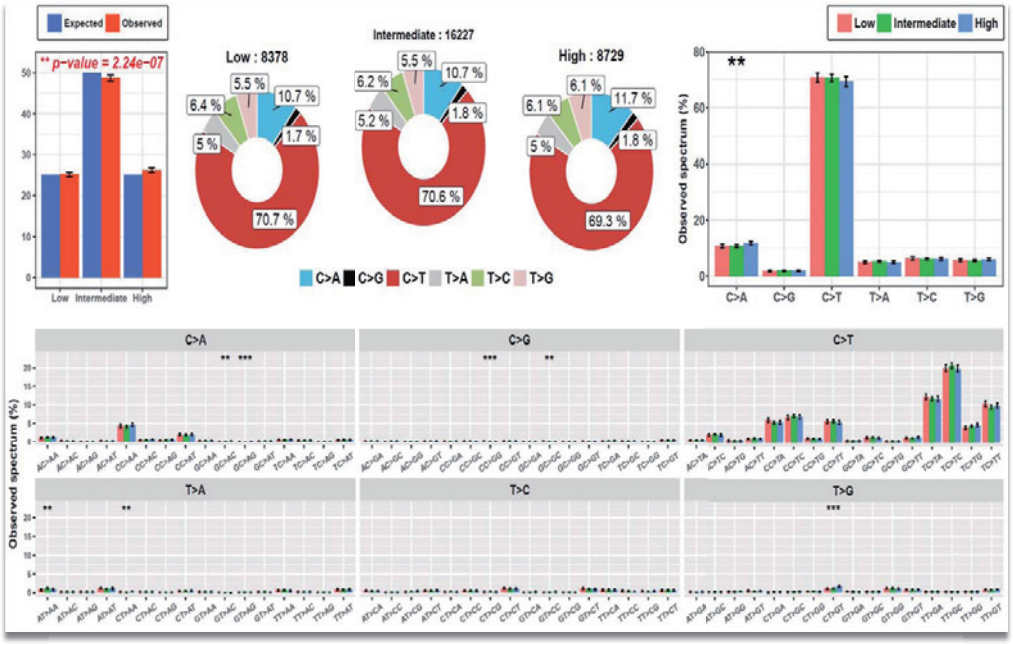
50

Mutalisk (6) – genomic/epigenomic modification analysis



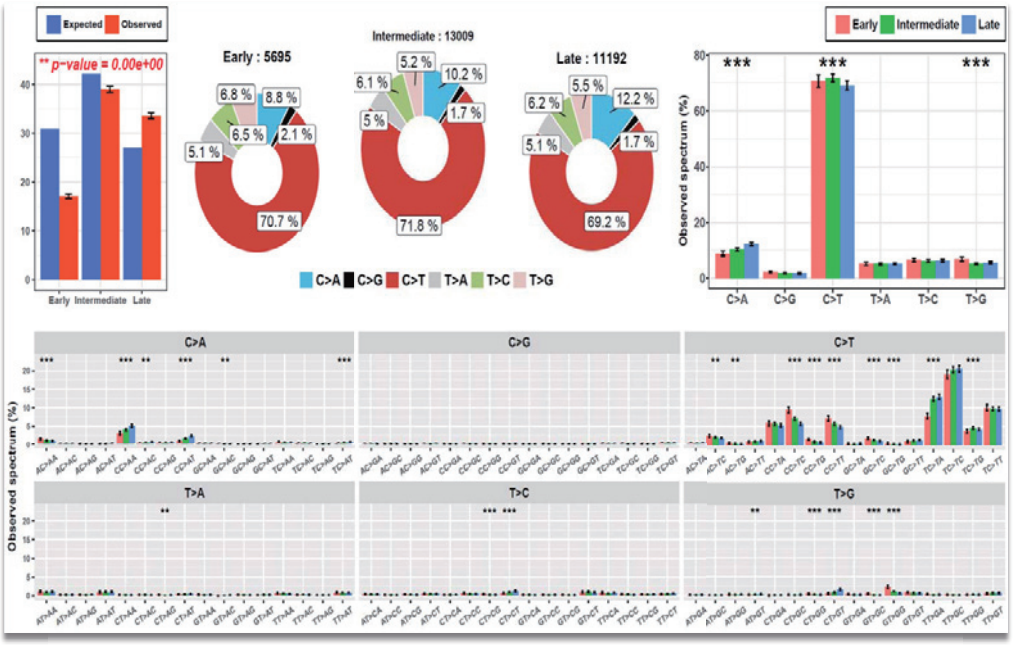
Mutalisk (6) – genomic/epigenomic modification analysis

H3k9me3 , melanoma sample (Pleasance et al., Nature 2010)



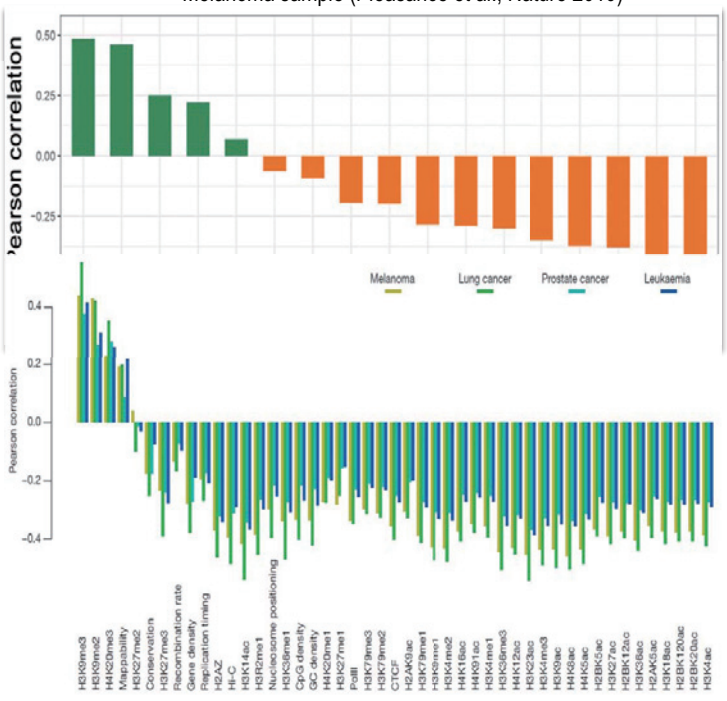
Mutalisk (6) – genomic/epigenomic modification analysis

DNA replication timing, melanoma sample (Pleasance et al., Nature 2010)



Mutalisk (6) – genomic/epigenomic modification analysis

Melanoma sample (Pleasance et al., Nature 2010)

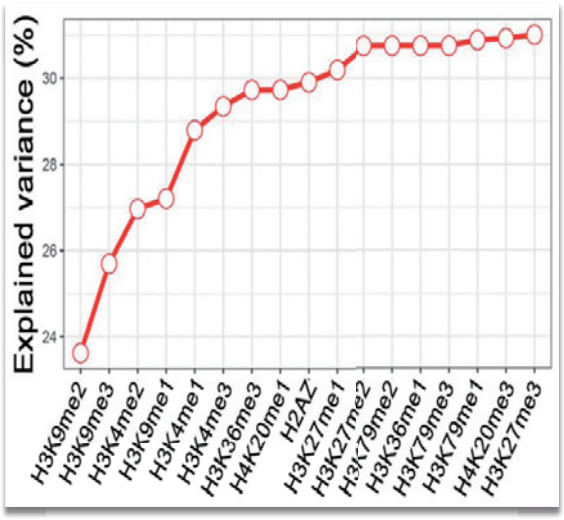


Mutalisk

Schuster-Bockler and Lehner, *Nature* 2012

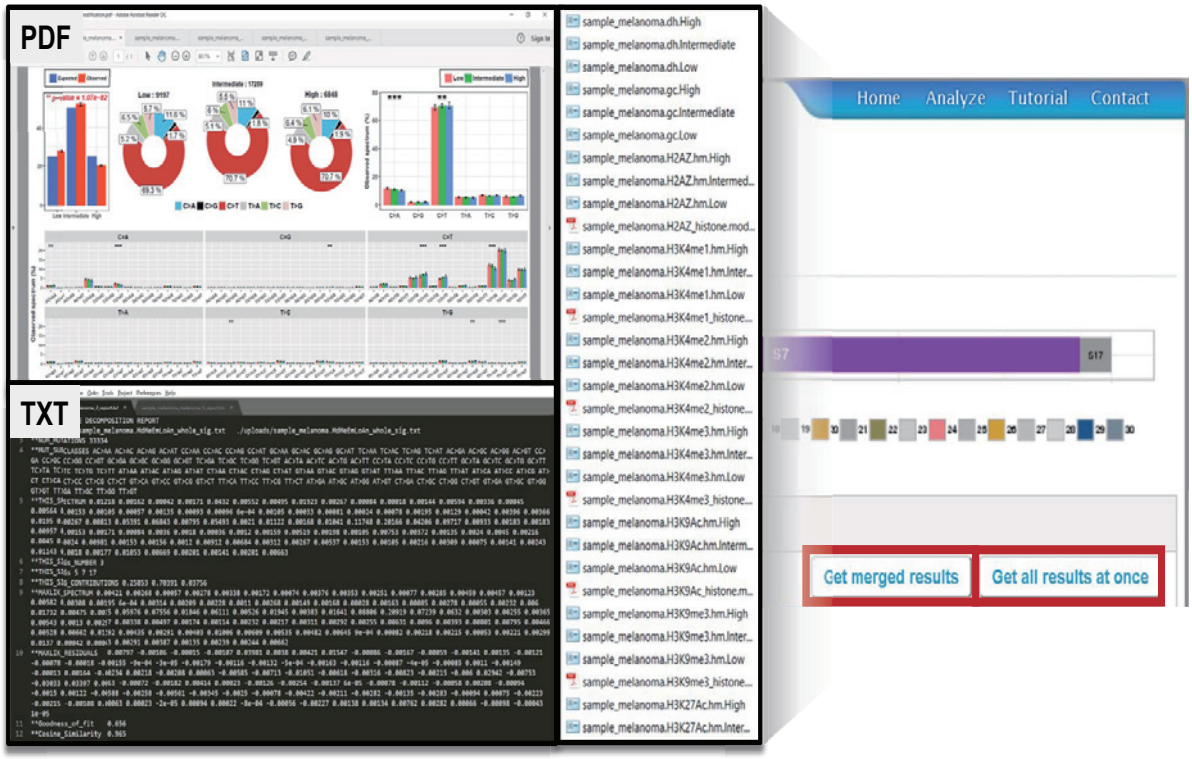
Mutalisk (6) – genomic/epigenomic modification analysis

Melanoma sample (Pleasance et al., Nature 2010)

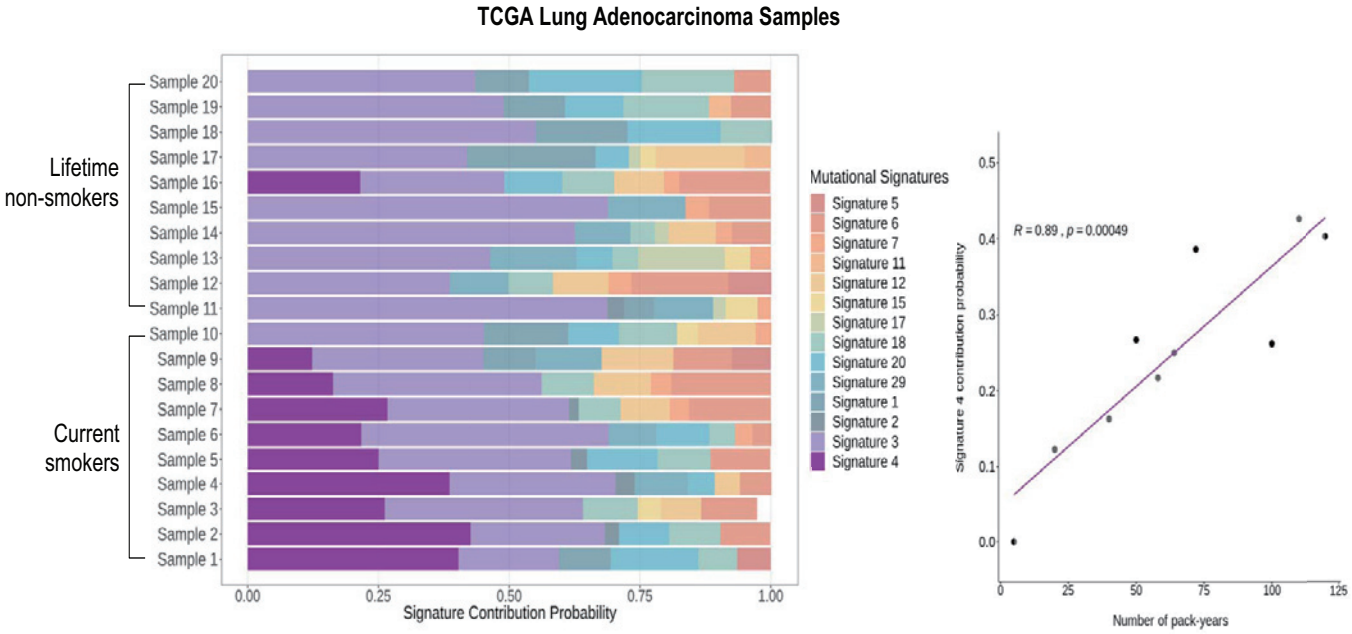


- Forward feature selection (generalized least-squares model and Akaike information criterion)
- Explained variance computed by linear regression

Mutalisk (7) – downloading results

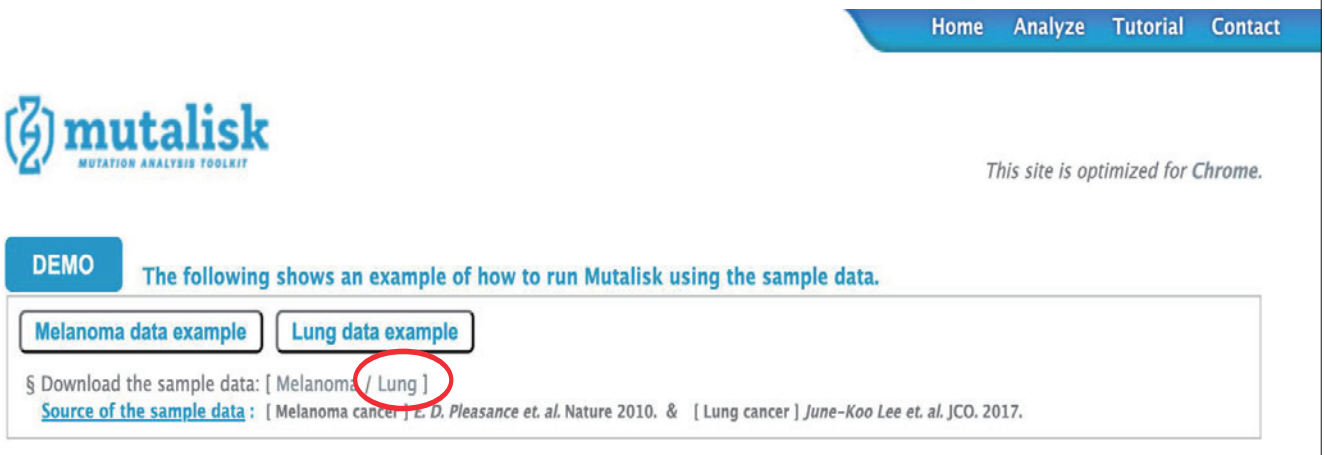


Tobacco-associated mutational signature #4



57

Run Mutalisk

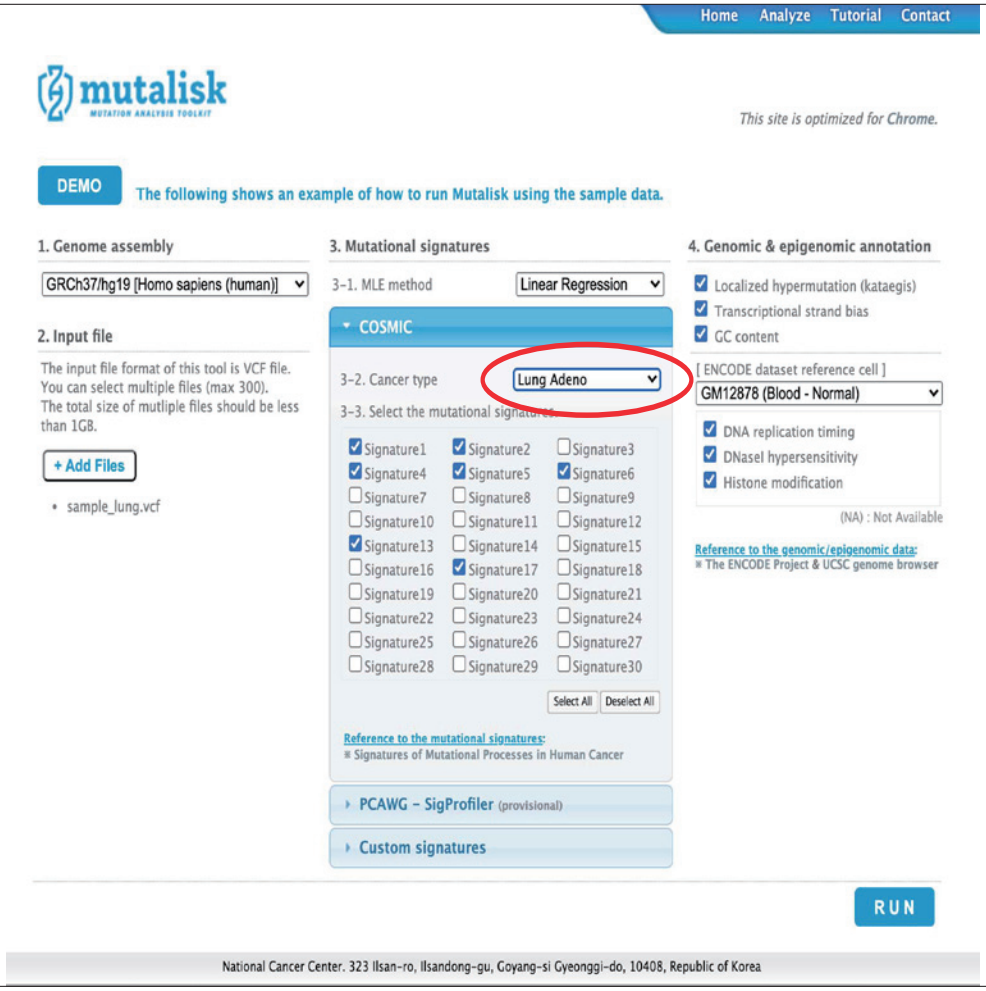


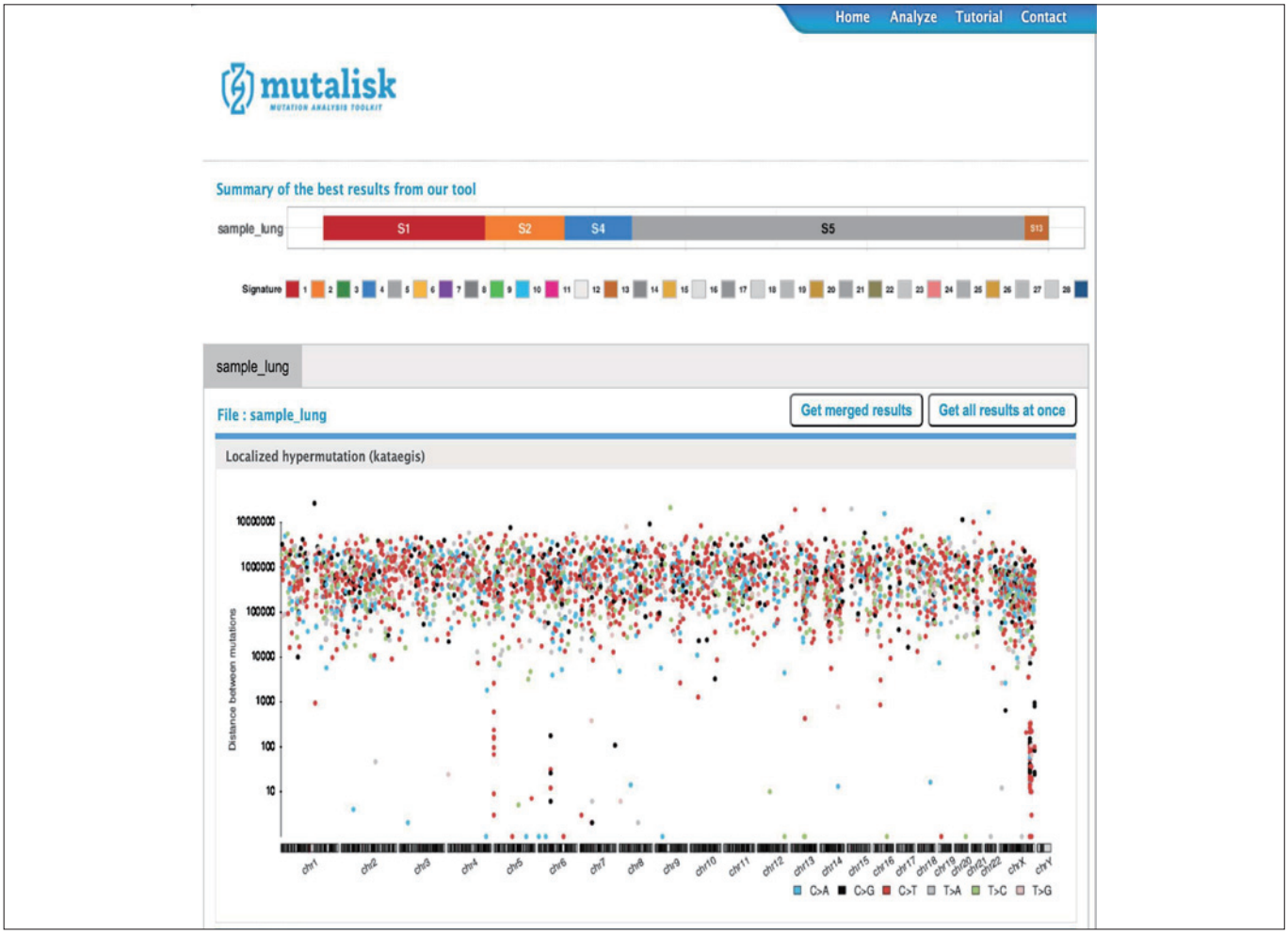
sample_lung.vcf

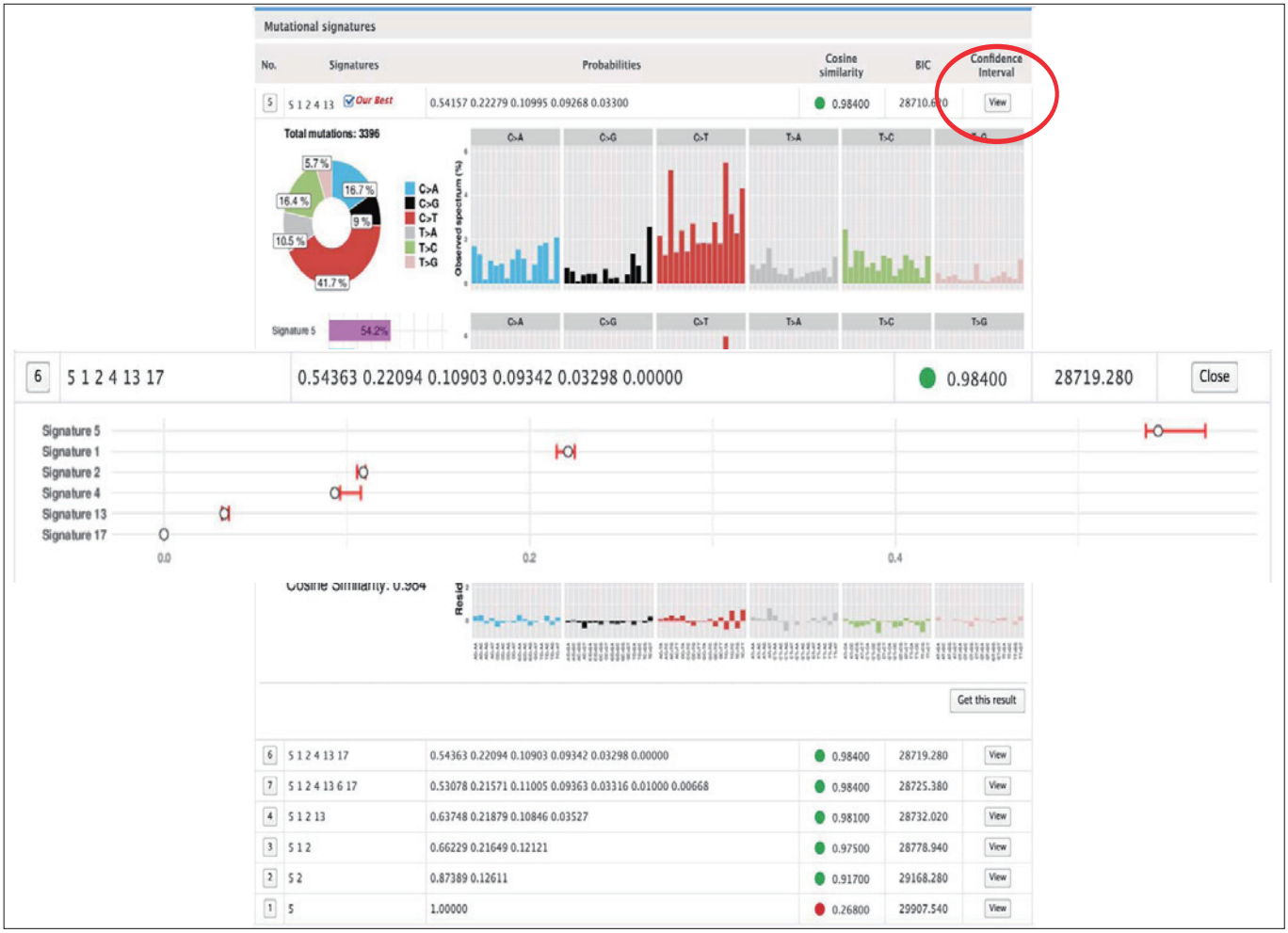
Variant Call Format (VCF): sample_lung.vcf

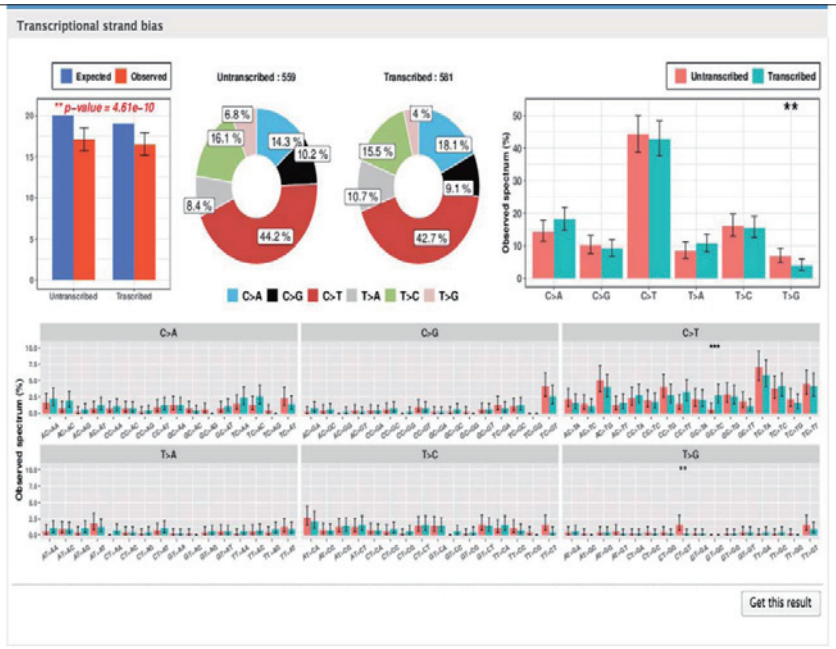
```
##fileformat=VCFv4.2
#CHROM  POS ID  REF ALT QUAL    FILTER  INFO
1   1910980 .   A   G   .   .   .
1   5148788 .   G   C   .   .   .
1   5867565 .   C   T   .   .   .
1   7146801 .   G   A   .   .   .
1   7665765 .   C   T   .   .   .
1   7749485 .   T   G   .   .   .
1   8710829 .   G   A   .   .   .
1   9804956 .   C   T   .   .   .
1   12381586    .   G   A   .   .   .
1   17274833    .   G   T   .   .   .
1   17365503    .   T   A   .   .   .
1   18099894    .   A   T   .   .   .
1   19665267    .   G   A   .   .   .
1   20753216    .   C   A   .   .   .
1   22905721    .   T   C   .   .   .
1   28496930    .   T   C   .   .   .
1   29464355    .   A   G   .   .   .
1   30253004    .   G   T   .   .   .
1   30346067    .   G   A   .   .   .
1   30627515    .   T   C   .   .   .
1   32251636    .   T   A   .   .   .
1   34081408    .   G   A   .   .   .
1   34435938    .   A   T   .   .   .
1   35909337    .   T   C   .   .   .
1   36062312    .   T   C   .   .   .
1   36414737    .   T   A   .   .   .
1   36729500    .   A   T   .   .   .
1   36936453    .   A   T   .   .   .
1   37261912    .   G   T   .   .   .
1   37277934    .   G   A   .   .   .
1   37708424    .   C   T   .   .   .
1   39672350    .   G   C   .   .   .
1   42038123    .   C   T   .   .   .
1   45810549    .   C   T   .   .   .
1   46950051    .   C   T   .   .   .
1   46984444    .   C   T   .   .   .
1   47098823    .   G   T   .   .   .
1   47446596    .   G   T   .   .   .
1   47619512    .   C   A   .   .   .
1   48781219    .   A   G   .   .   .
1   50032004    .   G   A   .   .   .
1   50642579    .   G   T   .   .   .
```

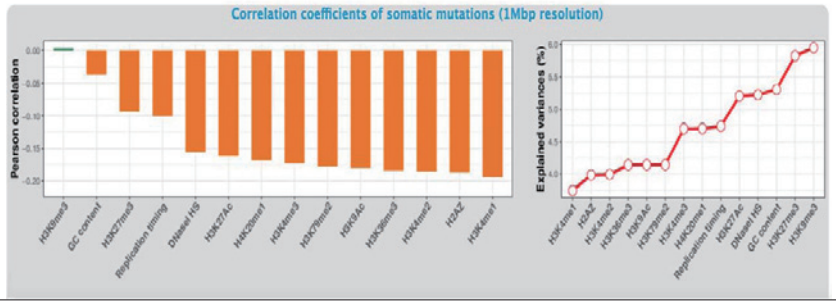
행 1, 열 1 – 3399 행




Home
Analyze
Tutorial
Contact
mutalisk
MUTATION ANALYSIS TOOLKIT
Summary of the best results from our tool
sample_lung
S1
S2
S4
S5
Signature
sample_lung
File : sample_lung
Get merged results
Get all results at once
Localized hypermutation (kataegis)
Distance between mutations
C>A C>G C>T T>A T>C T>G


Mutational signatures
No.
Signatures
Probabilities
Cosine similarity
BIC
Confidence Interval
5 1 2 4 13
Our Best
0.54157 0.22279 0.10995 0.09268 0.03300
0.98400
28710.610
View
Total mutations: 3396
5.7 %
16.7 %
16.4 %
9 %
10.5 %
41.7 %
C>A
C>G
C>T
T>A
T>C
T>G
Observed spectrum (%)
Signature 5
54.2%
6
5 1 2 4 13 17
0.54363 0.22094 0.10903 0.09342 0.03298 0.00000
0.98400
28719.280
Close
Signature 5
Signature 1
Signature 2
Signature 4
Signature 13
Signature 17
0.0
0.2
0.4
Resid
Get this result
6 5 1 2 4 13 17 0.54363 0.22094 0.10903 0.09342 0.03298 0.00000 0.98400 28719.280 View
7 5 1 2 4 13 6 17 0.53078 0.21571 0.11005 0.09363 0.03316 0.01000 0.00668 0.98400 28725.380 View
4 5 1 2 13 0.63748 0.21879 0.10846 0.03527 0.98100 28732.020 View
3 5 1 2 0.66229 0.21649 0.12121 0.97500 28778.940 View
2 5 2 0.87389 0.12611 0.91700 29168.280 View
1 5 1.00000 0.26800 29907.540 View

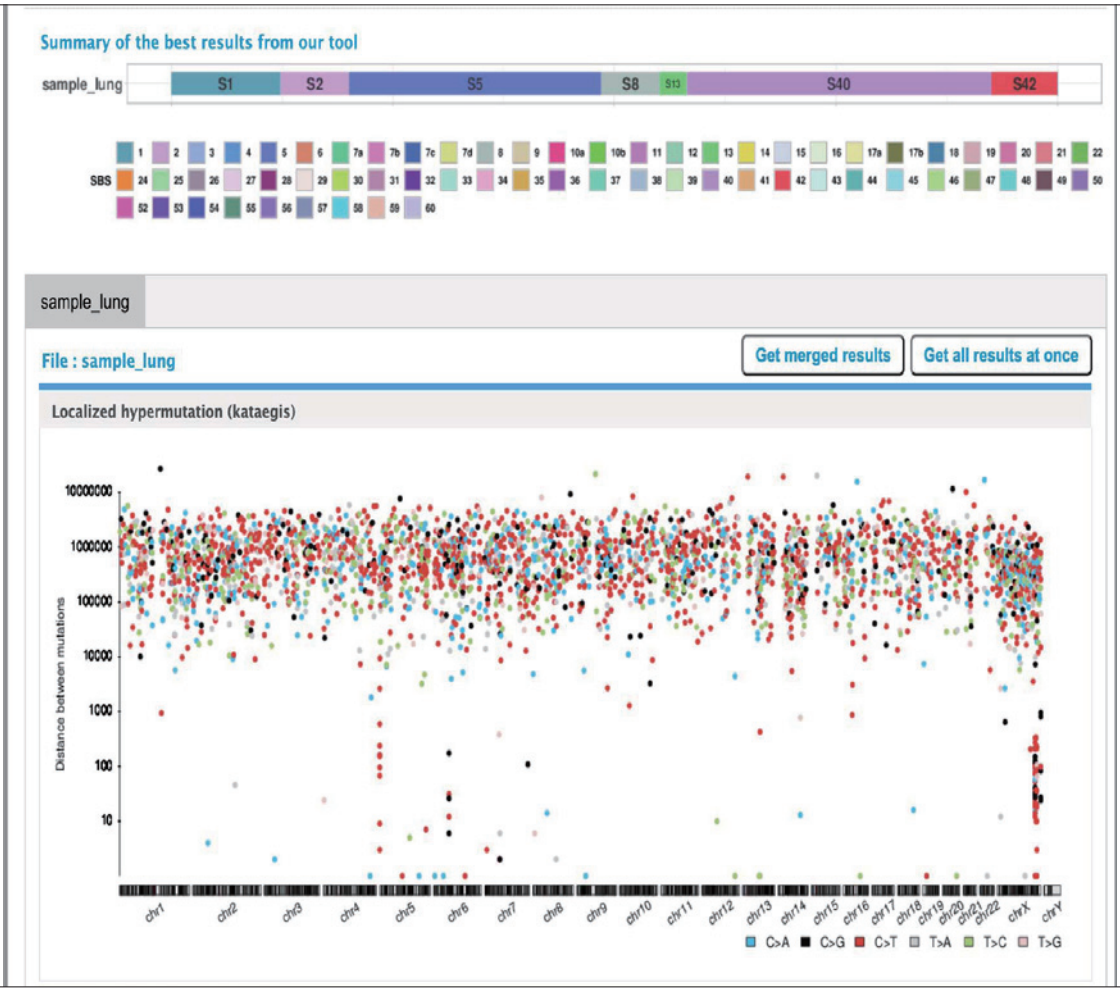

Transcriptional strand bias
Expected
Observed
** p-value = 4.61e-10
Untranscribed : 559
Transcribed : 581
Untranscribed
Transcribed
C>A
C>G
C>T
T>A
T>C
T>G
Observed spectrum (%)
Get this result

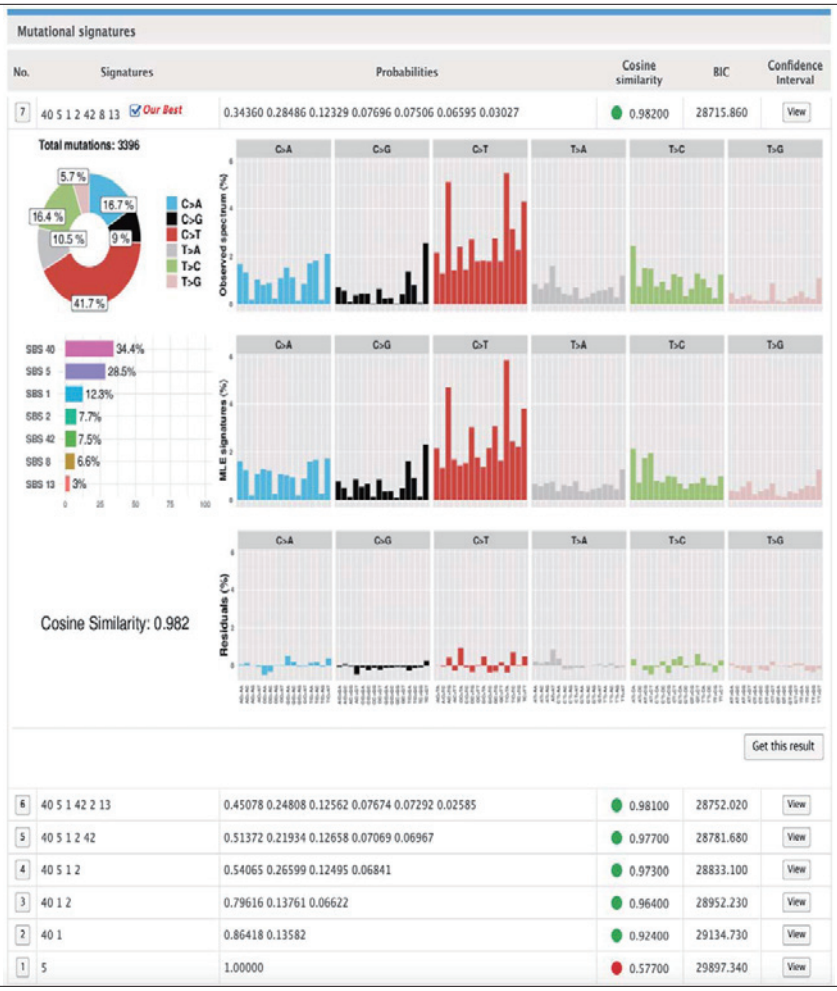

Correlation coefficients of somatic mutations (1Mbp resolution)
Pearson correlation
Explained variances (%)


DNA replication timing - Cell line : GM12878
Expected
Observed
** p-value = 2.37e-33
Early : 391
Intermediate : 988
Late : 846
Early
Intermediate
Late
C>A
C>G
C>T
T>A
T>C
T>G
Observed spectrum (%)
Get this result


DNaseI hypersensitivity – Cell line : GM12878
Expected
Observed
** p-value = 4.24e-43
Low Intermediate High
Low : 1166
5.8 %
17.5 %
8.1 %
18.5 %
13 %
37 %
Intermediate : 1632
5.8 %
17.2 %
16.1 %
9.1 %
9.7 %
42.2 %
High : 598
5.4 %
13.5 %
13 %
9.5 %
8.9 %
49.7 %
C>A C>G C>T T>A T>C T>G
Low
Intermediate
High
Observed spectrum (%)
C>A C>G C>T T>A T>C T>G
Get this result


Home
Analyze
Tutorial
Contact
mutalisk
Run Mutalisk (v3)
This site is optimized for Chrome.
DEMO
The following shows an example of how to run Mutalisk using the sample data.
1. Genome assembly
GRCh37/hg19 [Homo sapiens (human)]
2. Input file
The input file format of this tool is VCF file.
You can select multiple files (max 300).
The total size of mutliple files should be less than 1GB.
+ Add Files
sample_lung.vcf
3. Mutational signatures
3-1. MLE method
Linear Regression
COSMIC
PCAWG - SigProfiler
3-2. Cancer type
User Selection
3-3. Select the mutational signatures.
Full screening
Random sampling
SBS1 SBS2 SBS3 SBS4
SBS6 SBS7a SBS7b
SBS9
SBS12
SBS16
SBS19
SBS23
SBS27
SBS31
SBS35
SBS39
SBS43
SBS47
SBS51
SBS55
SBS56 SBS57 SBS58 SBS59
SBS60
Select All
Deselect All
An endogenous mutational process initiated by spontaneous or enzymatic deamination of 5-methylcytosine to thymine which generates G:T mismatches in double stranded DNA. Failure to detect and remove these mismatches prior to DNA replication results in fixation of the T substitution for C.
Custom signatures
4. Genomic & epigenomic annotation
Localized hypermutation (kataegis)
Transcriptional strand bias
GC content
[ENCODE dataset reference cell]
GM12878 (Blood - Normal)
DNA replication timing
DNaseI hypersensitivity
Histone modification
(NA) : Not Available
Reference to the genomic/epigenomic data:
= The ENCODE Project & UCSC genome browser
RUN


Summary of the best results from our tool
sample_lung
S1
S2
S5
S8
S13
S40
S42
SBS
sample_lung
File : sample_lung
Get merged results
Get all results at once
Localized hypermutation (kataegis)
Distance between mutations
10000000
1000000
100000
10000
1000
100
10
chr1
chr2
chr3
chr4
chr5
chr6
chr7
chr8
chr9
chr10
chr11
chr12
chr13
chr14
chr15
chr16
chr17
chr18
chr19
chr20
chr21
chr22
chrX
chrY
C>A
C>G
C>T
T>A
T>C
T>G


Mutational signatures
No.
Signatures
Probabilities
Cosine similarity
BIC
Confidence Interval
7
40 5 1 2 42 8 13
Our Best
0.34360 0.28486 0.12329 0.07696 0.07506 0.06595 0.03027
0.98200
28715.860
View
Total mutations: 3396
5.7 %
16.7 %
16.4 %
9 %
10.5 %
41.7 %
C>A
C>G
C>T
T>A
T>C
T>G
Observed spectrum (%)
SBS 40
34.4%
SBS 5
28.5%
SBS 1
12.3%
SBS 2
7.7%
SBS 42
7.5%
SBS 8
6.6%
SBS 13
3%
MLE signatures (%)
Residuals (%)
Cosine Similarity: 0.982
Get this result
6
40 5 1 42 2 13
0.45078 0.24808 0.12562 0.07674 0.07292 0.02585
0.98100
28752.020
View
5
40 5 1 2 42
0.51372 0.21934 0.12658 0.07069 0.06967
0.97700
28781.680
View
4
40 5 1 2
0.54065 0.26599 0.12495 0.06841
0.97300
28833.100
View
3
40 1 2
0.79616 0.13761 0.06622
0.96400
28952.230
View
2
40 1
0.86418 0.13582
0.92400
29134.730
View
1
5
1.00000
0.57700
29897.340
View

Interpretation of signature results

Proposed aetiology

Unknown.

Comments

Numbers of mutations attributed to SBS40 are correlated with patients' ages for some types of human cancer.

Proposed aetiology

Unknown. SBS5 mutational burden is increased in bladder cancer samples with ERCC2 mutations and in many cancer types due to tobacco smoking.

Comments

SBS5 is clock-like in that the number of mutations in most cancers and normal cells correlates with the age of the individual. Rates of acquisition of SBS5 mutations over time differ between different cancer types and different normal cell types. These differences do not clearly correlate with estimated rates of stem cell division in different tissues nor with differences in SBS1 mutation rates. SBS5 may be contaminated by SBS16.


Correlation coefficients of somatic mutations (1Mbp resolution)
Pearson correlation
Explained variances (%)
H3K9me3
GC content
H3K27me3
Replication timing
DNaseI HS
H3K27Ac
H4K20me1
H3K4me3
H3K79me2
H3K9Ac
H3K36me3
H3K4me2
H2AZ
H3K4me1
GC-content
Expected
Observed
** p-value = 8.42e-04
Low : 928
Intermediate : 1695
High : 773
Low
Intermediate
High
Observed spectrum (%)
C>A
C>G
C>T
T>A
T>C
T>G


DNA replication timing - Cell line : GM12878
Expected
Observed
** p-value = 2.37e-33
Early : 391
Intermediate : 988
Late : 846
Early
Intermediate
Late
Observed spectrum (%)
C>A
C>G
C>T
T>A
T>C
T>G
Get this result

TO Part II

Artificial Intelligence Study using Cancer Big Data

AI
Deep-learning is the hottest topic in cancer genomic research area

Latest Cancer Research Trend Analysis - **Top 15 Bigrams**

~250,000 articles / 1 year (pubmed)

As of August 1, 2019

Rank	Keyword	2015	2016	2017	2018	2019	Cumulative growth ratio (2018/2015)
1	deep learning	127	284	790	2,107	2,285	16.69
2	pd1 blockade	0	6	8	9	9	10.00
3	circular rna	53	96	249	512	458	9.50
4	health-related quality	0	3	4	8	5	9.00
5	checkpoint inhibitor	99	239	488	784	679	7.85
6	circular rnas	80	140	308	612	567	7.57
7	mutational burden	30	61	107	225	230	7.29
8	blood-brain barrier	5	8	9	40	23	6.83
9	epstein-barr virus	2	1	5	18	8	6.33
10	next-generation sequencing	2	9	15	17	18	6.00
11	progression-free survival	4	5	10	28	20	5.80
12	checkpoint inhibitors	318	767	1,292	1,844	1,594	5.78
13	endogenous rna	82	119	239	467	463	5.64
14	receptor t	57	110	194	320	262	5.53
15	liquid biopsies	47	124	193	250	179	5.23

Latest Cancer Research Trend Analysis - **Cancer Genomics**

Keyword	2015	2016	2017	2018	2019	Cumulative growth ratio (2018/2015)
deep learning	127	284	790	2,107	2,285	16.47
nextgeneration sequencing	2	9	15	17	18	6.00
cancer database	213	274	515	685	598	3.21
machine learning	1,731	2,280	3,287	5,405	4,834	3.12
cancer genome	789	1,017	1,359	1,904	1,614	2.41
germline variants	71	85	117	159	143	2.22

AI ?

Strong AI = General AI

공상과학 영화

터미네이터

A.I

아이로봇

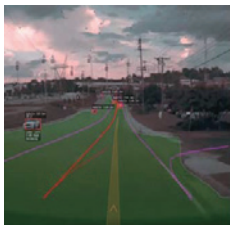
업그레이드

모든 부분에서 AR 가능한 로봇 또는 인간 수준 AI

Weak AI = Narrow AI

Google 광고 개인 최적화

Apple Watch 부정맥 감지



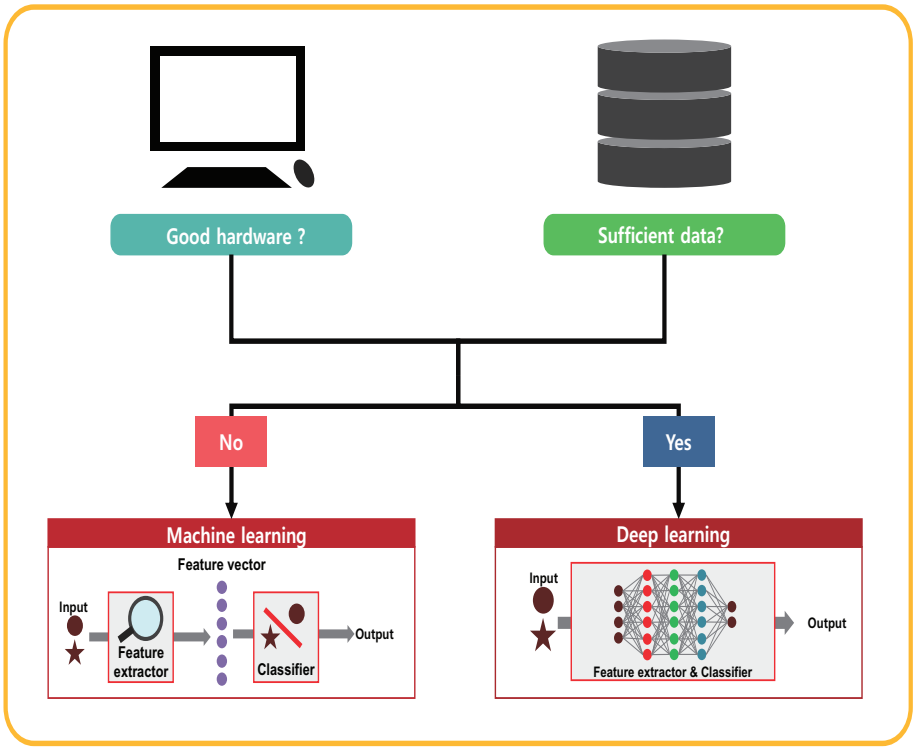
Tesla autopilot recognition

특정 임무를 수행하는 AI

Cancer drugs

- Vemurafenib and trametinib
  BRAF V600E mutations in melanoma
- Erlotibin and osimertinib
  EGFR mutations in NSCLC; L858R, Del (19), T790M
- Pembrolizumab (immune checkpoint inhibitor): FDA approved
  SOLID tumors from any tissue type
  Mismatch repair deficiency (dMMR)
- Nivolumab, ipilimumab and atezolizumab
  High tumor mutation burden

Which goal ?



컴퓨팅 파워의 발전

최소 출시: 2006년 11월 11일
최초 가격: $499
CPU: 3.2 GHz 셀 브로드밴드 엔진 1 PPE, 8 SPEs
RAM: 시스템 RAM: 256MB (XDR DRAM)
비디오 RAM: 256MB (GDDR3)
GPU: 550 MHz 엔비디아/SCEI RSX 리얼리 신시사이저

PS3 1대 FLOPS = 230.4 GFLOPS

미공군 336대의 ps3 를 이용한 도시감시용 슈퍼컴퓨터

500 TFLOPS

최소 출시: 2020년 11월 10일
최초 가격: $499
CPU: AMD ZEN 2 기반 커스텀 마이크로 아키텍처
제원: 8코어 16스레드, 3.6 GHz
RAM: 16 GB, GDDR6 ECC SGRAM
GPU: AMD RDNA 2 기반 커스텀 마이크로아키텍처

XBOX 1대 FLOPS = 12.1472 TFLOPS

÷

12.3 TFLOPS

2001 슈퍼 컴퓨터 ACSI white
핵무기 관련 시뮬레이션용 사용 (농구장 2배 크기)

*: Teraflops: 초당 10^{12}회의 연산을 처리 할 수 있는 계산 능력

컴퓨팅 능력의 저변 확대

Data 분석용 workstation 성능 변화

2002년 → 2018년~

	2002년	2018년~
CPU	Intel Pentium III 1400S @ 1400MHz	Intel Xeon Platinum 8268 @ 2.90GHz
Clockspeed	1.4 GHz	2.9 GHz
# of Physical Cores	1 (Threads: 1)	24 (Threads: 48)
CPU Mark	194	30,103

15.48 배

인공 지능을 이용한 연구 환경 조성 ??

ex)

AlphaGo
AlphaGo Zero

3hours
19hours
70hours

$361! = 2.6 \times 10^{845}$

가장 큰 수의 단위: 10^{68} 무량대수
읽을 수 있는 수: 10^{71} 천무량대수

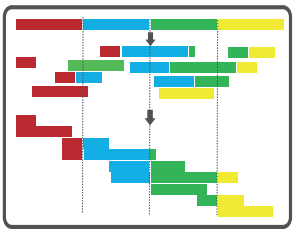
인간의 한계

오믹스 데이터

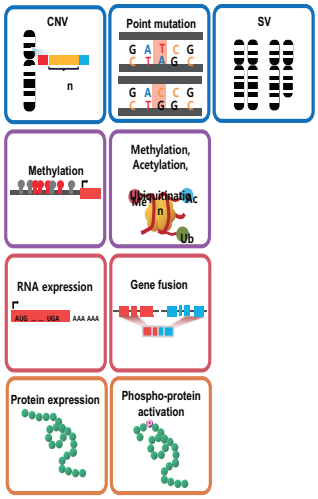
1) 일종의 디지털 데이터

A T G C
(30쌍)

2) 대량의 정보

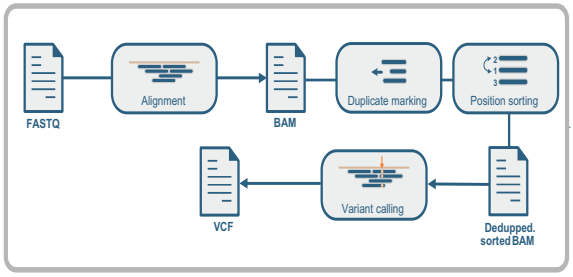


3) 복잡성

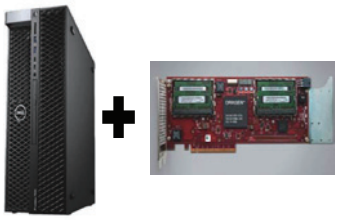


Pipeline 계산 능력

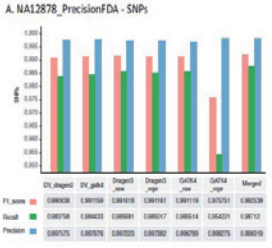
Germline variant calling pipelines

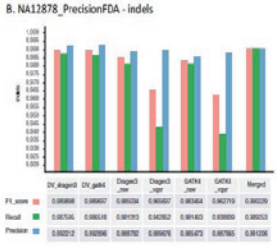


Workstation

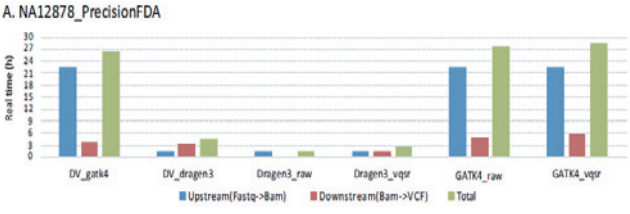


Workstation + Illumina DRAGEN Bio-IT Platform





DRAGEN3 vs GATK4 : 오차 범위 내 동일 수준 정확성



Sci Rep 2020 Nov 19;10(1):20222.

동일 데이터 처리 (fastq to vcf) 기준;
9배(GATK4; 27시간, dragen; 3시간) 시간 소요

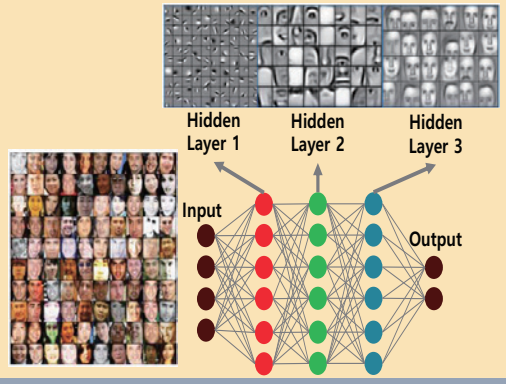
2.7. Machine learning 과 Deep learning

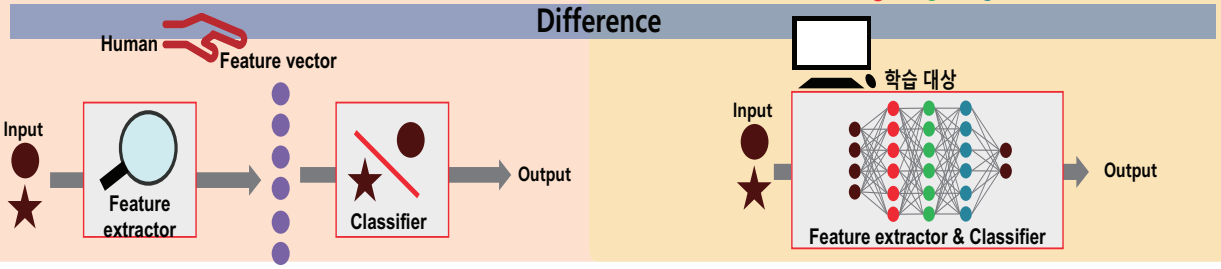
Machine learning
: 컴퓨터가 데이터를 통해 스스로 학습하여 예측이나 판단을 제공하는 기술

ex) 구글 광고 개인 최적화
(https://adssettings.google.com/authenticated)

Deep learning
: 깊은 인공신경망을 알고리즘을 활용하는 머신러닝 기술

ex) 딥러닝 알고리즘을 활용한 얼굴 인식 프로세스



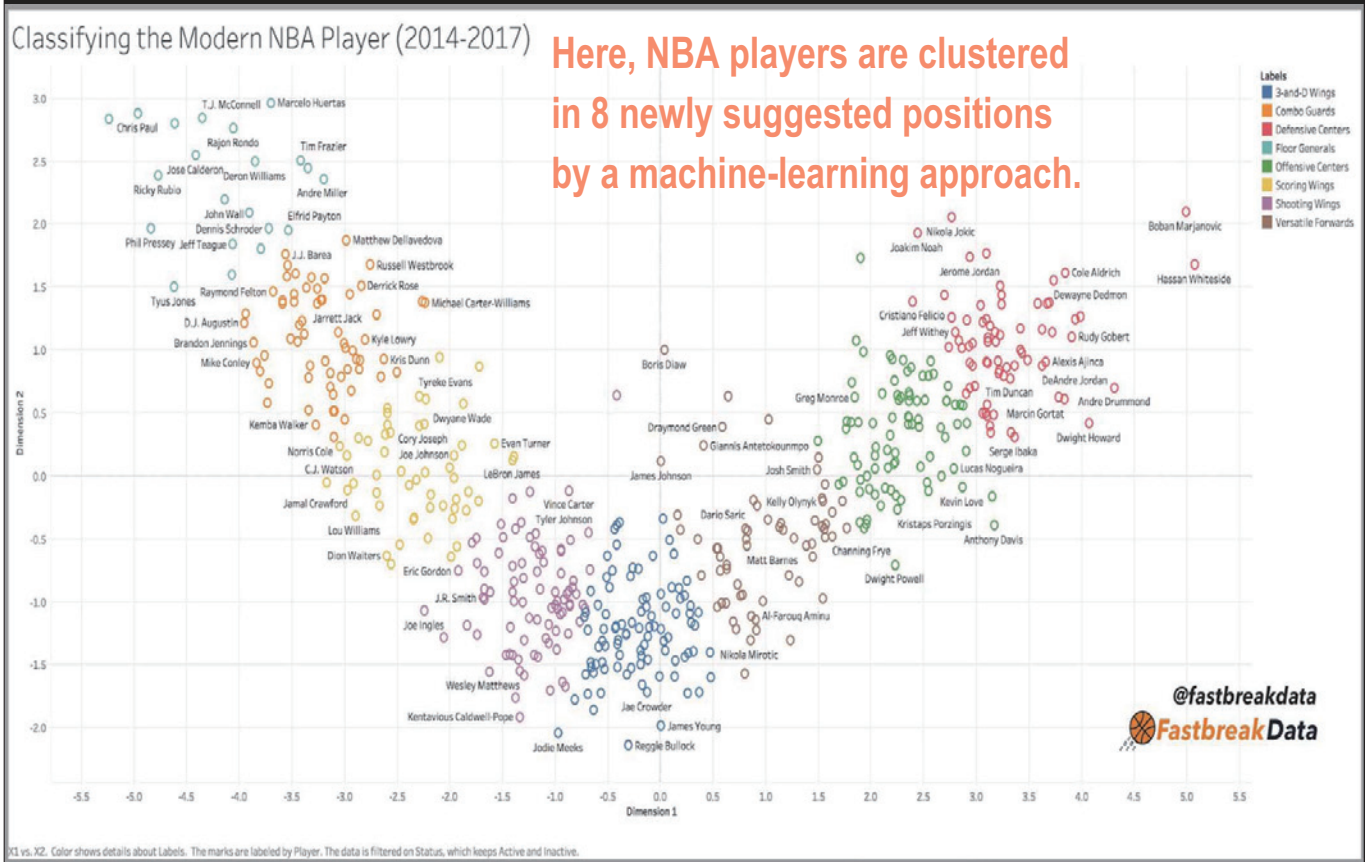


Three types of **research questions** driving application of **AI** in **genomics** (Ching *et al.*, J R Soc Interface 2018)

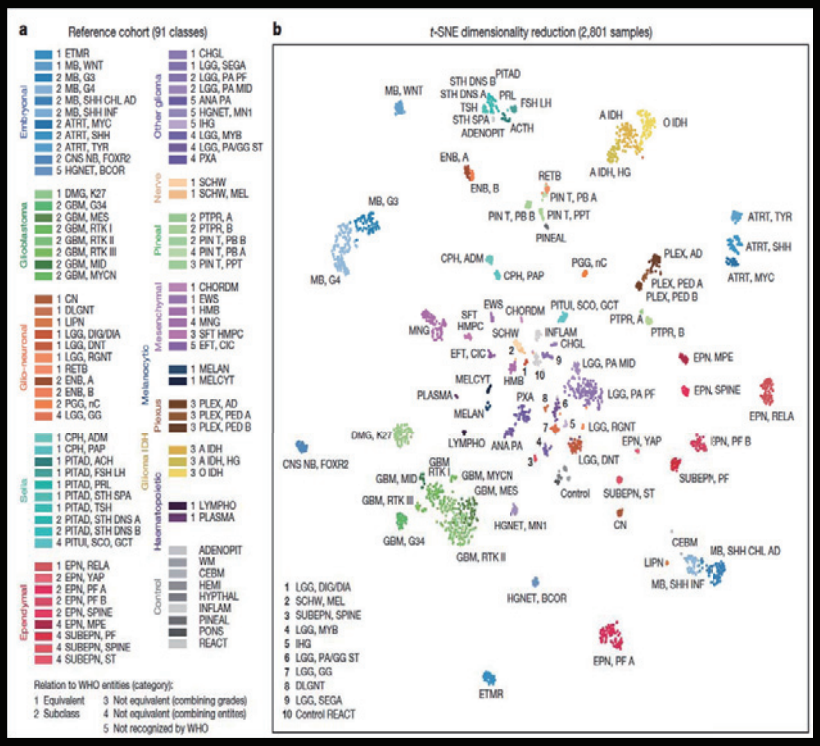
1. Disease and patient categorization
   (Gene expression, DNA methylation)
2. Functional and biological study (DNA sequences)
3. Treatment of patients (Gene expression)

Three types of **research questions** driving application of **AI** in **genomics** (Ching *et al.*, J R Soc Interface 2018)

1. **Disease and patient categorization**
2. Functional and biological study
3. Treatment of patients



Machine Learning Research in Genomics



Capper *et al.*, Nature 2018
Clustering of central nervous system (CNS) tumors based on **DNA methylation data**

Over 100 World Health Organization (WHO) CNS tumor subtypes

17 histological types

Three types of **research questions** driving application of **AI** in **genomics** (Ching *et al.*, J R Soc Interface 2018)

1. Disease and patient categorization
2. **Functional and biological study**
3. Treatment of patients

Different Tissues & Physiology

Caterpillar **Butterfly**

Different Tissues & Physiology, Same Genome

Nucleotide sequences

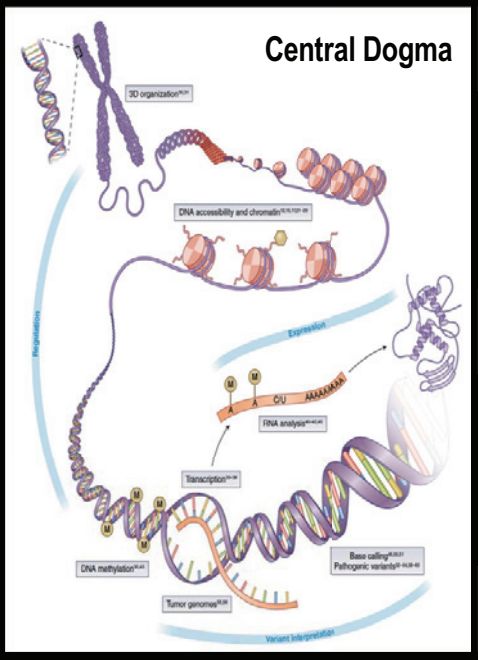
...CGCCGCTGACCTATCATCAGTTC
CAAGCGCTGATAGCGAGCATGCC
CCCGCCTCCGTCCGCCGAACCCA
CCATCAGTTTGGAGACACTCAACC
GCGCCGTTACACCTATCTCGGATA
ATCACGACGAACGATTTGGAGTGC
CGACACTCGAAGAACTTGGCTTCG
ATACGGAAGGTCTTAAACCTCCAA
TATGGATCGGCGGAGAAAACGAA
GCTCTGTTGAGACT...

=

...CGCCGCTGACCTATCATCAGTTC
CAAGCGCTGATAGCGAGCATGCC
CCCGCCTCCGTCCGCCGAACCCA
CCATCAGTTTGGAGACACTCAACC
GCGCCGTTACACCTATCTCGGATA
ATCACGACGAACGATTTGGAGTGC
CGACACTCGAAGAACTTGGCTTCG
ATACGGAAGGTCTTAAACCTCCAA
TATGGATCGGCGGAGAAAACGAA
GCTCTGTTGAGACT...

Caterpillar **Butterfly**

Many, So Many Components in Central Dogma



DNA → 19,000+ genes

RNA → 100,000+ transcripts

Protein → 1,000,000+ proteins

Zou *et al.*, Nat Genetics 2019

Current Problems in Applying Deep Learning to Genomics

To conduct optimal learning, we need n^2 samples for n features for correlated features

(Hua *et al.*, Bioinformatics 2005)

DNA → 19,000+ genes

361M+ samples?

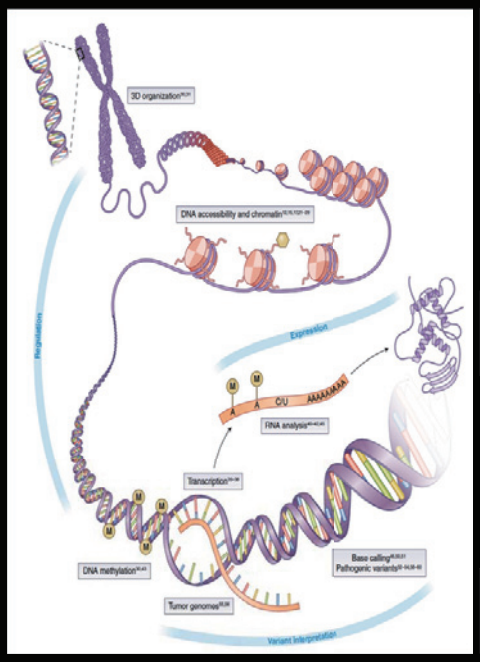
RNA → 100,000+ transcripts

10B+ samples??

Protein → 1,000,000+ proteins

1T+ samples???

Deep Learning Research in Genomics



DNA

SNV (Sundaram *et al.*, Nat Genetics 2018)
TF binding (Alipanahi *et al.*, Nat Biotech 2015)
Histone marks (Zhou *et al.*, Nat Methods 2015)
DNase hypersensitivity (Kelley *et al.*, Genom Res 2016)
DNA methylation (Angermueller *et al.*, Genom Biol 2017)

RNA

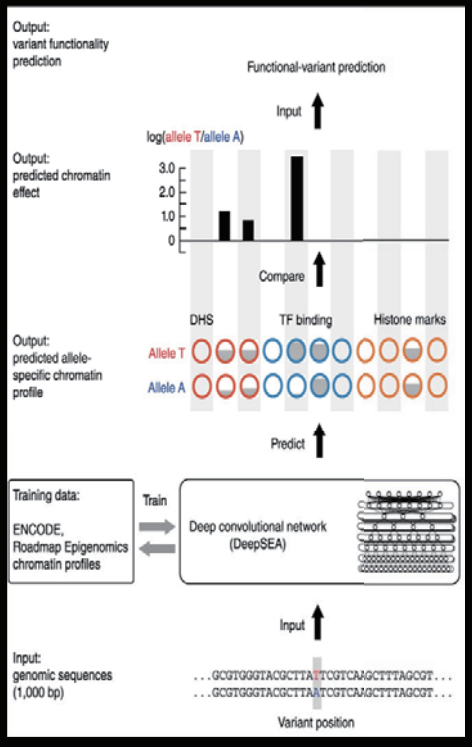
Alternative splicing (Jaganathan *et al.*, Cell 2019)
Polyadenylation (Bogard *et al.*, Cell 2019)
mRNA expression (Zhou *et al.*, Nat Genetics 2018)

Protein

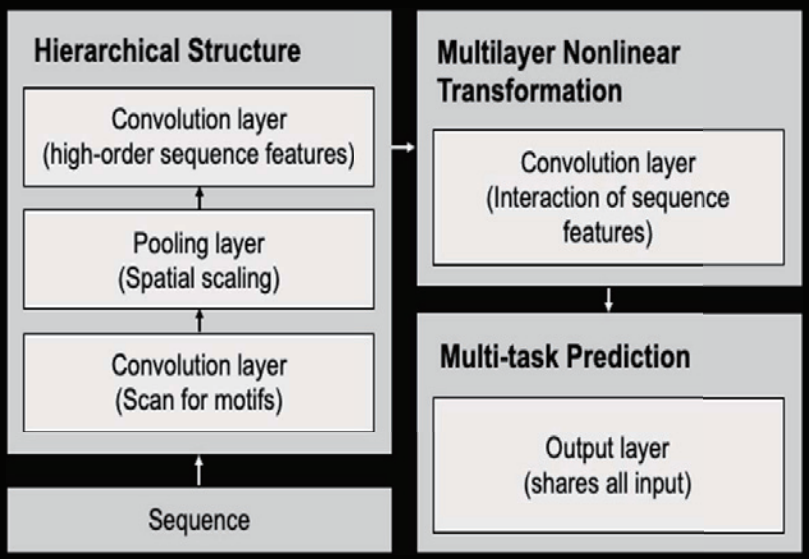
Enzyme commision (Ryu *et al.*, PNAS 2019)

Zou *et al.*, Nat Genetics 2019

Deep Learning Research in Genomics - DeepSEA



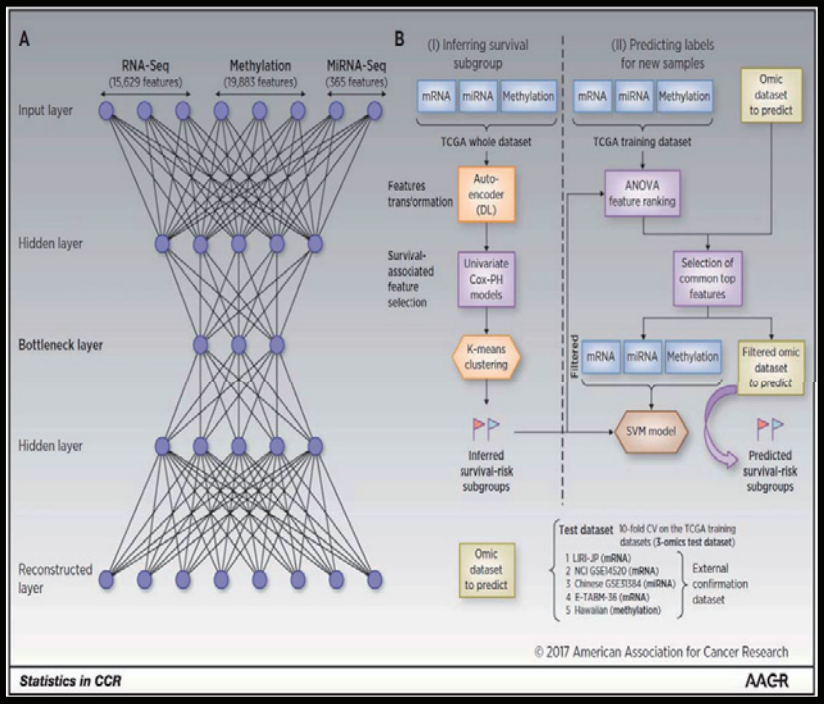
DeepSEA (Zhou *et al.*, Nat Methods 2015)
Using genomic sequences (1,000 bp) predict chromatin organization (transcription factor binding, histone marks, DNase sensitivity).



Three types of **research questions** driving application of **AI** in **genomics** (Ching *et al.*, J R Soc Interface 2018)

1. Disease and patient categorization
2. Functional and biological study
3. **Treatment of patients**

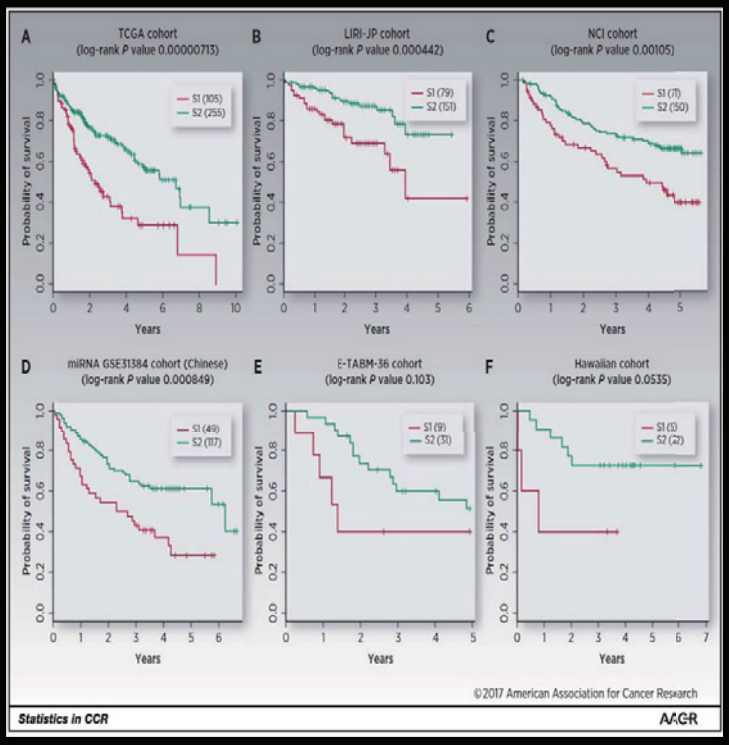
Deep Learning Research in Genomics - Predicting Prognosis



Chaudhary *et al.*, Clin Can Res 2018

- Predicting survival of liver cancer patients by training an **autoencoder**.
- Trained on 360 TCGA-HCC samples' **mRNA** and **miRNA sequencing** as well as **methylation data**

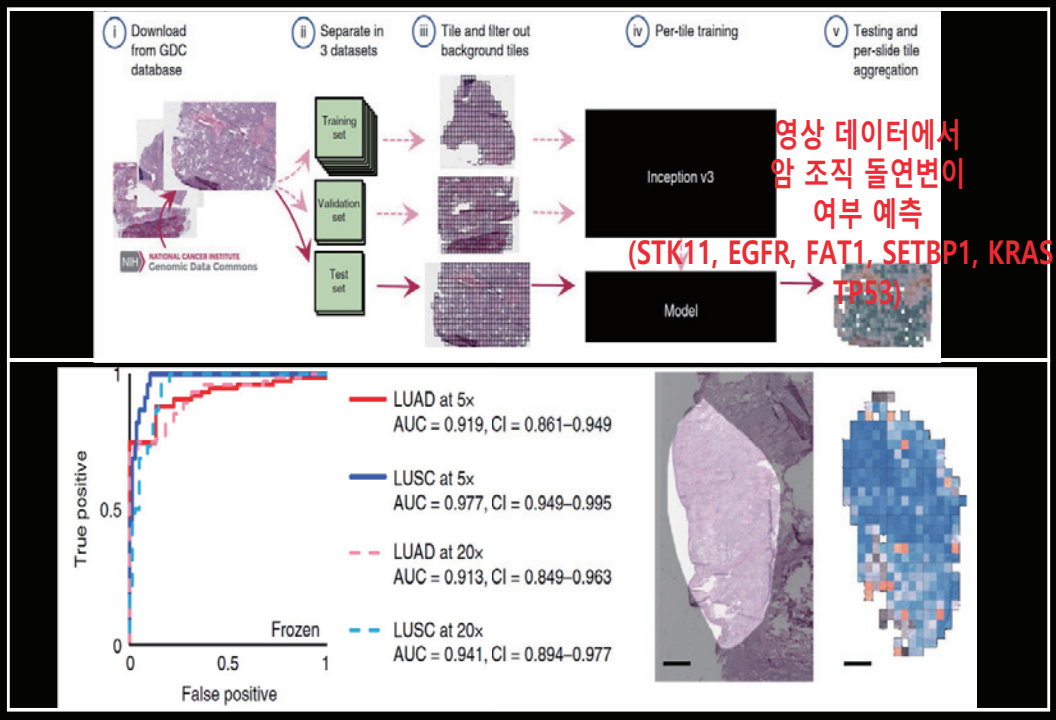
Deep Learning Research in Genomics - Predicting Prognosis



- Validated the deep learning model on 684 patients across 5 independent cohorts

Chaudhary *et al.*, Clin Can Res 2018

Deep Learning Research in Biomedicine



Coudray et al., Nature Medicine 2018

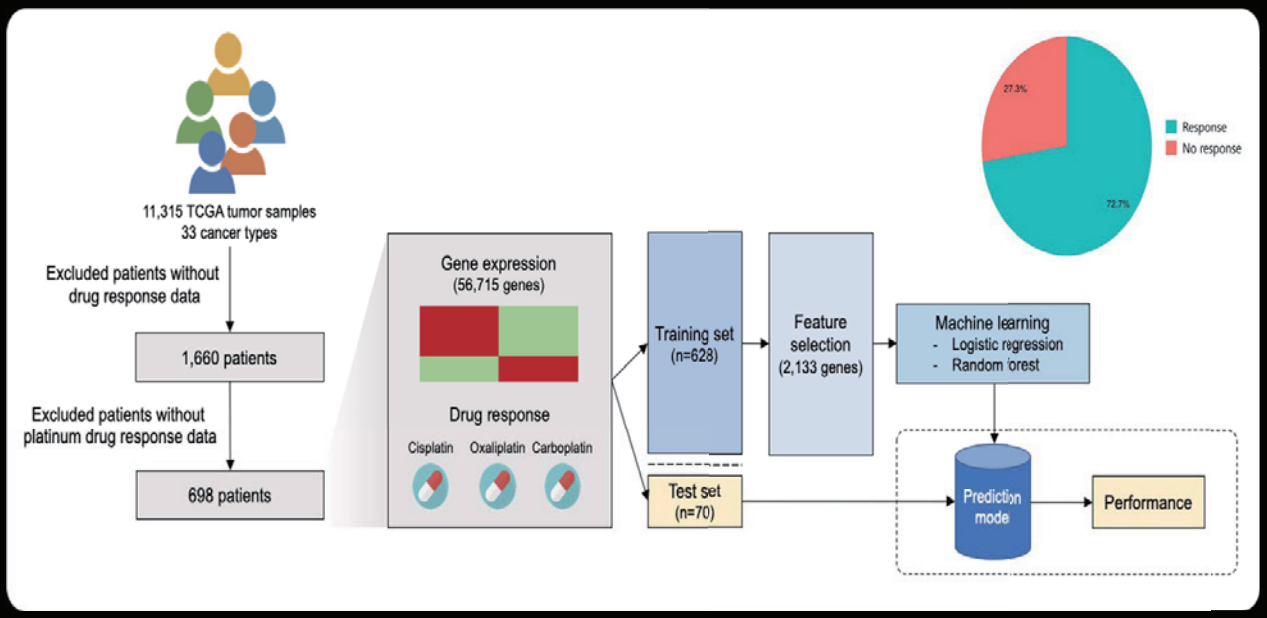
Use machine learning algorithm

arbitr
AI MODEL FOR CANCER GENOMICS

ARBITR: An aRtificially intelligent Bayesian approach to predIcting predisposition and evoluTionary deteRminants in human cancer

Challenges in Cancer Genomic Data for Deep Learning

Our pilot study predicting platinum therapy response using omics data



Challenges in Cancer Genomic Data for Deep Learning

Our pilot study predicting platinum therapy response using omics data

Method/Model	AUC
Random forest	**0.619***
SVM	0.612
Ada boost	0.609
Logistic regression	0.593
MLP	0.593

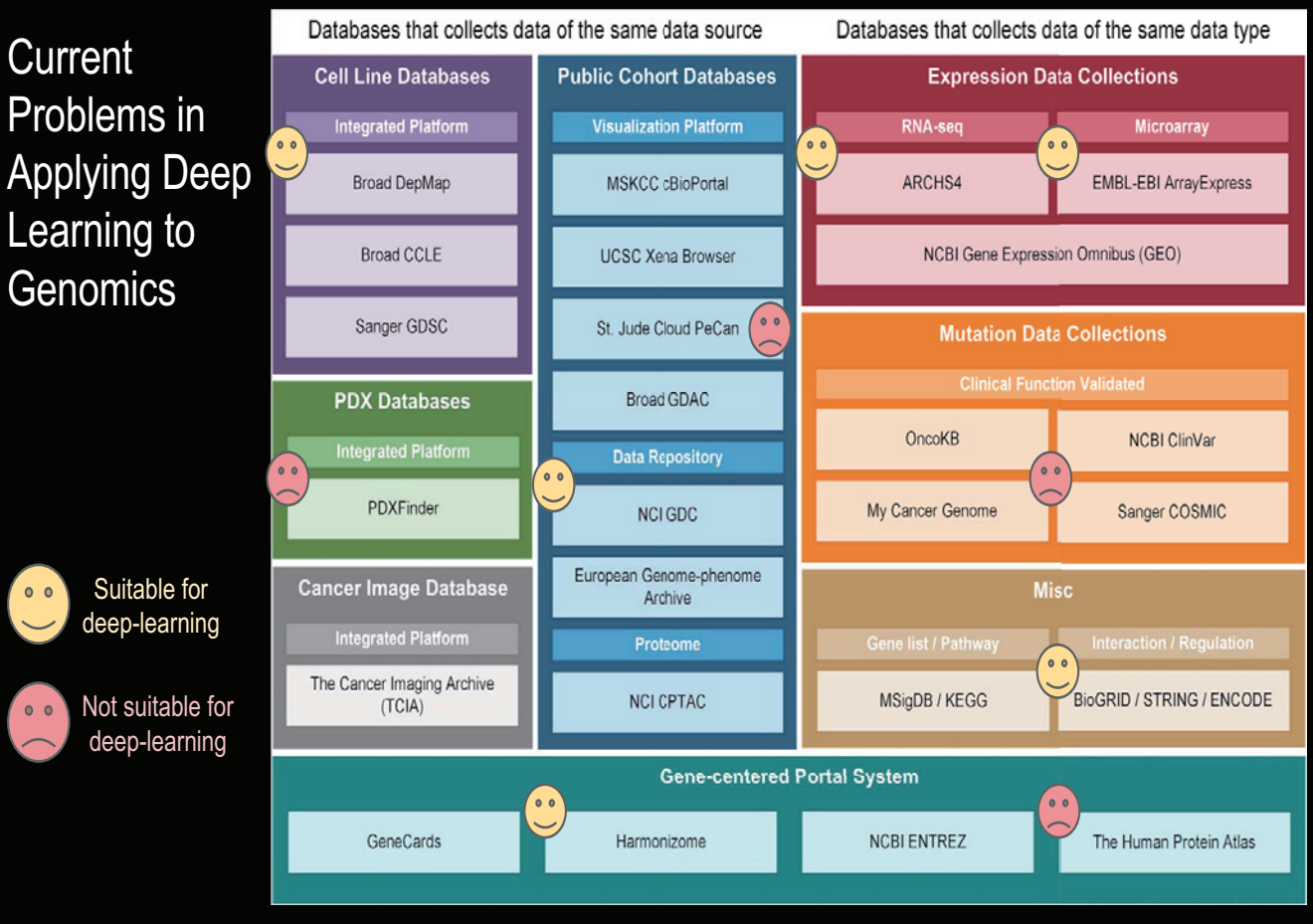
Genomic/transcriptomic features (selection) matter a great deal.

Due to currently limited sample size in publicly available datasets, we must devise new ways of tackling the problem of predicting therapeutic response in cancer patients

So why are genomic/transcriptomic features problematic (besides the dimensionality problem)?
Because of tumor heterogeneity

Dagogo-Jack *et al.*, Nat Rev Clin Oncol 2018

Current Problems in Applying Deep Learning to Genomics



Cancer Omics Data

Cell line data

Genomics of Drug Sensitivity in Cancer

https://www.cancerrxgene.org/

Summary

	GDSC1	GDSC2
Cell line	987	809
Compounds	367	198
IC50	310,904	135242

Methods & dataset

Exome sequencing
Array exome sequencing
Mutation
Copy Number
Methylation
Expression
Drug Screening – IC50s

CCLE Cancer Cell Line Encyclopedia

https://portals.broadinstitute.org/ccle

Summary

	CCLE
Cell line	1,457
Compounds	24 (504 cell line test)

Dataset

WES
Mutation
Fusion
structural variant
miRNA
Global Chromatin
RPPA
Antibody
RPKM
RSEM
Methylation
copy number
metabolomics

Cancer Omics Data

Human genomic data

NIH NATIONAL CANCER INSTITUTE GDC Data Portal

https://portal.gdc.cancer.gov/

Summary

	GDC
Projects	67
Primary sites	68
Cases	84,392
Genes	23,399
Files	596,758
Mutations	3,287,299

Method

Clinical data
Biospecimen data
Pathology Reports
SNP microarray
Copy number microarray
Low-Pass DNA Sequencing
Whole exome
Whole genome
SNP microarray
Sequence trace
Diagnostic image
Tissue image
Radiological image
Bisulfite sequencing
Bead array
miRNA Sequencing
Total RNA Sequencing
Microarray
Reverse-Phase Protein Array

ICGC Data Portal

https://dcc.icgc.org/

Summary

	ICGC
Data release 28	
cancer project	86
Cancer primer sites	22
Donor with molecular data in DCC	22,230
Total donors	24,289
Simple somatic mutations	81,782,588

Method

Clinical data
Biospecimen Data
WXS
WGS
RNA-Seq
miRNA-seq
Bisulfite-seq

NIH NATIONAL CANCER INSTITUTE Office of Cancer Clinical Proteomics Research

https://cptac-data-portal.georgetown.edu/

Summary

	ICGC
Studies	55
Tumor sites	12
Cases	2,549
Samples	3,639
Files	107,493
Data	25,576GB

Method

Proteome
Phosphoproteome
Acetylome
Gycoproteome
Ubiquitylome

가톨릭대학교

Issues to be considered

데이터 표기의 문제

▶ 각각의 데이터 표기 기준 안에 따른 데이터 구성의 문제 발생

◇ 약품 표기법

IDMP
Identification of Medicinal Products
Data elements and structures for the unique identification and exchange

RxNav
Navigating RxNorm Drugs

◇의학용어 표기법

SNOMED CT
The global language of healthcare

NIH National Institutes of Health

ex)1. IL2 = IL-2 = interleukin – 2 = interleukin–2
2. typing error

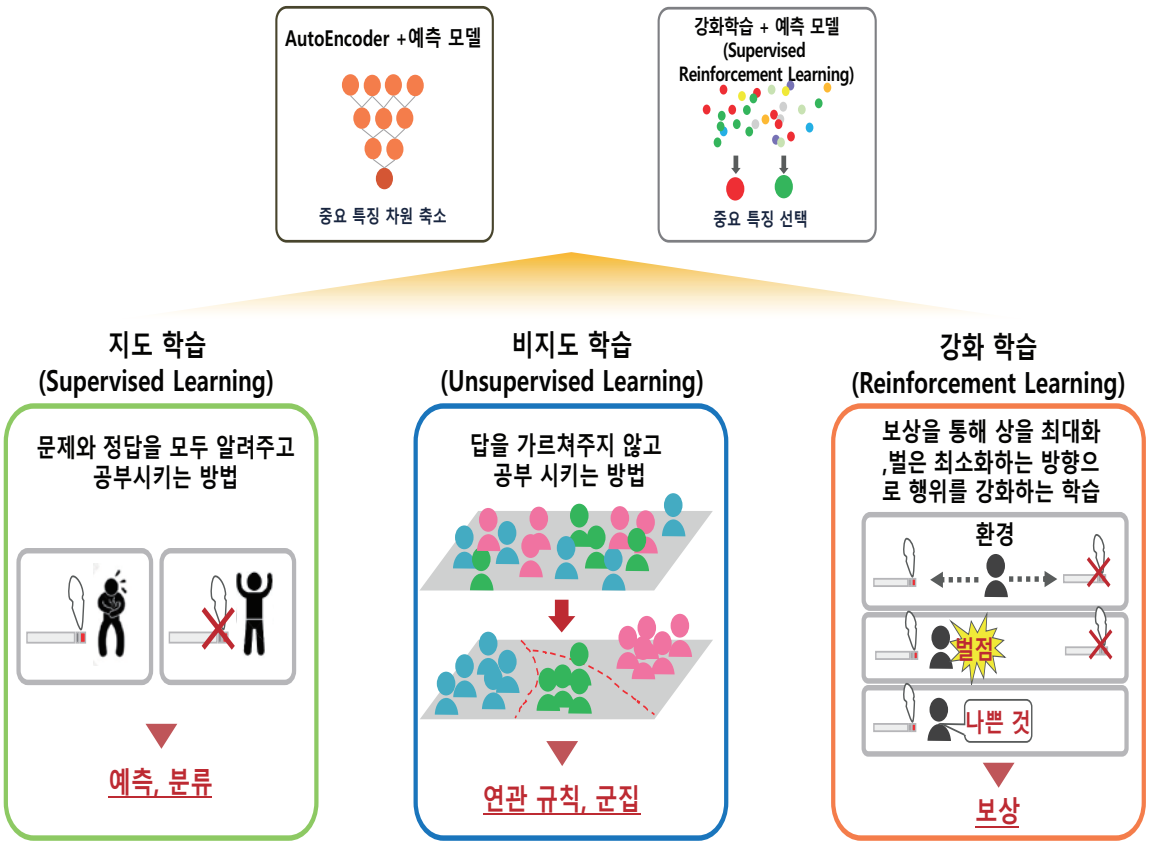
Table S1: Correcting drug names from TCGA to standard names

Recorded Name from TCGA	DrugBank ID	Standard drug name
IL2	DB00041	Aldesleukin
IL-2	DB00041	Aldesleukin
Interleukin - 2	DB00041	Aldesleukin
Interleukin-2	DB00041	Aldesleukin
Alvesin	NA	NA
Anastrozole	DB01217	Anastrozole
ANASTROZOLE	DB01217	Anastrozole
Arimidex	DB01217	Anastrozole
ARIMIDEX	DB01217	Anastrozole
PF-04605412	NA	anti-ASB1 integrin monoclonal antibody PF-04605412
MORAb-004	NA	anti-endosialin/TEM1 monoclonal antibody MORAb-004?
autologous vaccine	NA	autologous vaccine
Axitinib	DB06626	Axitinib
Axitnib	DB06626	Axitinib
Cediranib	DB04849	AZD2171
Bacillus Calmette-Guerin (BCG)	NA	BCG
BCG	NA	BCG
avastin	DB00112	Bevacizumab
Avastin	DB00112	Bevacizumab
bevacizumab	DB00112	Bevacizumab
Bevacizumab	DB00112	Bevacizumab
BEVACIZUMAB	DB00112	Bevacizumab
Bicalutamide	DB01128	Bicalutamide
casodex	DB01128	Bicalutamide
Casodex	DB01128	Bicalutamide
bleomycin	DB00290	Bleomycin
Bleomycin	DB00290	Bleomycin
BRAF inhibitor	NA	BRAF inhibitor
cabazitaxel	DB06772	Cabazitaxel
jevtana	DB06772	Cabazitaxel
Cabozantinib	DB08875	Cabozantinib
Cancer Vax	NA	Cancer Vax
capecitabine	DB01101	Capecitabine
Capecitabine	DB01101	Capecitabine

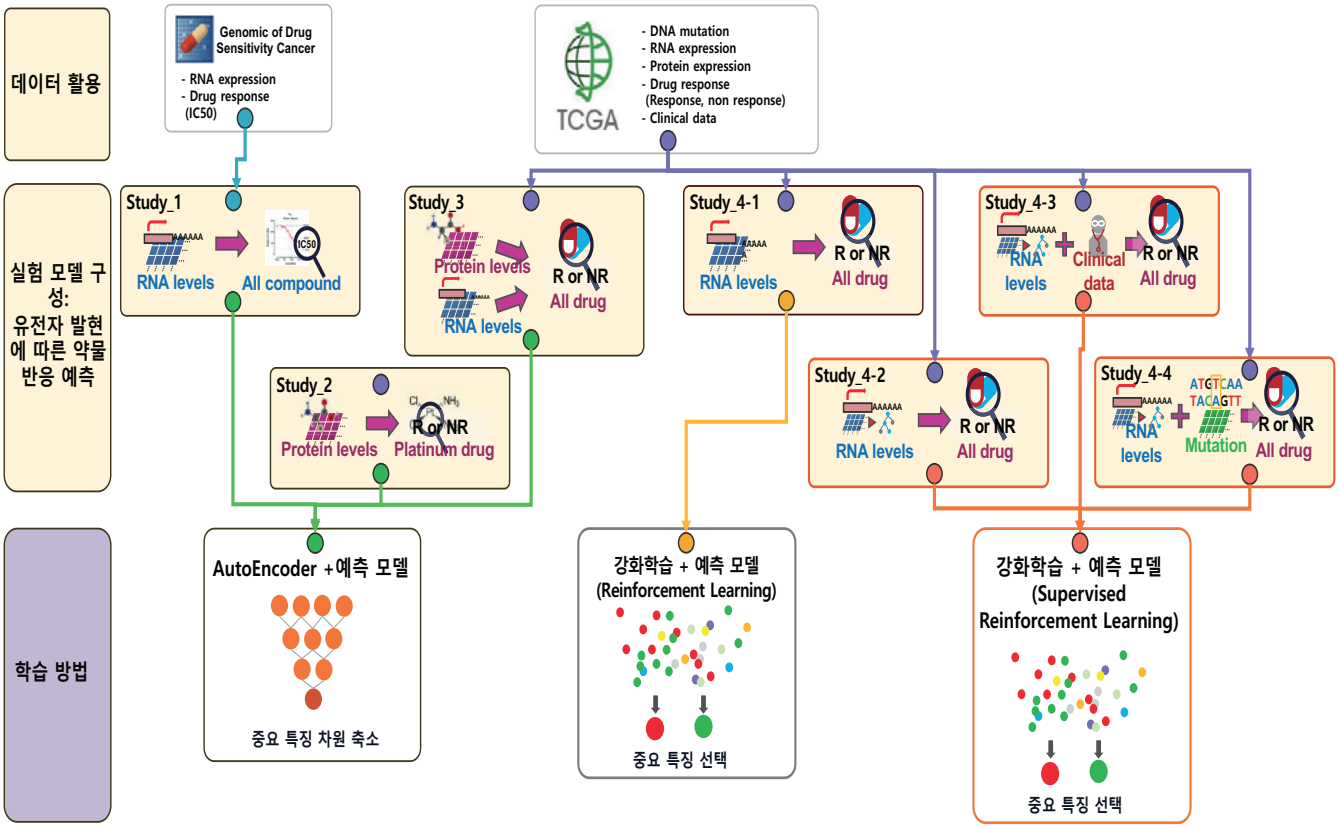
Bioinformatics, 32(19), 2891-2895.

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

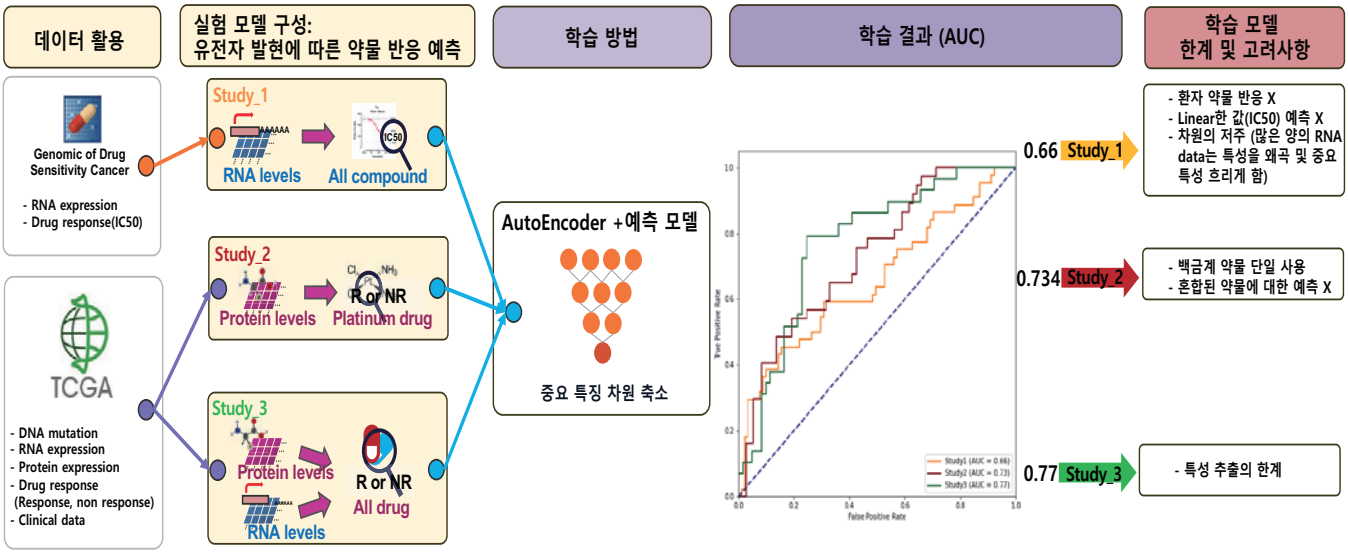
Preliminary study - methodology



Preliminary study

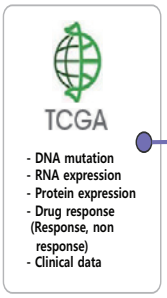


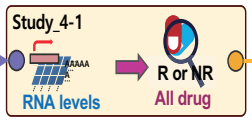
Results

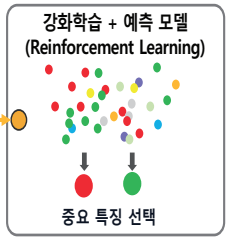


Results

데이터 활용 | 실험 모델 구성: 유전자 발현에 따른 약물 반응 예측 | 학습 방법 | 학습 결과 (AUC) | 학습 모델 한계 및 고려사항







Study_4-1 ??? Study_4-1

- 많은 차원에 의한 계산량 증가와 시간 증가
- 현실적으로 분석 X

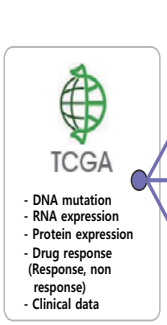
- The model needs least 10000 episodes for train
- 10000 episodes = 3350000 min = 6 years

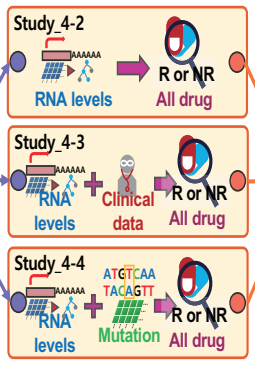
336개 유전자에 대한 강화학습 경우의 수

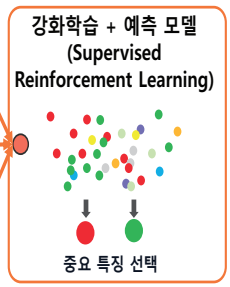
$$\sum_{n} \frac{336!}{(336-n)! \times n!} = 1.3998E + 101$$

Results

데이터 활용 | 실험 모델 구성: 유전자 발현에 따른 약물 반응 예측 | 학습 방법 | 학습 결과 (AUC)







Study_4-2 0.80

Study_4-3,4 진행 중

Results

학습 결과	학습 모델 한계 및 고려사항

Study_4-2

Study_4-2 결과

Cancer type	Sample size (R:NR)	Total gene (20531 genes) AUROC	Total gene (20531 genes) Loss	KEGG cancer pathway (525 genes) AUROC	KEGG cancer pathway (525 genes) Loss	COSMIC cancer gene census (683 genes) AUROC	COSMIC cancer gene census (683 genes) Loss
PANCAN	1794 (42:58)	**0.791**	0.795	**0.782**	0.875	**0.720**	0.715
BRCA	278 (15:85)	**0.902**	0.579	**0.913**	0.722	**0.910**	0.624
LGG	176 (80:20)	**0.939**	0.480	**0.908**	0.591	**0.840**	0.930
STAD	150 (35:65)	**0.586**	2.651	**0.620**	1.598	**0.584**	0.941
HNSC	59 (25:75)	**0.989**	0.10	**0.958**	0.225	**0.989**	0.139
KIRC	18 (89:11)	**0.750**	21965.61	**0.750**	8.888	**0.750**	12.087
KIRP	11 (73:27)	**0.333**	141.36	**1.000**	0.141	**1.000**	0.041
KICH	8 (87.5:12.5)	**0.500**	32591.15	**0.500**	13.325	**0.500**	17.119
LUAD	112 (47:53)	**0.752**	1.143	**0.811**	0.921	**0.750**	1.016
PRAD	43 (33:67)	**0.593**	1.230	**0.704**	1.371	**0.580**	1.827

- 특성 추출을 위한 여러 조건 연구

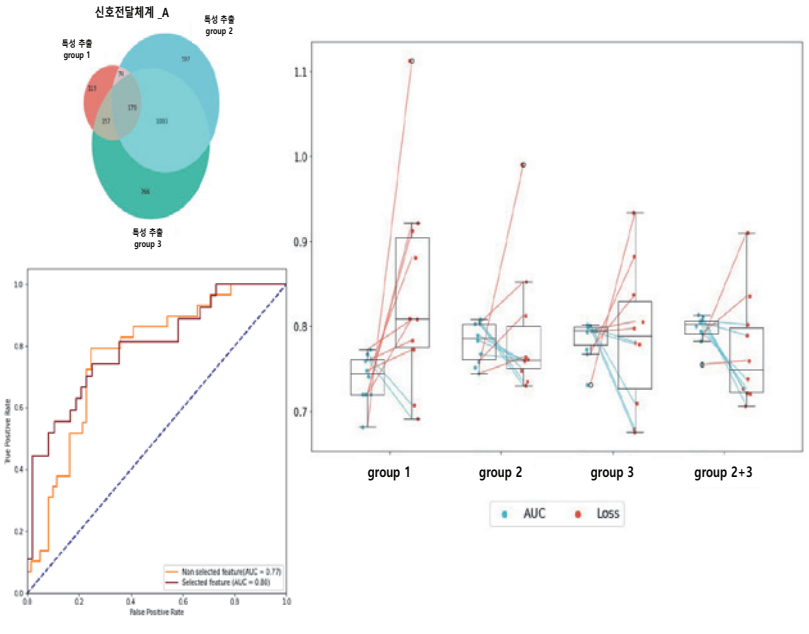
Results

학습 결과	개선점	학습 모델 한계 및 고려사항

Study_4-2

Study_4-2 결과

- 암세포의 신호전달체계 중 항암제 관련 신호전달체계 선택 후, 특성 추출
- 추출된 특성으로 예측모델 수행



- 항암제 관련 신호전달체계에서 특성 추출 후 예측모델 수행 시 학습 능력 향상되었고 (AUC=0.80) 예측의 불확실 정도가 개선됨.

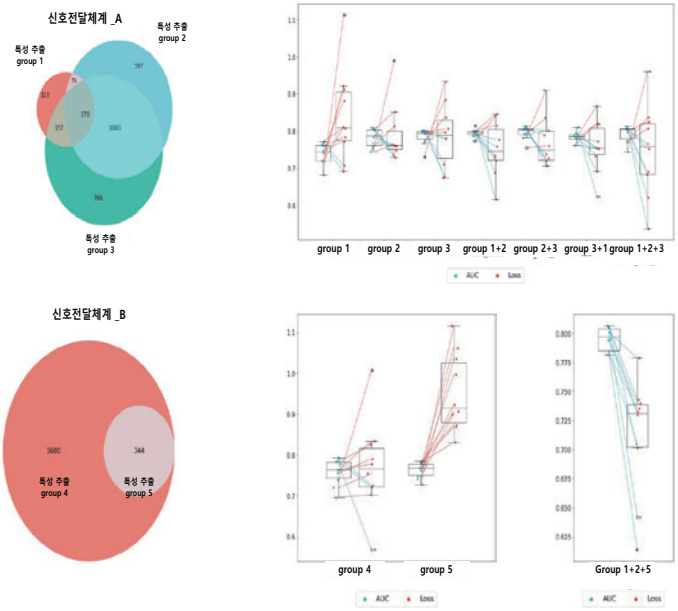
- 특성 추출 고려
- 예를 들어, cell signaling, cellular processes 등

Results

학습 결과	개선점	학습 모델 한계 및 고려사항
Study_4-2	- 항암제 관련 신호전달체계에서 특성 추출 후 예측모델 수행 시 학습 능력 향상되었고 (AUC=0.80) 예측의 불확실 정도가 개선됨.	- 특성 추출 고려 - 예를 들어, cell signaling, cellular processes 등

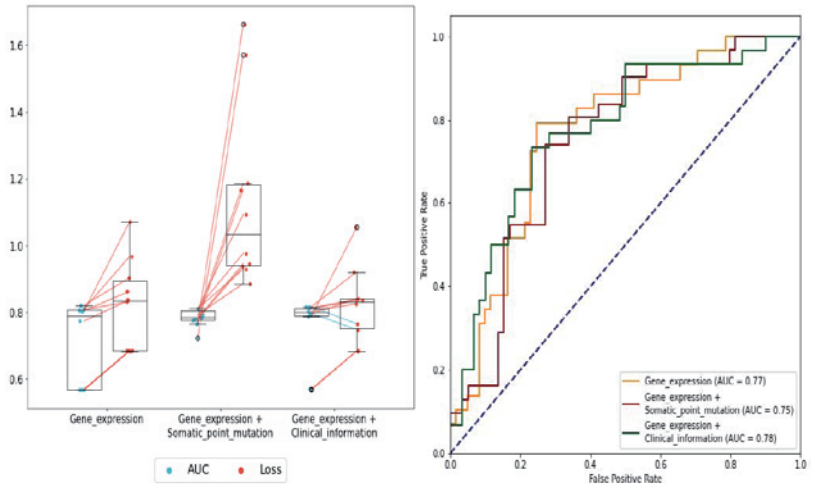
Study_4-2 결과

- 암세포의 신호전달체계 중 항암제 관련 신호전달체계 선택 후, 특성 추출
- 추출된 특성으로 예측모델 수행



Results

학습 결과	개선점	학습 모델 한계 및 고려사항
Study_4-3,4	- 특성 중 항암제 관련성이 반영 되지 않는 임상정보 및 돌연변이를 사용했을 경우 학습 능력 (+돌연변이:0.78, +임상정보: AUC=0.75)이 떨어지고 예측의 불확실 정도가 나쁨. - Layer 마다 특성을 고려해야 함.	- Layer 병합을 이용한 실험 모델에서는 각각 특성 추출 고려 - Layer와 layer 사이 관계 이해



알파폴드를 이용한
단백질 구조 예측 및 평가 I

Contents

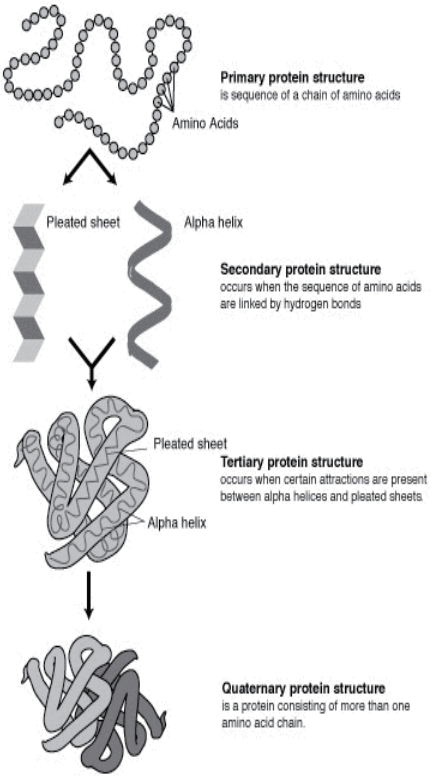
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

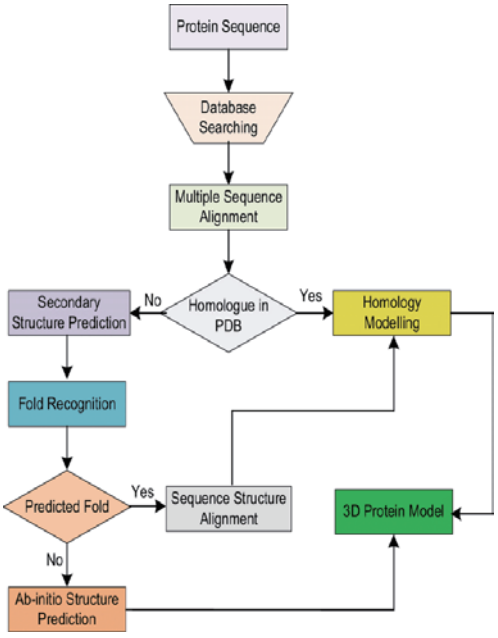
1

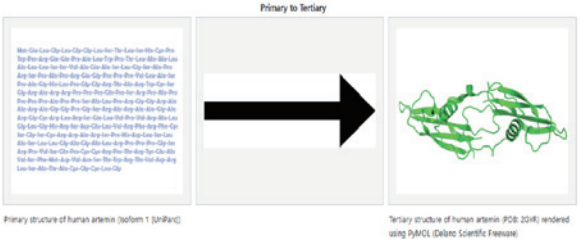
인공지능 및 AlphaFold의 소개

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 AlphaFold







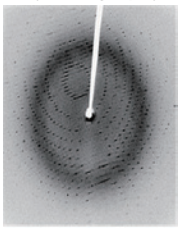
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

Analysis of Protein structure

1 AlphaFold

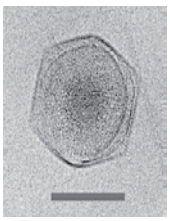
Past → present

X-ray crystallography

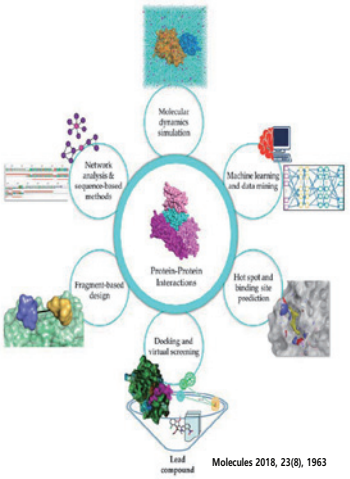


Nuclear magnetic Resonance (NMR)

Cryogenic electron Microscopy (Cryo-EM)



In silico



Molecules 2018, 23(8), 1963

- In the process of protein crystallization
  : pH, temperature, ion concentration in the crystal solution affect , etc : Too many factor
- Long run time and costs

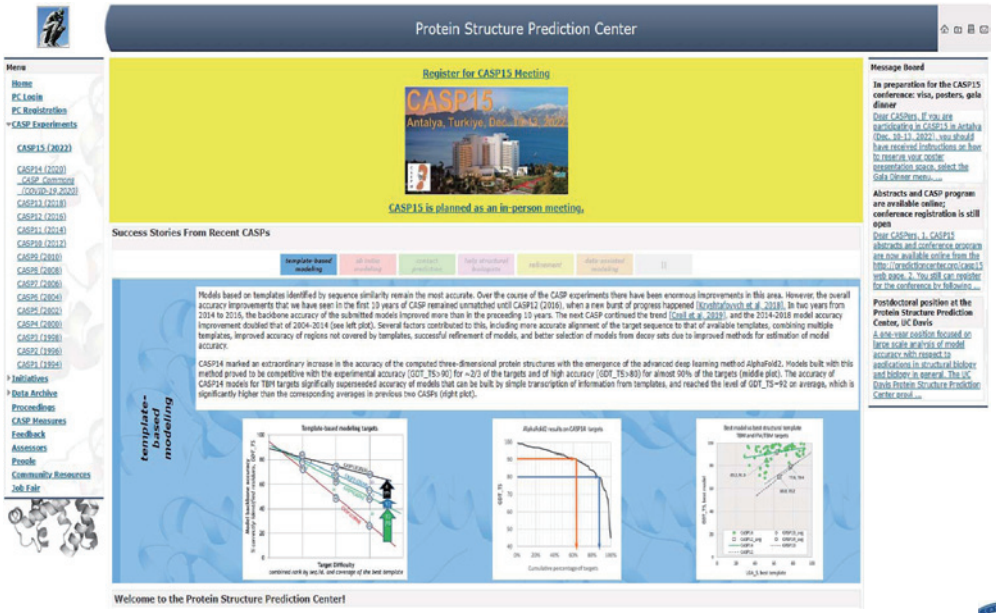
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

Protein structure prediction

1 AlphaFold

1994
Critical Assessment of protein Structure Prediction (CASP1)

2022
CASP15



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

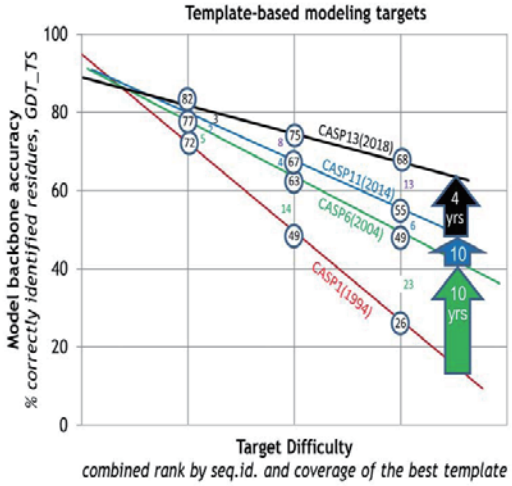
1 AlphaFold

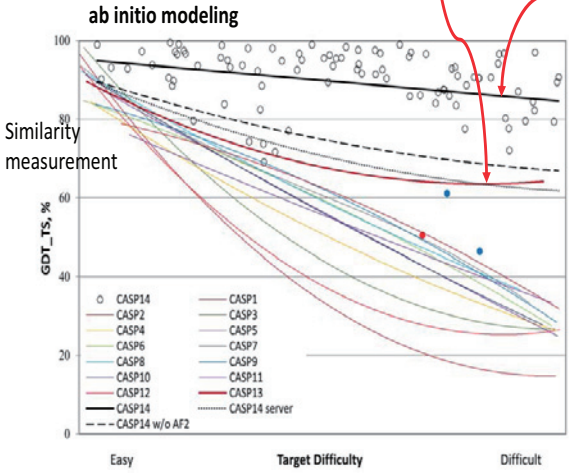
DeepMind AlphaFold & AlphaFold 2

1994
Critical Assessment of protein Structure Prediction (CASP)

2018
CASP13
AlphaFold1

2020
CASP14
AlphaFold2

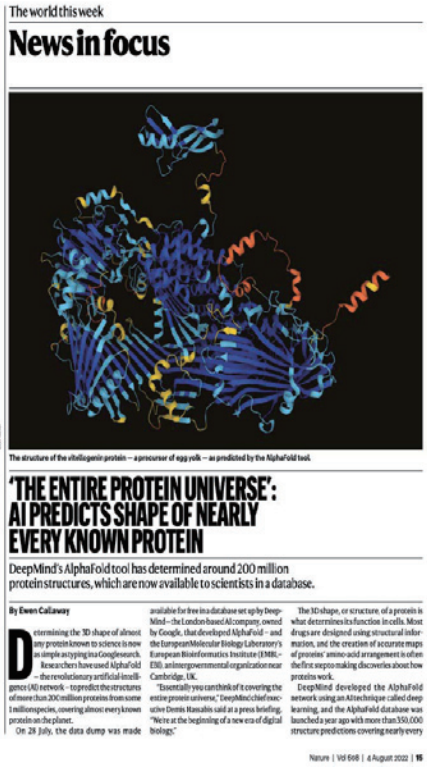




GDT; Global distance test

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 AlphaFold



The world this week

News in focus

The structure of the vitellogenin protein — a precursor of egg yolk — as predicted by the AlphaFold tool.

'THE ENTIRE PROTEIN UNIVERSE': AI PREDICTS SHAPE OF NEARLY EVERY KNOWN PROTEIN

DeepMind's AlphaFold tool has determined around 200 million protein structures, which are now available to scientists in a database.

By Ewen Callaway

Determining the 3D shape of almost any protein known to science is now as simple as typing in a Google search. Researchers have used AlphaFold — the revolutionary artificial-intelligence (AI) network — to predict the structures of more than 200 million proteins from some 1 million species, covering almost every known protein on the planet.

On 28 July, the data dump was made available for free in a database set up by DeepMind — the London-based AI company, owned by Google, that developed AlphaFold — and the European Molecular Biology Laboratory's European Bioinformatics Institute (EMBL-EBI), an intergovernmental organization near Cambridge, UK.

"Essentially you can think of it covering the entire protein universe," DeepMind's chief executive Demis Hassabis said at a press briefing. "We're at the beginning of a new era of digital biology."

The 3D shape, or structure, of a protein is what determines its function in cells. Most drugs are designed using structural information, and the creation of accurate maps of proteins' amino-acid arrangement is often the first step to making discoveries about how proteins work.

DeepMind developed the AlphaFold network using an AI technique called deep learning, and the AlphaFold database was launched a year ago with more than 350,000 structure predictions covering nearly every

News in focus

protein made by humans, mice and 19 other widely studied organisms. Over the months that followed, the catalogue swelled to around 1 million structures.

"We're bracing ourselves for the release of this huge trove," says Christine Orengo, a computational biologist at University College London, who has used the AlphaFold database to identify new families of proteins. "Having all the data predicted for us is just fantastic."

High-quality structures

The release of AlphaFold last year made a splash in the life-sciences community, whose members have since been scrambling to use the tool. The network produces highly accurate predictions of many proteins' structures. It also provides information about the accuracy of its predictions, so researchers know whether they can be relied on. Conventionally, scientists have needed to use time-consuming and costly experimental methods such as X-ray crystallography and cryo-electron microscopy to solve protein structures.

According to EMBL-EBI, around 35% of the more than 214 million predictions are deemed to be highly accurate, which means they are as good as experimentally determined structures. Another 45% are considered to be accurate enough for many applications.

Many AlphaFold structures are good enough to replace experimental structures for some applications. In other cases, researchers use AlphaFold predictions to validate and make sense of experimental data. Poor predictions are often obvious, and some of them are caused by intrinsic disorder in the protein itself: that means it has no defined shape — at least, not without other molecules present.

The 200 million predictions released last week are based on the sequences in another database, called UniProt. It's likely that scientists will have already had an idea about the shapes of some of these proteins, because they are included in databases of experimental structures or resemble other proteins in such repositories, says Eduard Porta Pardo, a computational biologist at Josep Carreras Leukaemia Research Institute (IJC) in Barcelona, Spain.

But such entries tend to be skewed towards human, mouse and other mammalian proteins, Portas says. It's likely that the AlphaFold dump will add significant knowledge, because it includes a diverse set of organisms. "It's going to be an awesome resource," says Porta.

Because AlphaFold's software has been available for a year, researchers have already had the capacity to predict the structure of any protein they wish. But many say that the availability of predictions in a single database will save researchers time, money — and, as Porta says, "It's another barrier of entry that you remove."

"I've used a lot of AlphaFold models. I have not ever run AlphaFold myself."

Jan Kosinski, a structural modeller at EMBL Hamburg in Germany who has been running the AlphaFold network over the past year, can't wait for the database expansion. His team once spent three weeks predicting the proteome — the set of all of an organism's proteins — of a pathogen. "Now we can just download all the models," he said at the briefing.

Having almost every known protein in the database will also make new types of study possible. Orengo and her team have used the AlphaFold database to identify new protein families, and they will now do this on a much larger scale. They will also use the expanded repository to help them to understand the evolution of proteins with helpful properties — such as the ability to consume plastic — or worrying ones, like those that can drive cancer. The identification of distant relatives of these proteins in the database can pinpoint the basis for their properties.

Martin Steinegger, a computational biologist at Seoul National University who helped to develop a cloud-based version of AlphaFold, is excited about seeing the database expand. But he says that researchers are still likely to need to run the AI network themselves. Increasingly, people are using AlphaFold to determine how proteins interact, and such predictions are not in the database. Other predictions that are not there include microbial proteins identified by sequencing genetic material from soil, ocean water and other 'metagenomic' sources.

Some sophisticated applications of the expanded AlphaFold database might also depend on downloading its entire 23-terabyte contents, which won't be feasible for many teams. Steinegger says. Cloud-based storage could also prove costly. Steinegger has co-developed a software tool called FoldSeek that can quickly find structurally similar proteins and which should also be able to squash the AlphaFold data down.

Even with almost every known protein included, the AlphaFold database will need updating as new organisms are discovered. AlphaFold's predictions can also be improved as new structural information becomes available. Hassabis says DeepMind hopes to update the database annually. His hope is that the repository will have a lasting impact on the life sciences. "It's going to require quite a big change in thinking."

DeepMind chief executive Demis Hassabis.

HOW LONG IS COVID INFECTIOUS? WHAT SCIENTISTS KNOW SO FAR

People with SARS-CoV-2 are told to isolate for a few days. But some can pass on the virus for much longer.

By David Adam

When the US Centers for Disease Control and Prevention (CDC) halved its recommended isolation time for people with COVID-19 to five days back in December, it said that the change was motivated by science. Specifically, the CDC said that most SARS-CoV-2 transmission occurs early in the course of the illness, in the one to two days before the onset of symptoms and for two to three days after.

Many scientists disputed that decision then and they continue to do so. Such dissent is bolstered by a series of studies confirming that many people with COVID-19 remain infectious well into the second week after they first experience symptoms. Reductions in the length of the recommended isolation period — now common worldwide — are driven by politics, they say, rather than any reassuring new data.

"The facts of how long people are infectious for have not really changed," says Amy Barczak, an infectious-disease specialist at Massachusetts General Hospital in Boston. "There is not data to support five days or anything

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 AlphaFold

GOLD (PROTEIN) RUSH !

What can I do for a medical research … ?

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 AlphaFold

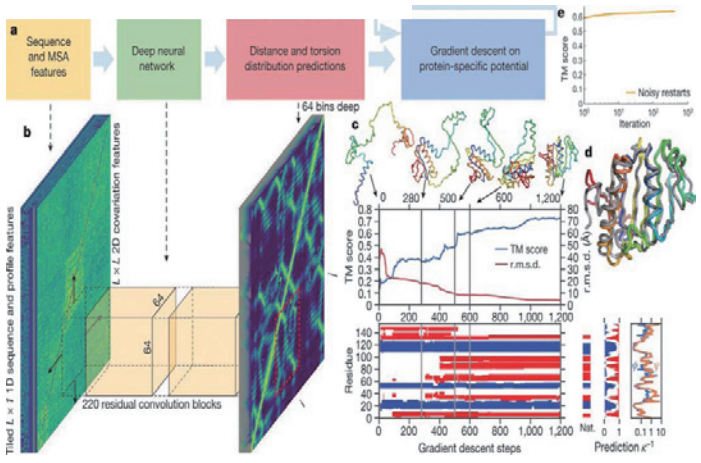
Article

DeepMind

Improved protein structure prediction using potentials from deep learning

https://doi.org/10.1038/s41586-019-1923-7
Received: 2 April 2019
Accepted: 10 December 2019
Published online: 15 January 2020

Andrew W. Senior[1,4*], Richard Evans[1,4], John Jumper[1,4], James Kirkpatrick[1,4], Laurent Sifre[1,4], Tim Green[1], Chongli Qin[1], Augustin Žídek[1], Alexander W. R. Nelson[1], Alex Bridgland[1], Hugo Penedones[1], Stig Petersen[1], Karen Simonyan[1], Steve Crossan[1], Pushmeet Kohli[1], David T. Jones[2,3], David Silver[1], Koray Kavukcuoglu[1] & Demis Hassabis[1]



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

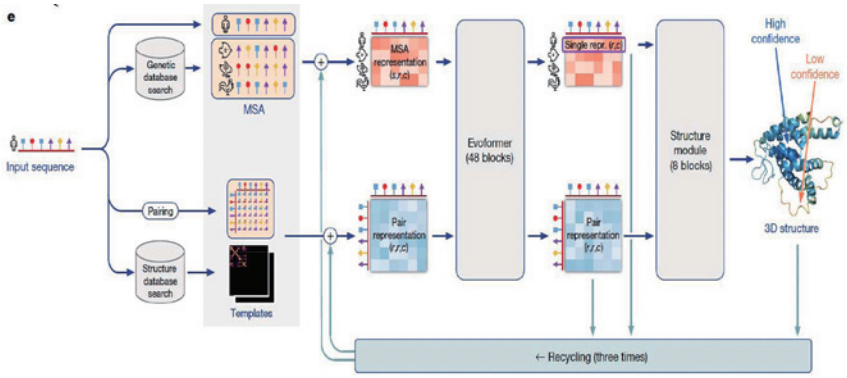
1 AlphaFold

DeepMind **AlphaFold2** Nature. 2021 Aug;596(7873):583-589

Highly accurate protein structure prediction with AlphaFold

https://doi.org/10.1038/s41586-021-03819-2
Received: 11 May 2021
Accepted: 12 July 2021
Published online: 15 July 2021
Open access
Check for updates

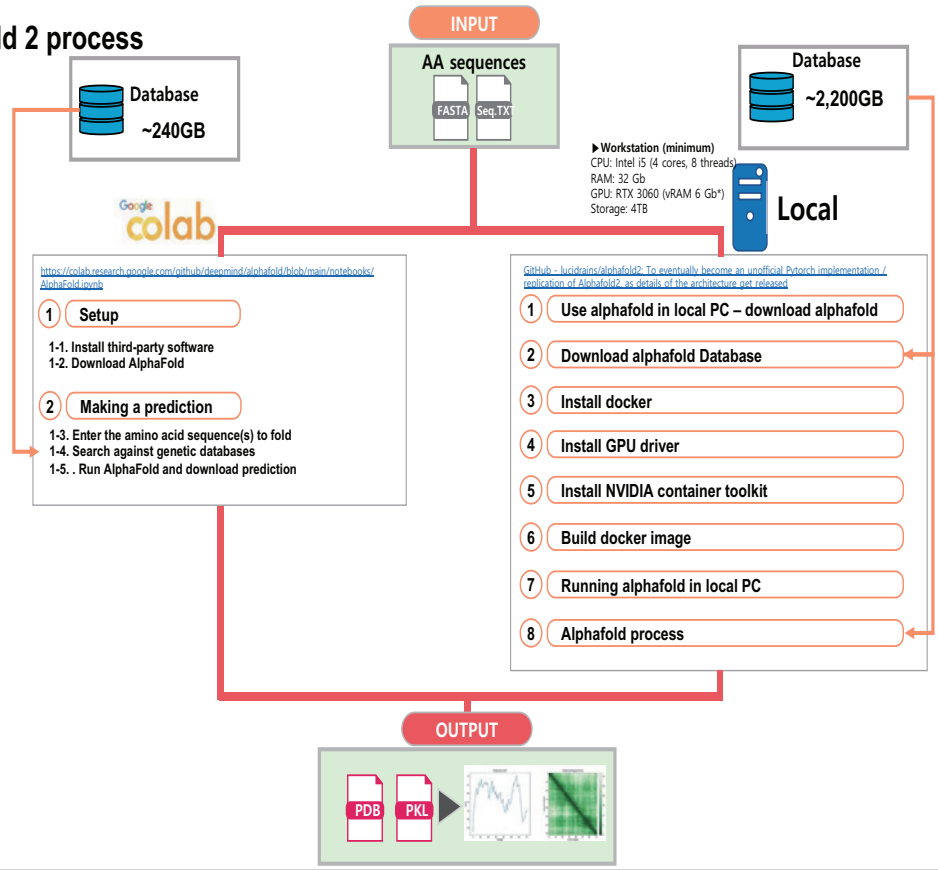
John Jumper[1,4✉], Richard Evans[1,4], Alexander Pritzel[1,4], Tim Green[1,4], Michael Figurnov[1,4], Olaf Ronneberger[1,4], Kathryn Tunyasuvunakool[1,4], Russ Bates[1,4], Augustin Žídek[1,4], Anna Potapenko[1,4], Alex Bridgland[1,4], Clemens Meyer[1,4], Simon A. A. Kohl[1,4], Andrew J. Ballard[1,4], Andrew Cowie[1,4], Bernardino Romera-Paredes[1,4], Stanislav Nikolov[1,4], Rishub Jain[1,4], Jonas Adler[1], Trevor Back[1], Stig Petersen[1], David Reiman[1], Ellen Clancy[1], Michal Zielinski[1], Martin Steinegger[2,3], Michalina Pacholska[1], Tamas Berghammer[1], Sebastian Bodenstein[1], David Silver[1], Oriol Vinyals[1], Andrew W. Senior[1], Koray Kavukcuoglu[1], Pushmeet Kohli[1] & Demis Hassabis[1,4✉]



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Colab 환경에서의 AlphaFold 사용법

AlphaFold 2 process



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Colab 환경에서의 AlphaFold 사용법

AlphaFold database usage

DB list

```
$DOWNLOAD_DIR/                  # Total: ~ 2.2 TB (download: 438 GB)
    bfd/                        # ~ 1.7 TB (download: 271.6 GB)
        # 6 files.
    mgnify/                     # ~ 64 GB (download: 32.9 GB)
        mgy_clusters_2018_12.fa
    params/                     # ~ 3.5 GB (download: 3.5 GB)
        # 5 CASP14 models,
        # 5 pTM models,
        # 5 AlphaFold-Multimer models,
        # LICENSE,
        # = 16 files.
    pdb70/                      # ~ 56 GB (download: 19.5 GB)
        # 9 files.
    pdb_mmcif/                  # ~ 206 GB (download: 46 GB)
        mmcif_files/
            # About 180,000 .cif files.
        obsolete.dat
    pdb_seqres/                 # ~ 0.2 GB (download: 0.2 GB)
        pdb_seqres.txt
    small_bfd/                  # ~ 17 GB (download: 9.6 GB)
        bfd-first_non_consensus_sequences.fasta
    uniclust30/                 # ~ 86 GB (download: 24.9 GB)
        uniclust30_2018_08/
            # 13 files.
    uniprot/                    # ~ 98.3 GB (download: 49 GB)
        uniprot.fasta
    uniref90/                   # ~ 58 GB (download: 29.7 GB)
        uniref90.fasta
```

Local

- Get MSA
  - uniref90
  - mgnify
  - uniclust30
  - bfd
- Search templates
  - pdb mmcif
  - pdb70
- AF multimer
  - uniprot
  - pdb seqres

Google colab

- Get MSA
  - uniref90
  - mgnify
  - small bfd
  - uniprot

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Colab 환경에서의 AlphaFold 사용법 : AlphaFold2

README.md

AlphaFold

This package provides an implementation of the inference pipeline of AlphaFold v2.0. This is a completely new model that was entered in CASP14 and published in Nature. For simplicity, we refer to this model as AlphaFold throughout the rest of this document.

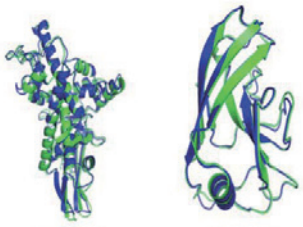
We also provide an implementation of AlphaFold-Multimer. This represents a work in progress and AlphaFold-Multimer isn't expected to be as stable as our monomer AlphaFold system. Read the guide for how to upgrade and update code.

Any publication that discloses findings arising from using this source code or the model parameters should cite the AlphaFold paper and, if applicable, the AlphaFold-Multimer paper.

Please also refer to the Supplementary Information for a detailed description of the method.

You can use a slightly simplified version of AlphaFold with this Colab notebook or community-supported versions (see below).

If you have any questions, please contact the AlphaFold team at alphafold@deepmind.com.



T1037 / 6vr4
90.7 GDT
(RNA polymerase domain)

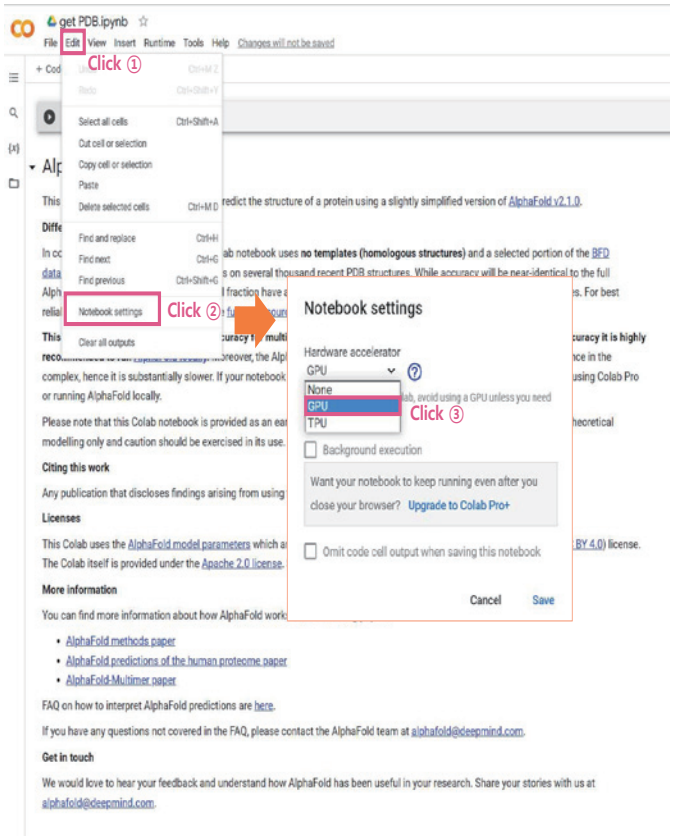
T1049 / 6y4f
93.3 GDT
(adhesin tip)

Experimental result
Computational prediction

Google colab

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Colab 환경에서의 AlphaFold 사용법 : AlphaFold2



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Colab 환경에서의 AlphaFold 사용법 : AlphaFold2

1. Install third-party software

Please execute this cell by pressing the *Play* button on the left to download and import third-party software in this Colab notebook. (See the acknowledgements in our readme.)

Note: This installs the software on the Colab notebook in the cloud and not on your computer.

코드 표시

2. Download AlphaFold

Please execute this cell by pressing the *Play* button on the left.

코드 표시

Five steps to run AlphaFold2

Making a prediction

Please paste the sequence of your protein in the text box below, then run the remaining cells via *Runtime* > *Run after*. You can also run the cells individually by pressing the *Play* button on the left.

Note that the search against databases and the actual prediction can take some time, from minutes to hours, depending on the length of the protein and what type of GPU you are allocated by Colab (see FAQ below).

3. Enter the amino acid sequence(s) to fold

Enter the amino acid sequence(s) to fold:

- If you enter only a single sequence, the monomer model will be used.
- If you enter multiple sequences, the multimer model will be used.

input length range: min: 16, max: 2500

sequence_1: 여기에 text 입력

sequence_2: 여기에 text 입력

sequence_3: 여기에 text 입력

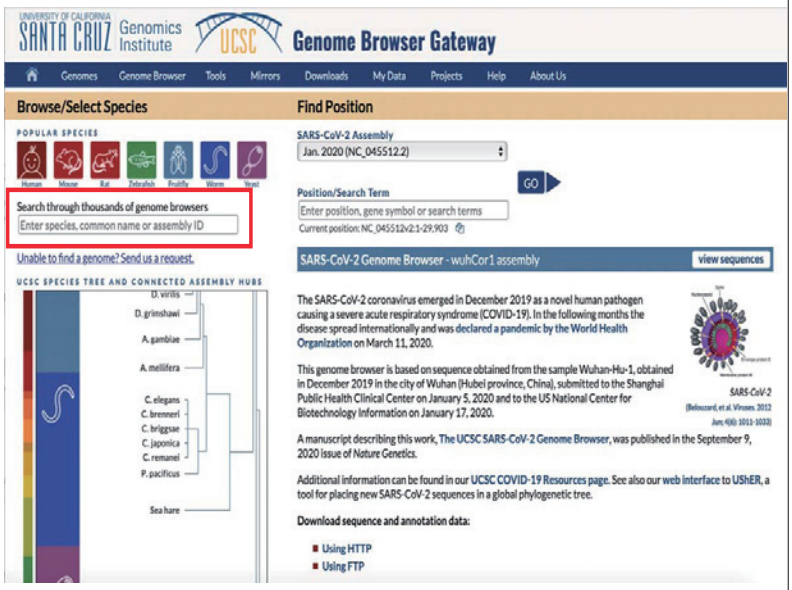
sequence_4: 여기에 text 입력

sequence_5: 여기에 text 입력

sequence_6: 여기에 text 입력

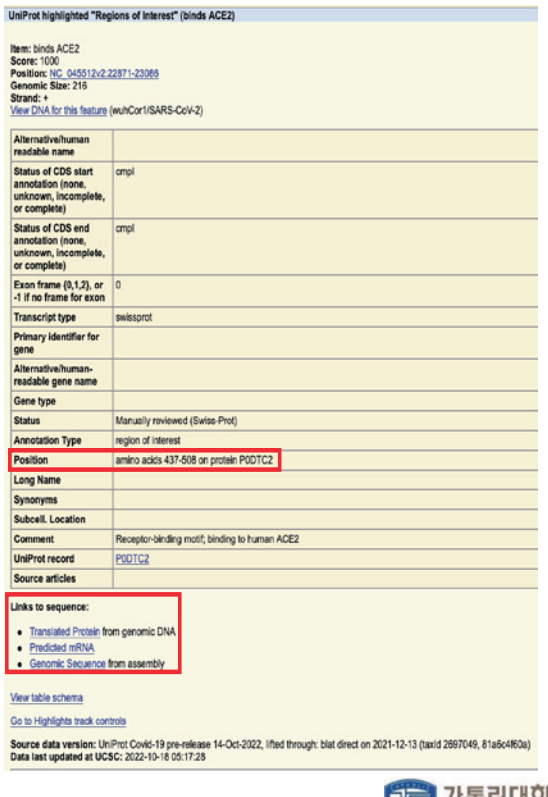
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측



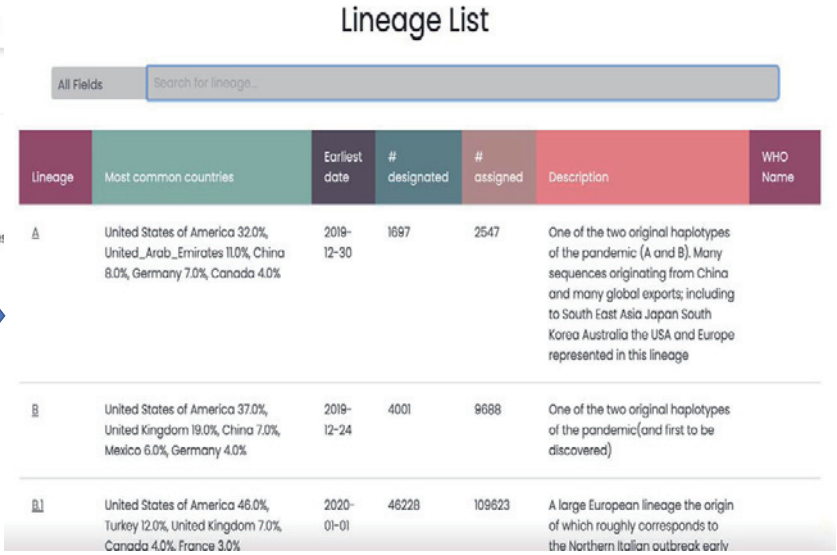
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측



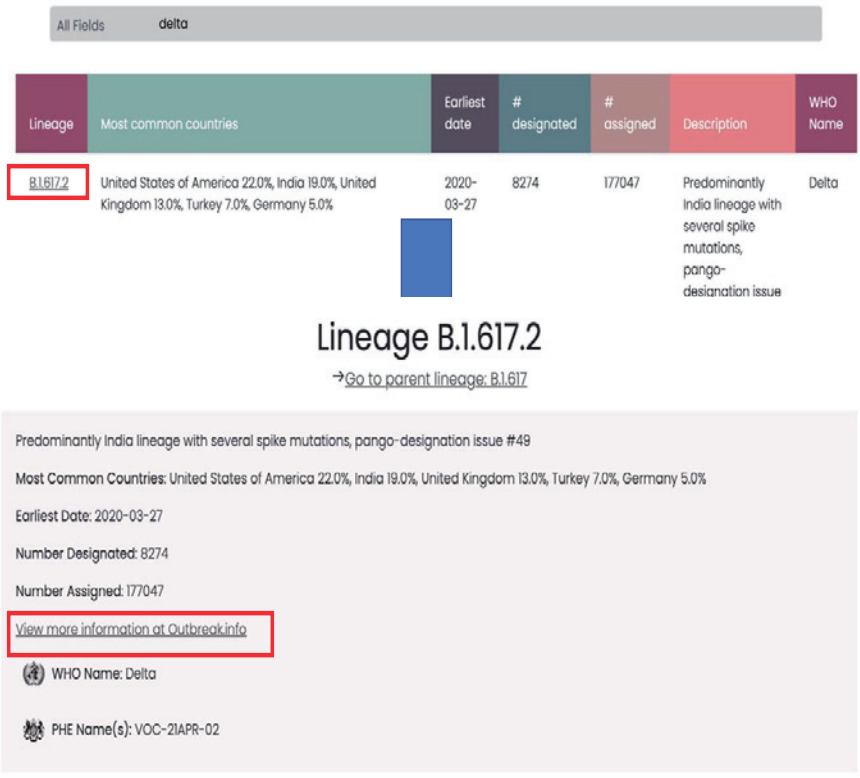
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

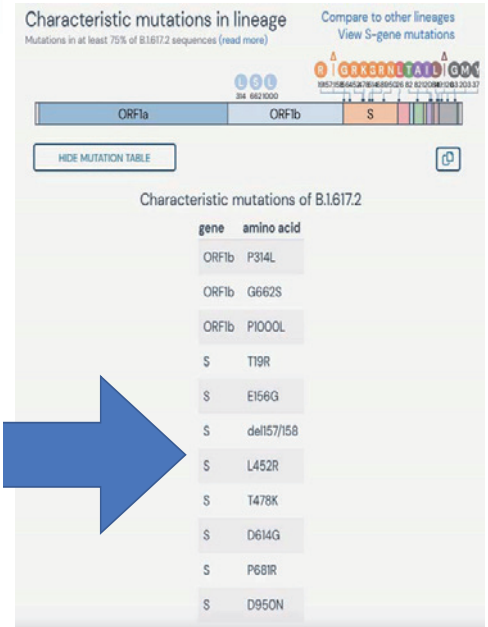
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측





가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Setup

Start by running the 2 cells below to set up AlphaFold and all required software.

[1] 1. Install third-party software

Please execute this cell by pressing the *Play* button on the left to download and import third-party software in this Colab notebook. (See the acknowledgements in our readme.)

Note: This installs the software on the Colab notebook in the cloud and not on your computer.

코드 표시

```
100% 100/100 [elapsed: 04:37 remaining: 00:00]
```

[2] 2. Download AlphaFold

Please execute this cell by pressing the *Play* button on the left.

코드 표시

```
100% 100/100 [elapsed: 01:39 remaining: 00:00]
Running with Tesla T4 GPU
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3. Enter the amino acid sequence(s) to fold

Enter the amino acid sequence(s) to fold:

- If you enter only a single sequence, the monomer model will be used.
- If you enter multiple sequences, the multimer model will be used.

sequence_1: AATTCTAACAATCTTGATTCTAAGGTTGGTGGTAATTATAATTACCTGTATAGATTGTTTAGGAAGTCTAATCTCAAACCTTTTGAGAGAGATATTTCAACTGAAATCTATCAGGCCGGTAGCACACCTTGTAATGGTGTTGAAGGTTTTAATTGTTACTTTCCTTTACAATCATATGGTTTCCAACCCACTAATGGTGTTGGTTACCAACCATAC

sequence_2: 여기에 text 입력

sequence_3: 여기에 text 입력

sequence_4: 여기에 text 입력

sequence_5: 여기에 text 입력

sequence_6: 여기에 text 입력

sequence_7: 여기에 text 입력

sequence_8: 여기에 text 입력

코드 표시

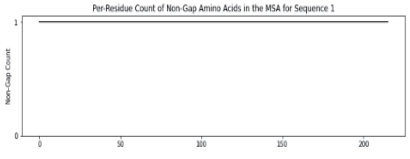
```
Using the single-chain model.
```

4. Search against genetic databases

[8] Once this cell has been executed, you will see statistics about the multiple sequence alignment (MSA) that will be used by AlphaFold. In particular, you'll see how well each residue is covered by similar sequences in the MSA.

코드 표시

```
Getting MSA for sequence 1
Searching mgnify: 100% 147/147 [elapsed: 36:06 remaining: 00:00]
1 unique sequences found in uniref90 for sequence 1
1 unique sequences found in smallbfd for sequence 1
1 unique sequences found in mgnify for sequence 1

1 unique sequences found in total for sequence 1
```



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

5. Run AlphaFold and download prediction

Once this cell has been executed, a zip-archive with the obtained prediction will be automatically downloaded to your computer.

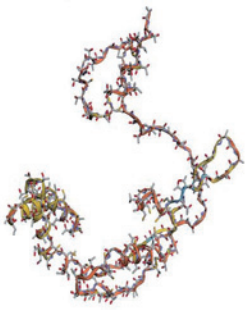
In case you are having issues with the relaxation stage, you can disable it below. Warning: This means that the prediction might have distracting small stereochemical violations.

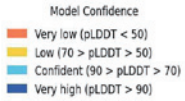
run_relax: ☐

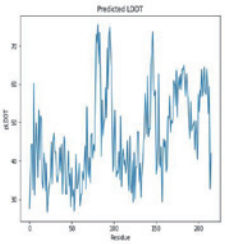
Relaxation is faster with a GPU, but we have found it to be less stable. You may wish to enable GPU for higher performance, but if it doesn't converge we suggested reverting to using without GPU.

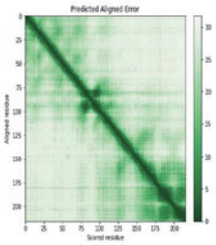
relax_use_gpu: ☐

코드 표시









가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

```
MODEL     1
ATOM      1  N   ALA A   1      11.310  45.250  12.074  1.00 27.48           N
ATOM      2  CA  ALA A   1      10.784  44.580  13.260  1.00 27.48           C
ATOM      3  C   ALA A   1      10.026  43.310  12.882  1.00 27.48           C
ATOM      4  CB  ALA A   1       9.877  45.523  14.047  1.00 27.48           C
ATOM      5  O   ALA A   1       9.012  43.370  12.183  1.00 27.48           O
ATOM      6  N   ALA A   2      10.663  42.210  12.688  1.00 35.26           N
ATOM      7  CA  ALA A   2       9.972  40.934  12.528  1.00 35.26           C
ATOM      8  C   ALA A   2      10.841  39.775  13.009  1.00 35.26           C
ATOM      9  CB  ALA A   2       9.571  40.725  11.069  1.00 35.26           C
ATOM     10  O   ALA A   2      11.836  39.430  12.368  1.00 35.26           O
ATOM     11  N   THR A   3      11.091  39.784  14.373  1.00 44.04           N
ATOM     12  CA  THR A   3      11.033  38.576  15.189  1.00 44.04           C
ATOM     13  C   THR A   3       9.720  38.510  15.964  1.00 44.04           C
ATOM     14  CB  THR A   3      12.217  38.509  16.171  1.00 44.04           C
ATOM     15  O   THR A   3       9.443  39.372  16.800  1.00 44.04           O
ATOM     16  CG2 THR A   3      12.379  37.103  16.740  1.00 44.04           C
ATOM     17  OG1 THR A   3      13.420  38.877  15.486  1.00 44.04           O
ATOM     18  N   THR A   4       8.656  37.925  15.358  1.00 44.39           N
ATOM     19  CA  THR A   4       7.840  37.025  16.165  1.00 44.39           C
ATOM     20  C   THR A   4       7.094  36.031  15.279  1.00 44.39           C
ATOM     21  CB  THR A   4       6.831  37.807  17.027  1.00 44.39           C
ATOM     22  O   THR A   4       5.959  35.655  15.579  1.00 44.39           O
ATOM     23  CG2 THR A   4       7.475  38.293  18.321  1.00 44.39           C
ATOM     24  OG1 THR A   4       6.357  38.939  16.287  1.00 44.39           O
ATOM     25  N   CYS A   5       7.714  35.364  14.361  1.00 32.47           N
ATOM     26  CA  CYS A   5       7.085  34.230  13.693  1.00 32.47           C
ATOM     27  C   CYS A   5       7.618  32.911  14.240  1.00 32.47           C
ATOM     28  CB  CYS A   5       7.321  34.298  12.184  1.00 32.47           C
ATOM     29  O   CYS A   5       7.032  31.853  14.001  1.00 32.47           O
ATOM     30  SG  CYS A   5       5.952  35.039  11.267  1.00 32.47           S
ATOM     31  N   THR A   6       7.951  32.750  15.488  1.00 60.19           N
ATOM     32  CA  THR A   6       8.169  31.370  15.906  1.00 60.19           C
ATOM     33  C   THR A   6       7.118  30.941  16.926  1.00 60.19           C
ATOM     34  CB  THR A   6       9.576  31.183  16.504  1.00 60.19           C
ATOM     35  O   THR A   6       6.667  29.794  16.916  1.00 60.19           O
ATOM     36  CG2 THR A   6      10.014  29.724  16.433  1.00 60.19           C
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

3. Enter the amino acid sequence(s) to fold

Enter the amino acid sequence(s) to fold:

- If you enter only a single sequence, the monomer model will be used.
- If you enter multiple sequences, the multimer model will be used.

Sequence of Receptor Binding Domain (RBD)

sequence_1: RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTYGVGYQPYF

sequence_2: 여기에 text 입력

sequence_3: 여기에 text 입력

sequence_4: 여기에 text 입력

sequence_5: 여기에 text 입력

sequence_6: 여기에 text 입력

sequence_7: 여기에 text 입력

sequence_8: 여기에 text 입력

코드 표시

4. Search against genetic databases

Once this cell has been executed, you will see statistics about the multiple sequence alignment (MSA) that will be used by AlphaFold. In particular, you'll see how well each residue is covered by similar sequences in the MSA.

코드 표시

5. Run AlphaFold and download prediction

Once this cell has been executed, a zip-archive with the obtained prediction will be automatically downloaded to your computer.

In case you are having issues with the relaxation stage, you can disable it below. Warning: This means that the prediction might have distracting small stereochemical violations.

run_relax:

코드 표시

+ 코드 + 텍스트

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

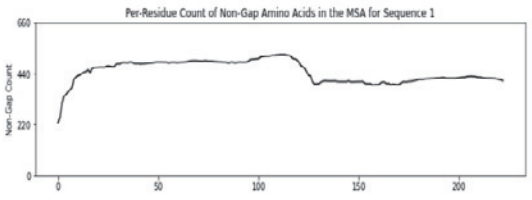
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

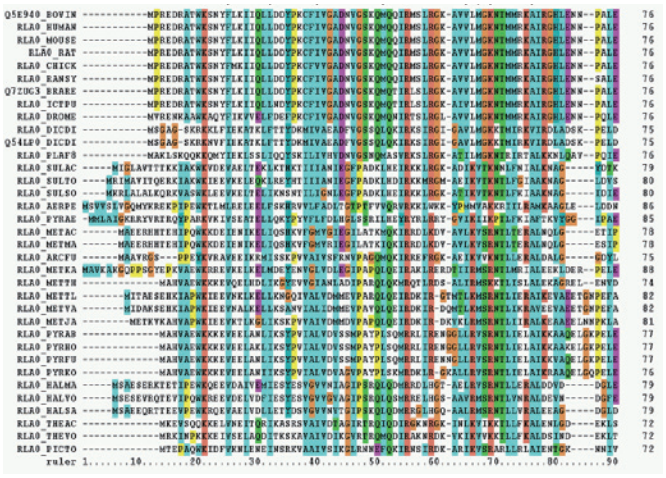
[4] 4. Search against genetic databases

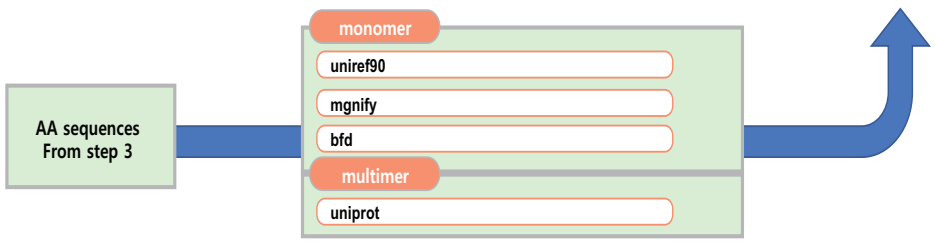
Once this cell has been executed, you will see statistics about the multiple sequence alignment (MSA) that will be used by AlphaFold. In particular, you'll see how well each residue is covered by similar sequences in the MSA.

코드 표시

```
Getting MSA for sequence 1
Searching mgnify: 100% 147/147 [elapsed: 17:09 remaining: 00:00]
658 unique sequences found in uniref90 for sequence 1
4 unique sequences found in smallbfd for sequence 1
1 unique sequences found in mgnify for sequence 1

660 unique sequences found in total for sequence 1
```

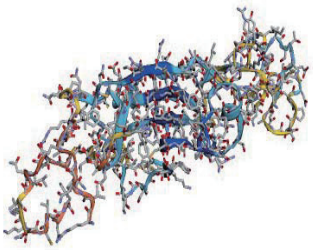


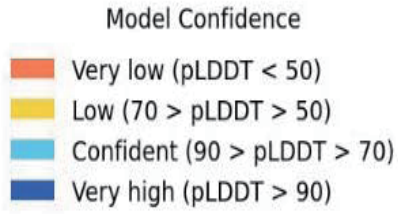


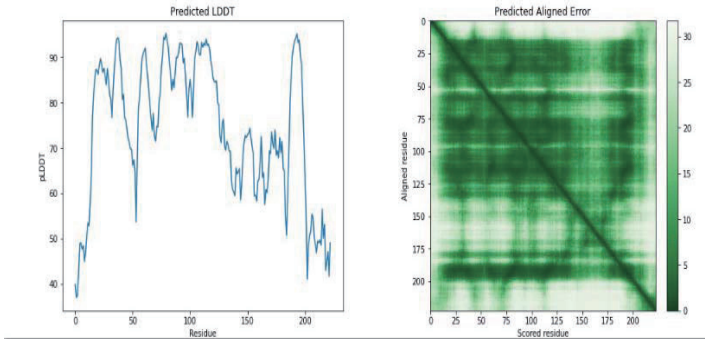


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측





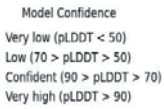


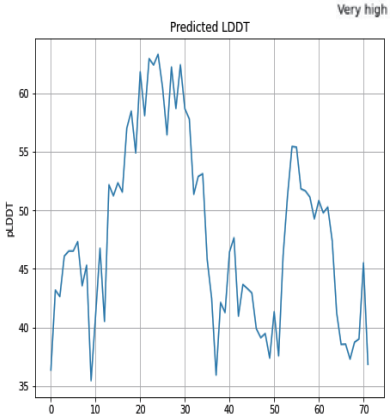
Local Distance Difference Test (LDDT)

pFAM uses a quality score (LDDT)

>= 0.6 : considered a reasonable model
> 0.8 : great model

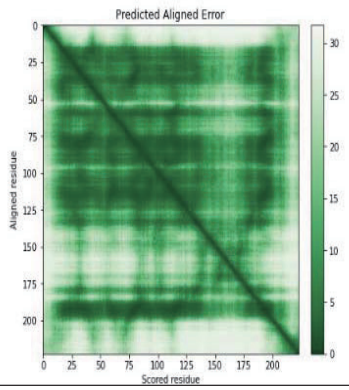
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA





pLDDT(predicted Local Distance Difference Test)
pLDDT는 LDDT값을 예측한 수치로 예측 모델의 각 residue에서의 신뢰도를 의미합니다.
실제 모델의 residue와 얼마나 일치하는지 예측한 값인 동시에 해당 위치에서 단백질 구조가 folding이 잘 되는지를 나타냅니다.
pLDDT값이 낮음은 신뢰도가 낮음을 의미하며 해당 위치의 residue들이 무질서한 구조를 가짐을 의미합니다.

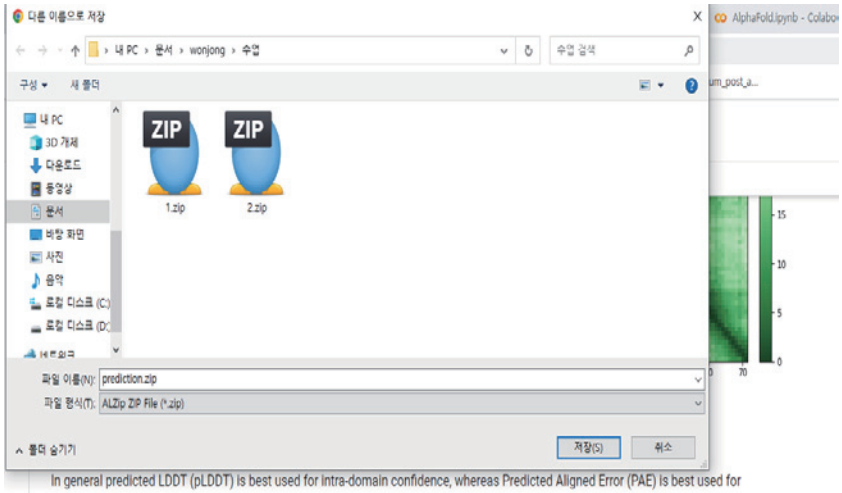
LDDT : 예측된 모델이 실제 단백질과 얼만큼 일치하는지를 나타내는 [0,1]의 범위를 가진 값으로 1에 가까울 수록 실제 단백질과 일치함을 의미합니다.



PAE(Predicted Aligned Error)
PAE는 모델의 residue간의 위치 에너지가 실제 모델과 얼마나 차이를 가지는지 예측한 값으로 해당 값이 낮으면 두 residue간 위치의 정확도가 높음을 의미합니다.

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측



In general predicted LDDT (pLDDT) is best used for intra-domain confidence, whereas Predicted Aligned Error (PAE) is best used for determining between domain or between chain confidence.

Please see the AlphaFold methods paper, the AlphaFold predictions of the human proteome paper, and the AlphaFold-Multimer paper as well as our FAQ on how to interpret AlphaFold predictions.

사용자 › User › 문서 › wonjong › 수업 › prediction › prediction

prediction 검색

이름	수정한 날짜	유형	크기
predicted_aligned_error.json	2022-05-03 오전 9:05	JSON 파일	54KB
selected_prediction.pdb	2022-05-03 오전 9:05	Protein Data Bank...	89KB

PDB file


PyMOL


ChimeraX

Visualization

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

pLDDT

PDB

Record Name	Atom serial number	Atom name	Residue Name	Chain ID	Residue sequnce number	X	Y	Z	Occupancy	temperature factor (B-factor)	Element symbol
ATOM	1	N	MET	A	1	-6.594	-16.75	58.3	1	23.69	N
ATOM	2	H	MET	A	1	-6.533	-15.777	58.035	1	23.69	H
ATOM	3	H2	MET	A	1	-7.551	-16.959	58.547	1	23.69	H
ATOM	4	H3	MET	A	1	-6.011	-16.91	59.109	1	23.69	H
ATOM	5	CA	MET	A	1	-6.158	-17.624	57.184	1	23.69	C
ATOM	6	HA	MET	A	1	-6.298	-18.659	57.494	1	23.69	H
ATOM	7	C	MET	A	1	-4.656	-17.501	56.924	1	23.69	C
ATOM	8	CB	MET	A	1	-6.99	-17.429	55.907	1	23.69	C
ATOM	9	HB2	MET	A	1	-6.503	-17.961	55.09	1	23.69	H
ATOM	10	HB3	MET	A	1	-7.043	-16.372	55.649	1	23.69	H
ATOM	11	O	MET	A	1	-3.943	-18.391	57.354	1	23.69	O
ATOM	12	CG	MET	A	1	-8.406	-17.996	56.06	1	23.69	C
ATOM	13	HG2	MET	A	1	-8.337	-19.033	56.39	1	23.69	H
ATOM	14	HG3	MET	A	1	-8.953	-17.425	56.81	1	23.69	H
ATOM	15	SD	MET	A	1	-9.333	-17.958	54.511	1	23.69	S
ATOM	16	CE	MET	A	1	-10.835	-18.857	54.988	1	23.69	C
ATOM	17	HE1	MET	A	1	-11.339	-18.332	55.8	1	23.69	H
ATOM	18	HE2	MET	A	1	-10.578	-19.867	55.307	1	23.69	H
ATOM	19	HE3	MET	A	1	-11.507	-18.914	54.132	1	23.69	H
ATOM	20	N	PHE	A	2	-4.184	-16.412	56.3	1	22.95	N
ATOM	21	H	PHE	A	2	-4.856	-15.744	55.949	1	22.95	H
ATOM	22	CA	PHE	A	2	-2.816	-16.168	55.783	1	22.95	C
ATOM	23	HA	PHE	A	2	-2.798	-16.448	54.73	1	22.95	H
ATOM	24	C	PHE	A	2	-1.599	-16.889	56.41	1	22.95	C
ATOM	25	CB	PHE	A	2	-2.557	-14.651	55.862	1	22.95	C
ATOM	26	HB2	PHE	A	2	-2.966	-14.246	56.788	1	22.95	H
ATOM	27	HB3	PHE	A	2	-1.482	-14.476	55.896	1	22.95	H
ATOM	28	O	PHE	A	2	-0.756	-17.388	55.674	1	22.95	O
ATOM	29	CG	PHE	A	2	-3.099	-13.873	54.68	1	22.95	C
ATOM	30	CD1	PHE	A	2	-2.249	-13.598	53.592	1	22.95	C
ATOM	31	HD1	PHE	A	2	-1.221	-13.931	53.602	1	22.95	H
ATOM	32	CD2	PHE	A	2	-4.434	-13.423	54.656	1	22.95	C

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

AlphaFold v.2.2.3(2022.08.25 released)

●Change the Colab PAE json output to new format that matches the format used in the new release of the AlphaFold Protein Structure Database (AFDB).

Old version

```
[
  {
    "residue1": [1, 1, 1, 1, 1, ...],
    "residue2": [1, 2, 3, 4, 5, ...],
    "predicted_aligned_error": [0, 1, 4, 7, 9, ..., ...],
    "max_predicted_aligned_error": 31.75
  }
]
```

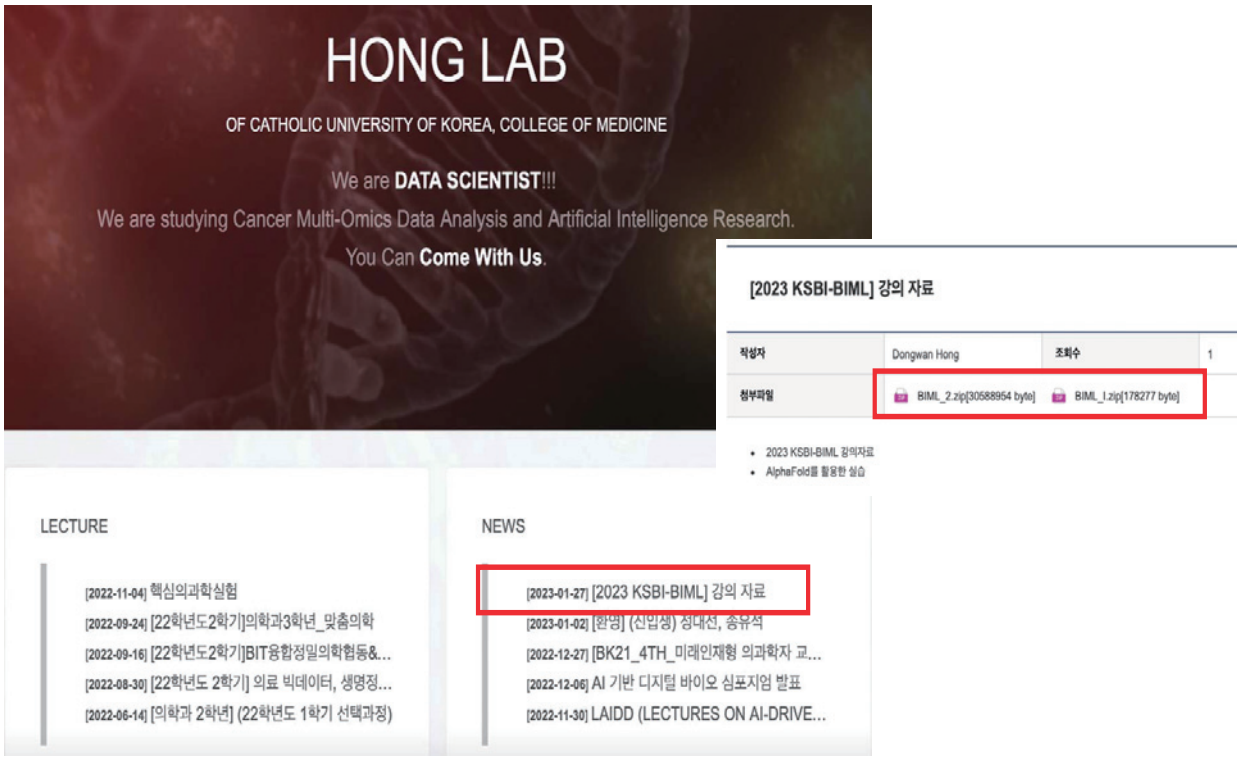
Latest version

```
[
  {
    "predicted_aligned_error": [[0, 1, 4, 7, 9, ...], ...],
    "max_predicted_aligned_error": 31.75
  }
]
```

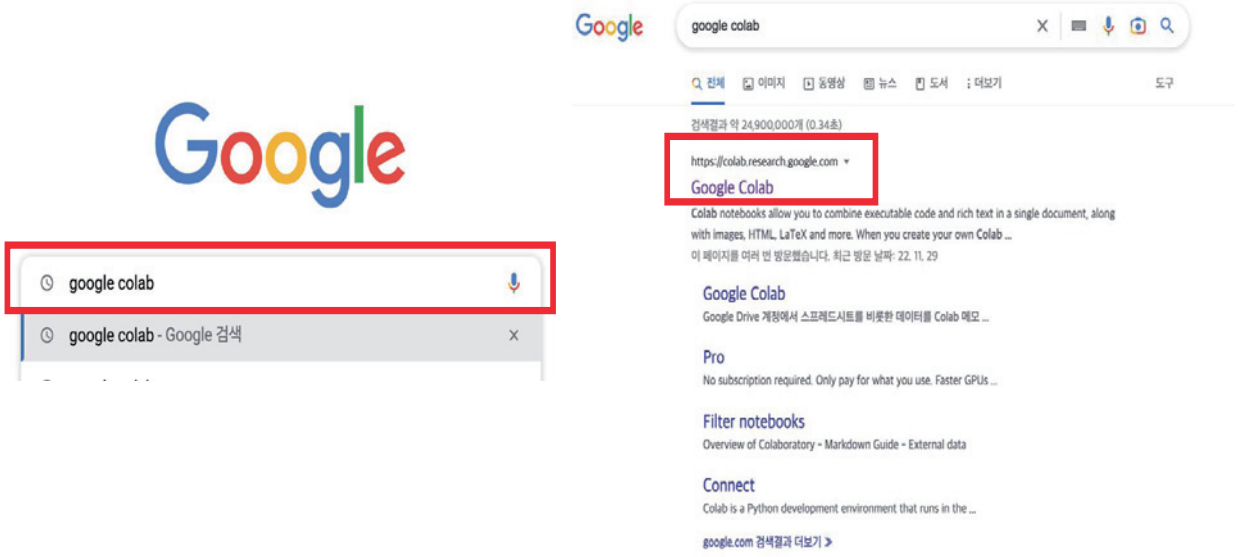
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

http://honglab.catholic.ac.kr



Google colab을 이용한 예측 구조의 해석

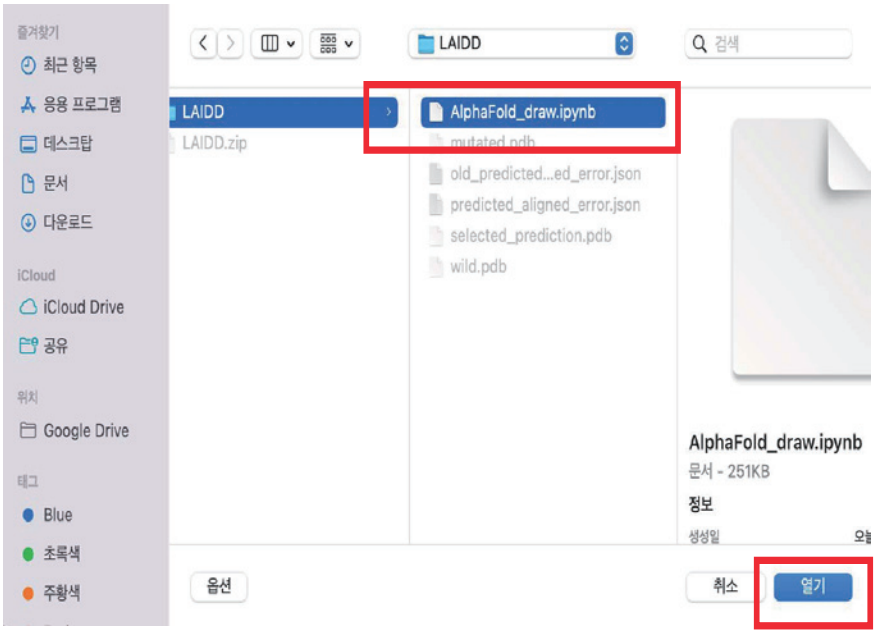


3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Google colab을 이용한 예측 구조의 해석

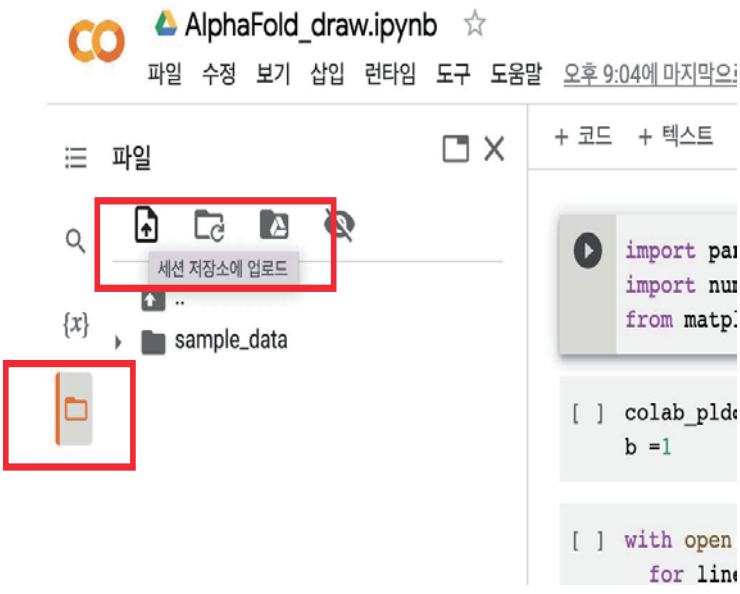
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

Google colab을 이용한 예측 구조의 해석



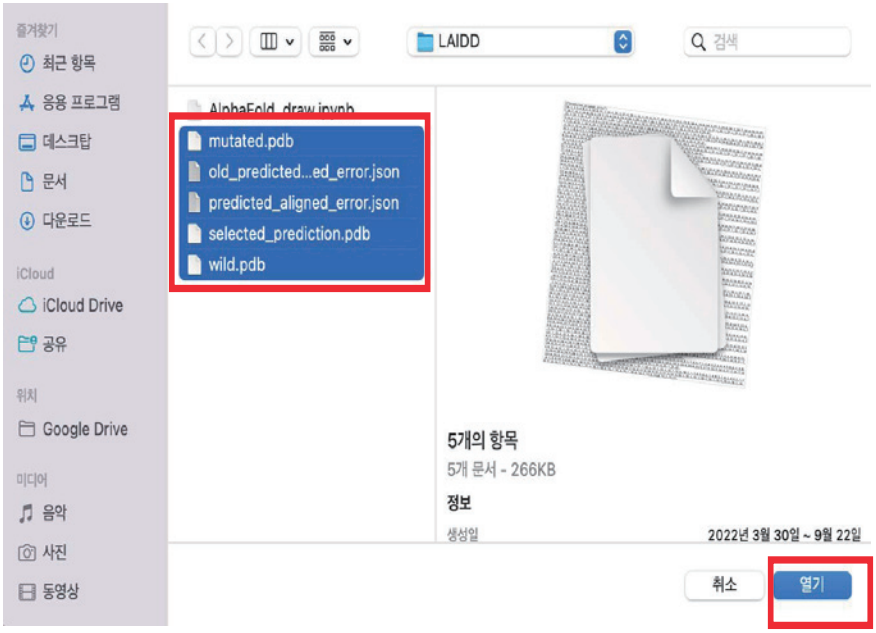
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Google colab을 이용한 예측 구조의 해석



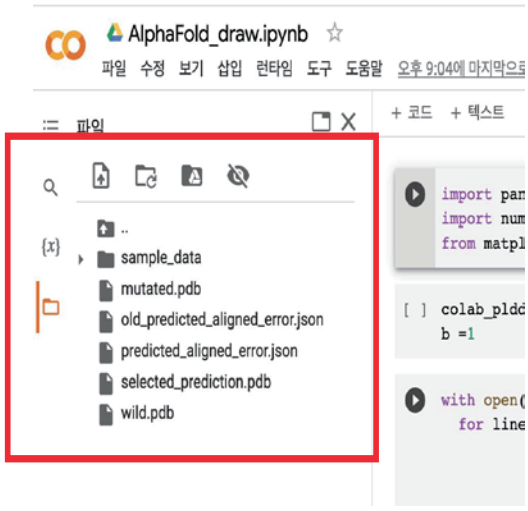
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

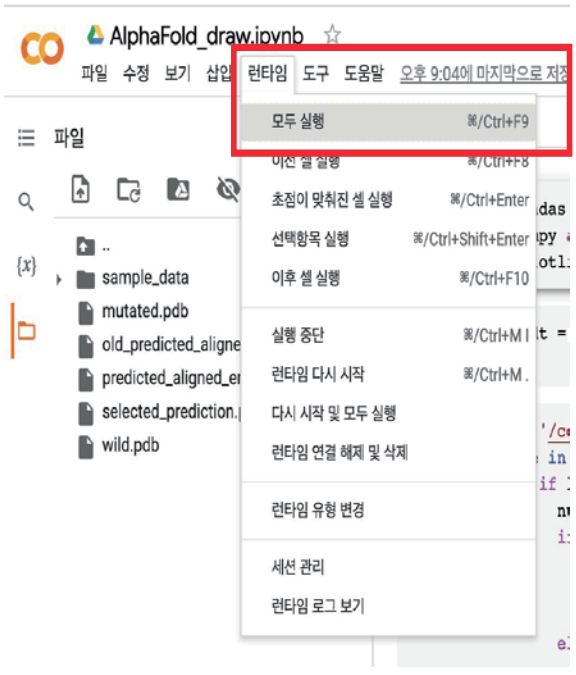
Google colab을 이용한 예측 구조의 해석



3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Google colab을 이용한 예측 구조의 해석





가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

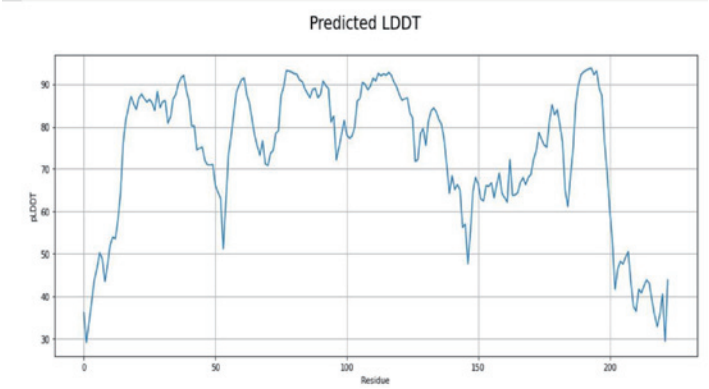
Get information from PDB & JSON file – draw pLDDT & PAE

```
[1]  import json
     import pandas as pd
     import numpy as np
     from matplotlib import pyplot as plt
```

```
[2]  colab_plddt =[]
     b =1
```

```
[3]  with open('/content/selected_prediction.pdb', 'r') as file:
       for line in file:
             if line.startswith('ATOM'):
               number = int(line[22:26])
               if number == b:
                 b+=1
                 score = line[61:66].strip()
                 colab_plddt.append(float(score))
               elif number == 1 and b > 2:
                 b=1
                 b+=1
                 score = line[61:66].strip()
                 colab_plddt.append(float(score))
```

```
plt.figure(figsize=[16, 6])
plt.plot(colab_plddt,linestyle='solid')
plt.grid('True')
plt.xlabel('Residue')
plt.ylabel('pLDDT')
plt.suptitle('Predicted LDDT',fontsize=20)
plt.savefig('/content/pLDDT.png', dpi=300)
```



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

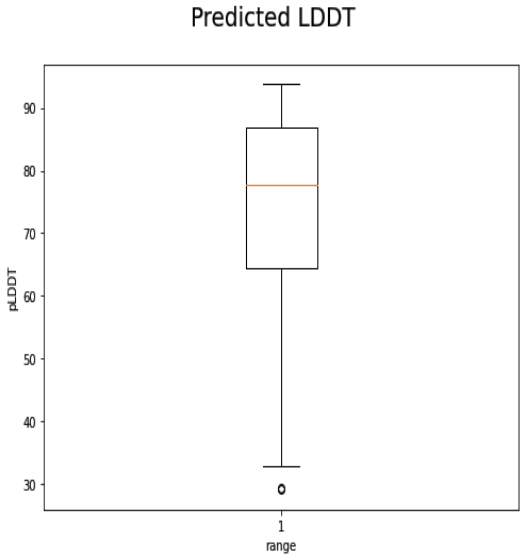
Get information from PDB & JSON file – draw pLDDT & PAE

```
[1]  import json
     import pandas as pd
     import numpy as np
     from matplotlib import pyplot as plt
```

```
[2]  colab_plddt =[]
     b =1
```

```
[3]  with open('/content/selected_prediction.pdb', 'r') as file:
       for line in file:
             if line.startswith('ATOM'):
               number = int(line[22:26])
               if number == b:
                 b+=1
                 score = line[61:66].strip()
                 colab_plddt.append(float(score))
               elif number == 1 and b > 2:
                 b=1
                 b+=1
                 score = line[61:66].strip()
                 colab_plddt.append(float(score))
```

```
[9]  plt.figure(figsize=[8, 6])
     plt.boxplot([colab_plddt])
     plt.xlabel('range')
     plt.ylabel('pLDDT')
     plt.suptitle('Predicted LDDT',fontsize=20)
     plt.savefig('/content/pLDDT.png', dpi=300)
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

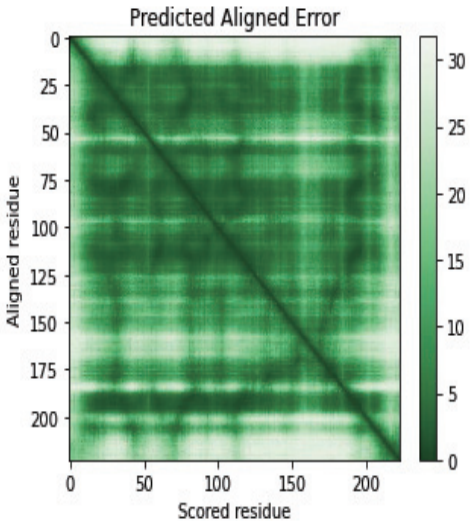
Get information from PDB & JSON file – draw pLDDT & PAE

```
#colab AlphaFold latest version result file
```

```
import json
import pandas as pd
import numpy as np
from matplotlib import pyplot as plt
```

```
with open('/content/predicted_aligned_error.json', 'r') as pae:
  info = json.load(pae)
  pae = info[0]['predicted_aligned_error']
  max_pae = info[0]['max_predicted_aligned_error']
```

```
plt.imshow(pae, vmin=0., vmax=max_pae, cmap='Greens_r')
plt.colorbar(fraction=0.046, pad=0.04)
plt.title('Predicted Aligned Error')
plt.xlabel('Scored residue')
plt.ylabel('Aligned residue')
plt.savefig('/content/PAE.png', dpi = 300)
```



3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – draw pLDDT & PAE


```
#colab AlphaFold old version result file
```

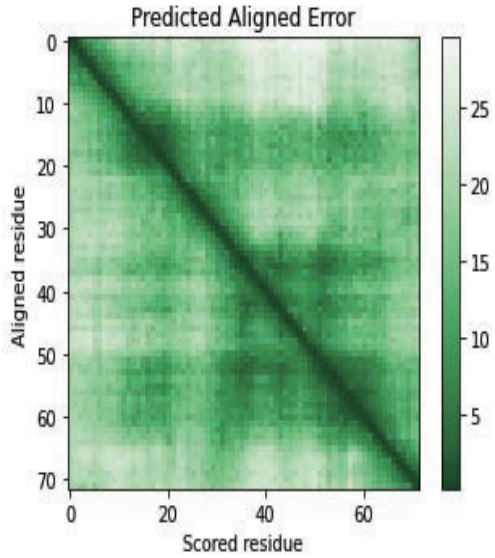
```
import json
import pandas as pd
import numpy as np
from matplotlib import pyplot as plt
```

```
with open('/content/predicted_aligned_error.json', 'r') as pae:
  info = json.load(pae)
  residue1 = info[0]['residue1']
  residue2 = info[0]['residue2']
  pae_score = info[0]['distance']
```

```
pae_array = np.ones((max(residue1),(max(residue2))))
```

```
for x, y, z in zip(residue1, residue2, pae_score):
  pae_array[int(x-1),int(y-1)] = z
```

```
plt.subplot(1, 1, 1)
plt.imshow(pae_array, alpha=1, cmap='Greens_r')
plt.colorbar(fraction=0.046, pad=0.04)
plt.title('Predicted Aligned Error')
plt.xlabel('Scored residue')
plt.ylabel('Aligned residue')
plt.savefig('/content/PAE.png', dpi = 300)
```



3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – draw pLDDT & PAE

```
import pandas as pd
import numpy as np
from matplotlib import pyplot as plt
```

```
#1.Wuhan-hu-1의 pLDDT 값 추출
```

```
wild_plddt =[]
b =1
```

```
with open('/content/wild.pdb', 'r') as file:
  for line in file:
          if line.startswith('ATOM'):
            number = int(line[22:26])
            if number == b:
              b+=1
              score = line[61:66].strip()
              wild_plddt.append(float(score))
            elif number == 1 and b > 2:
              b=1
              b+=1
              score = line[61:66].strip()
              wild_plddt.append(float(score))
```

```
#2.delta의 pLDDT 값 추출
```

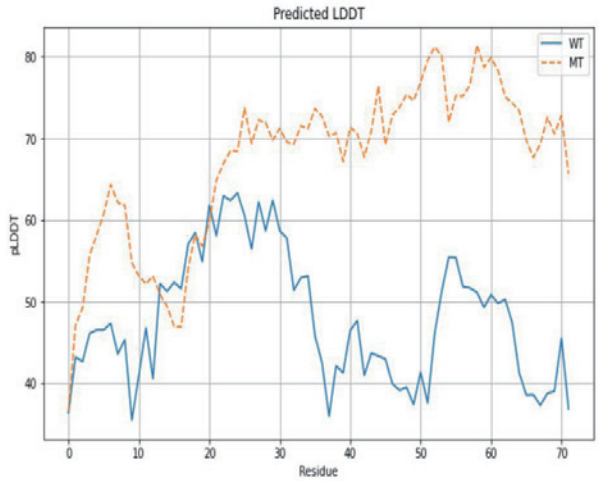
```
mutated_plddt =[]
b =1
```

```
with open('/content/mutated.pdb', 'r') as file:
  for line in file:
          if line.startswith('ATOM'):
            number = int(line[22:26])
            if number == b:
              b+=1
              score = line[61:66].strip()
              mutated_plddt.append(float(score))
            elif number == 1 and b > 2:
              b=1
              b+=1
              score = line[61:66].strip()
              mutated_plddt.append(float(score))
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

```
#3. 비교 그래프 그리기
```

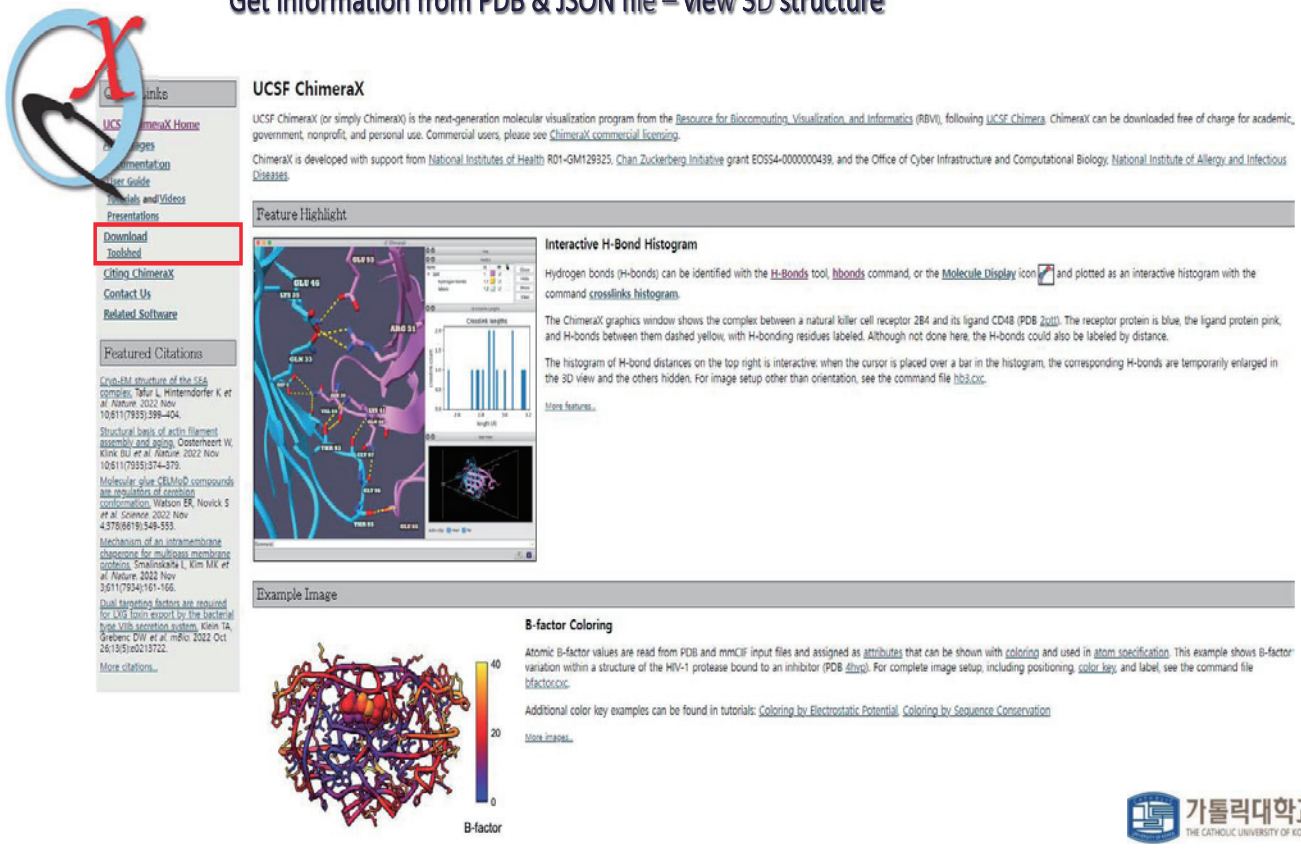
```
plt.figure(figsize=[10, 6])
plt.plot(wild_plddt,linestyle='solid',label='WT')
plt.plot(mutated_plddt,linestyle='dashed',label='MT')
plt.legend()
plt.grid('True')
plt.title('Predicted LDDT')
plt.xlabel('Residue')
plt.ylabel('pLDDT')
plt.savefig('/content/compare_plddt.png', dpi=300)
```



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

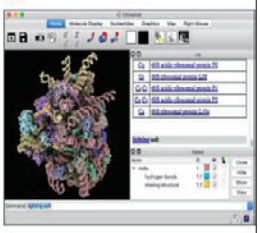
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – view 3D structure



3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – view 3D structure



Download UCSF ChimeraX

ChimeraX is the state-of-the-art visualization program from the Resource for Biocomputing, Visualization, and Informatics at UC San Francisco. It is free for academic, government, nonprofit, and personal use; commercial users, please see commercial licensing. Please cite ChimeraX in publications.

See also: Features and Missing Features, Change Log, System Requirements, Older Releases, Common Platform Problems, Download & Citation Counts

ChimeraX version 1.5

Production releases are stable versions for ChimeraX Toolshed bundles to work with. You may need to use an older release if a bundle you wish to use has not been updated yet. Showing releases for Windows 10.

Operating System	Distribution	Date	Notes
Windows	ChimeraX-1.5.exe	2022년 11월 23일	Download is a Windows installer. Tested on Windows 10 and Windows 11. ▸ More Info...

▸ Other releases

Daily Build

Daily builds are generated automatically each night from the development source code (see the change log). While a given build may have unforeseen problems, these are often fixed by the next day. Showing releases for Windows 10.

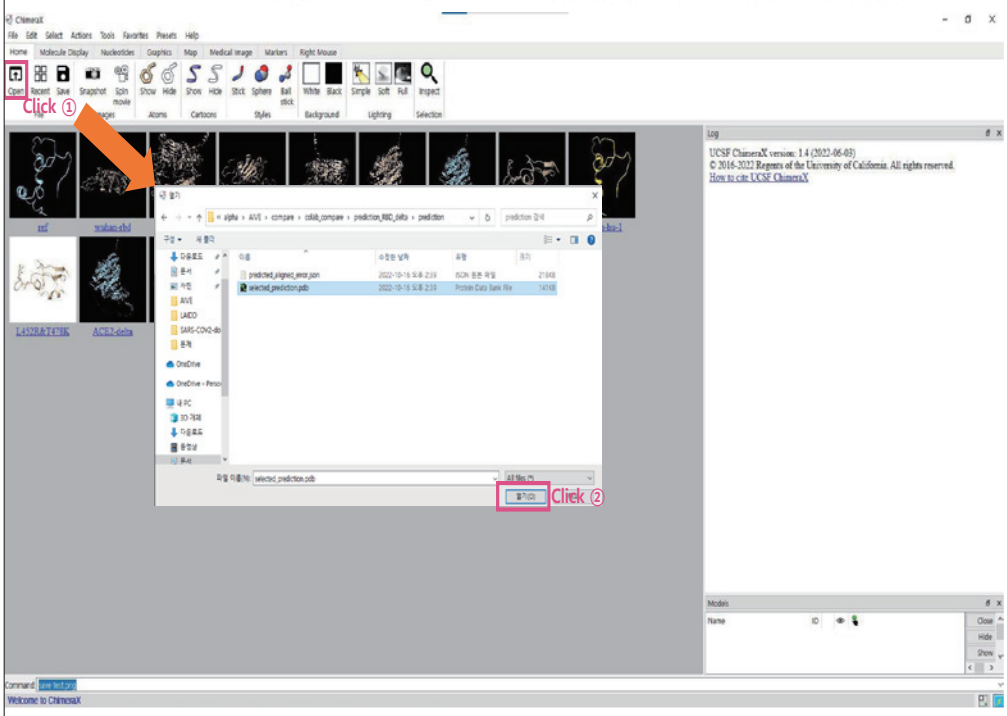
Operating System	Distribution	Date	Notes
Windows	chimerax-daily.exe	2022년 11월 28일	Download is a Windows installer. Tested on Windows 10 and Windows 11. ▸ More Info...

▸ Other releases

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

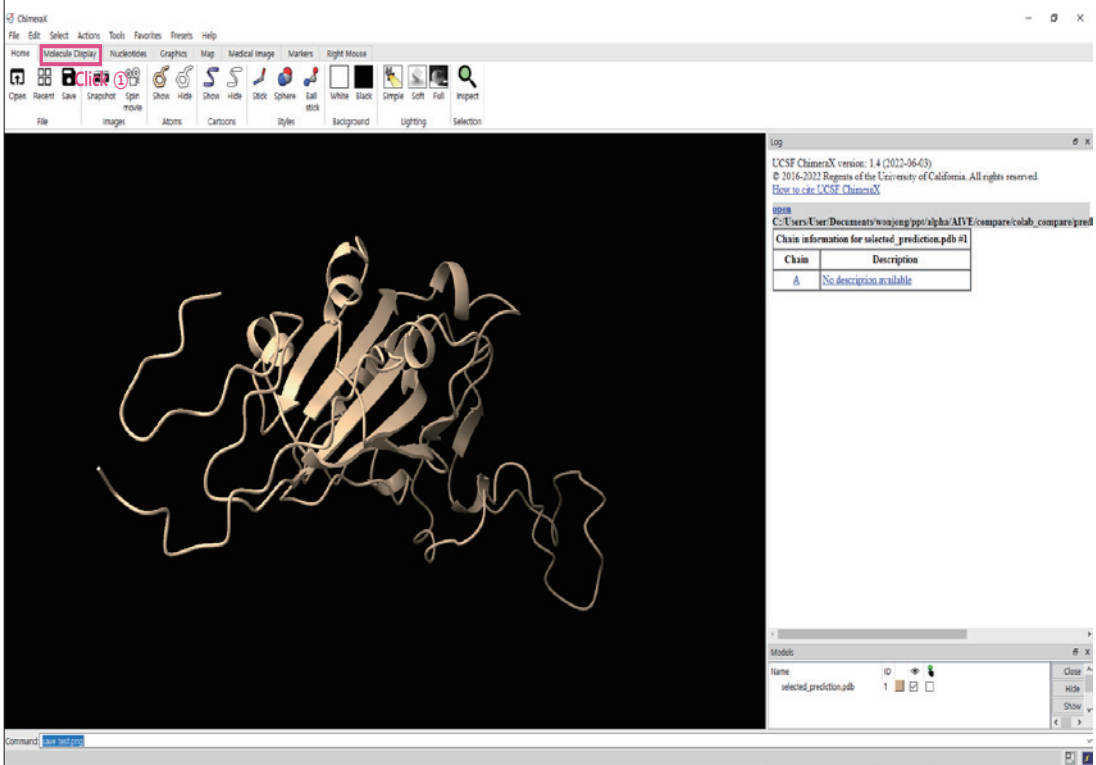
Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

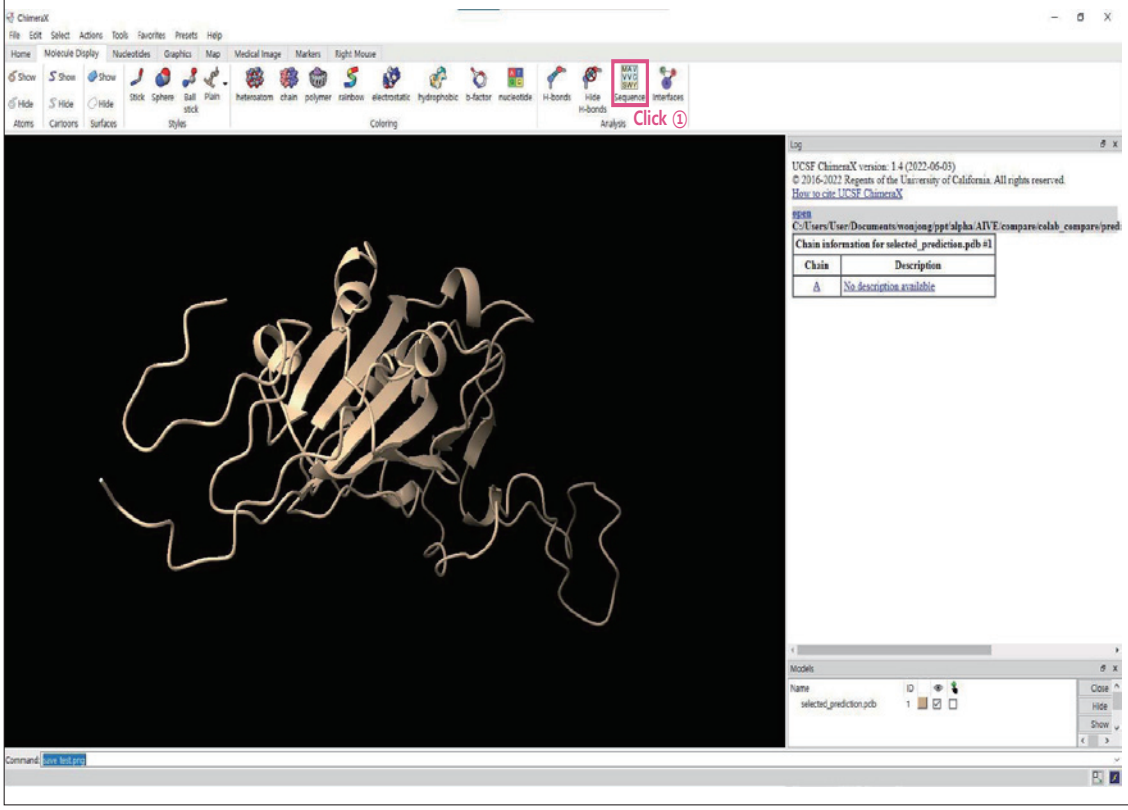
Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

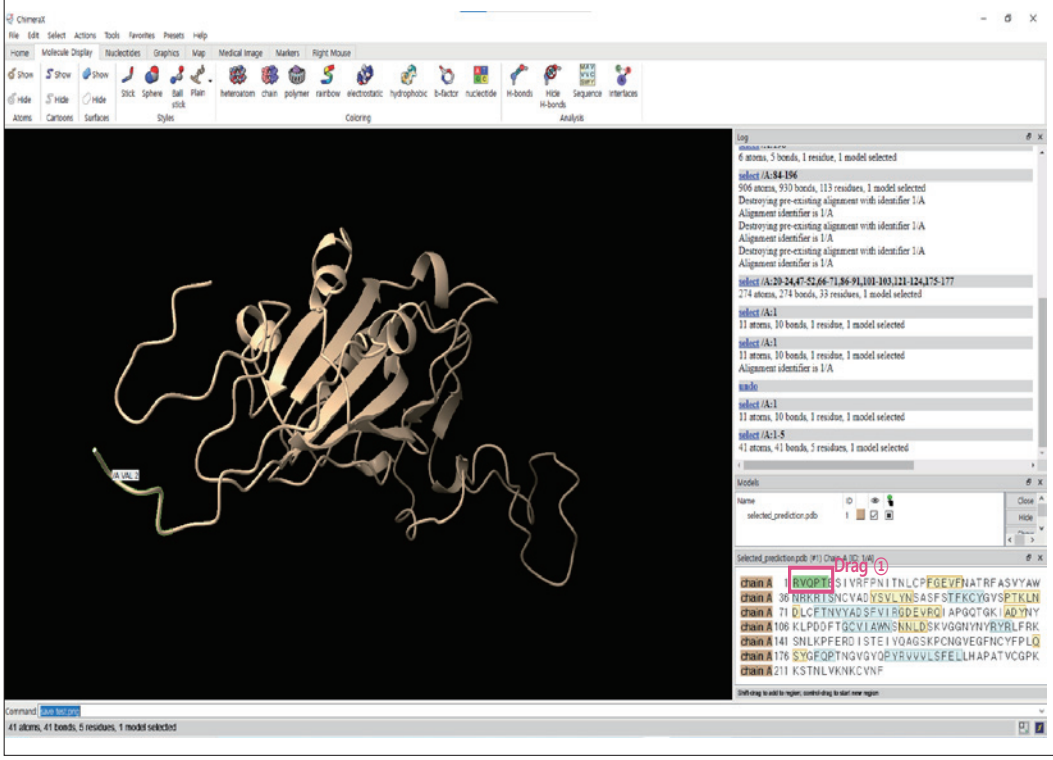
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – view 3D structure



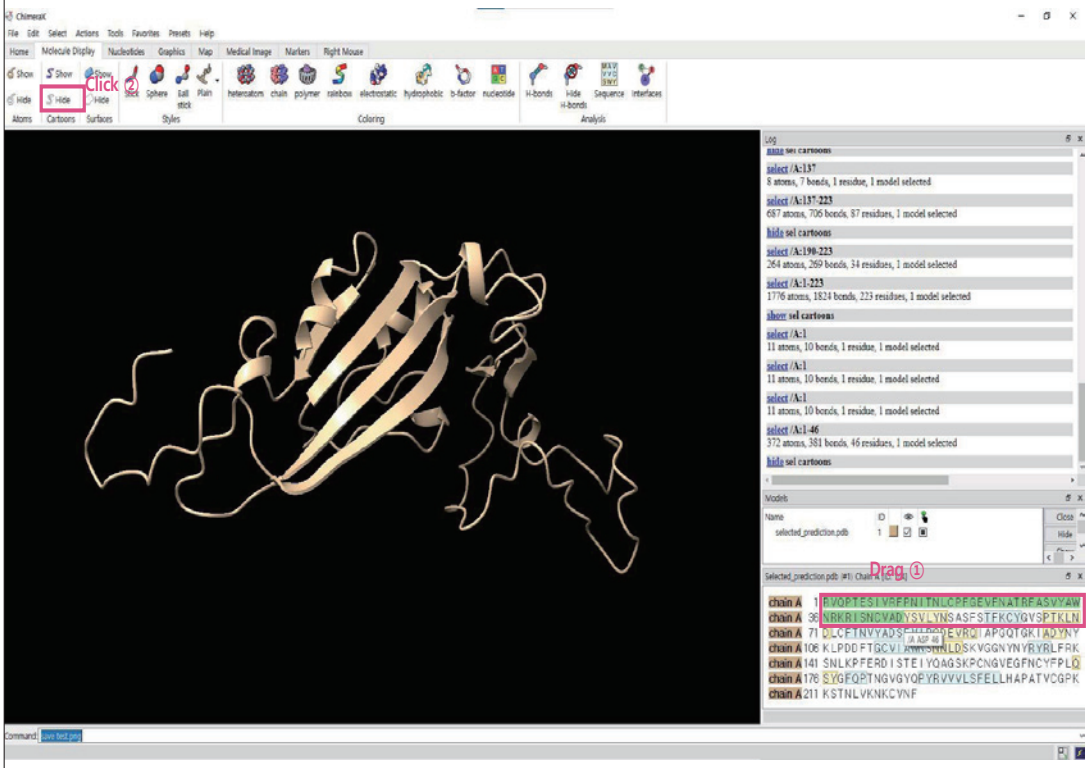
3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – view 3D structure



3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

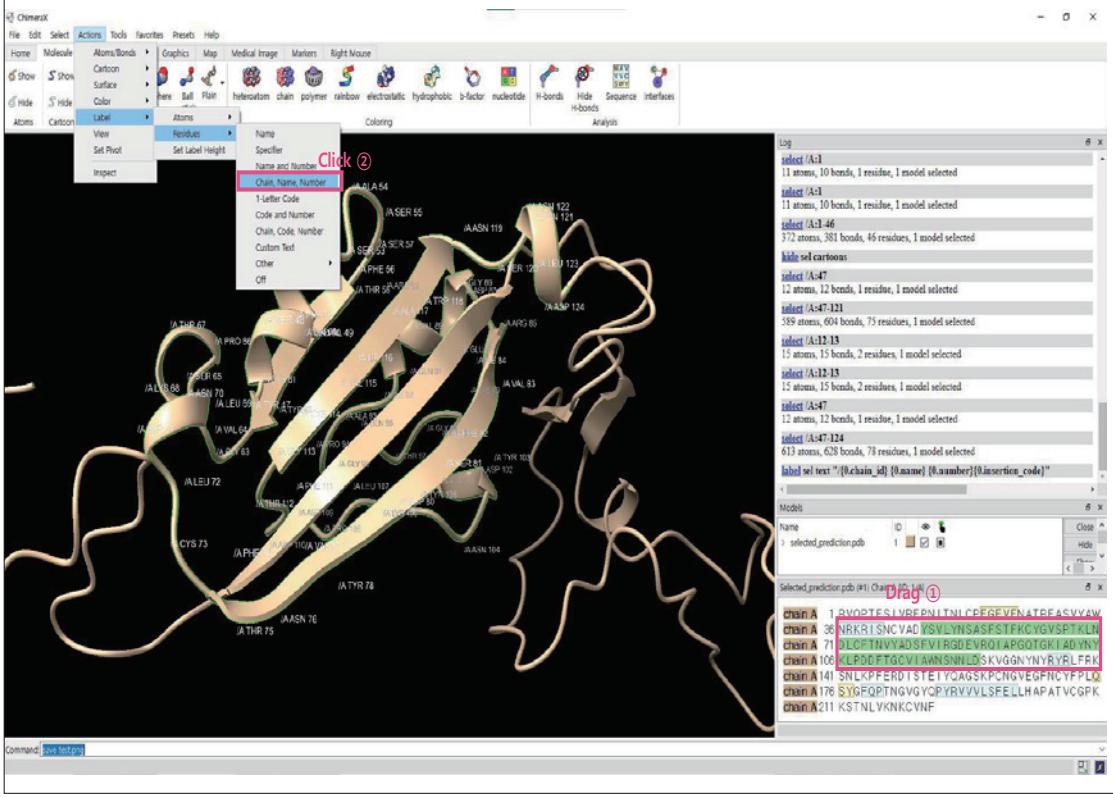
Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

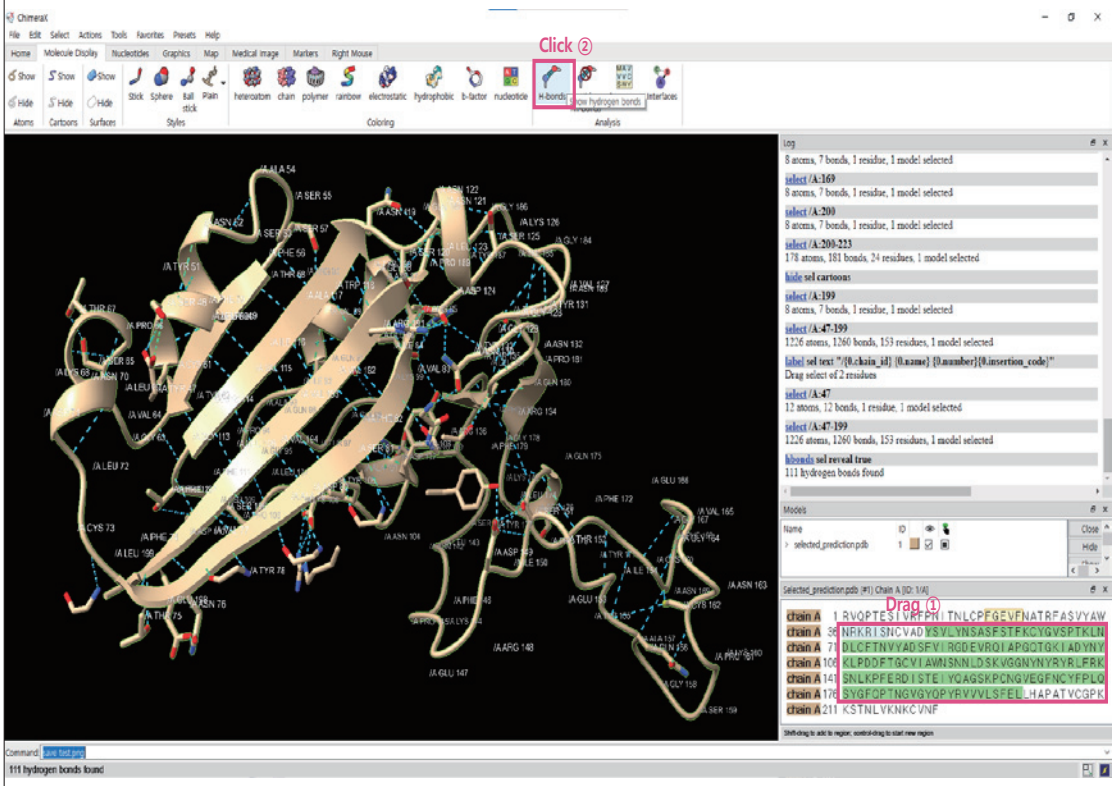
Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

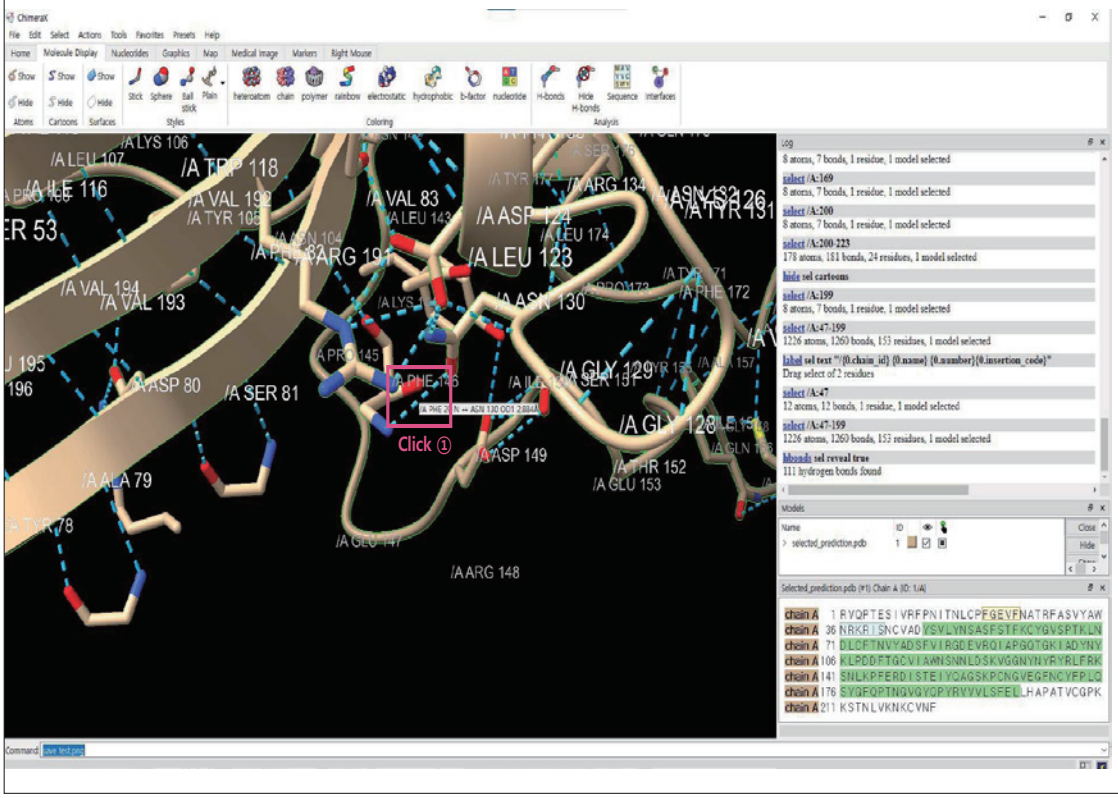
Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 AlphaFold를 이용한 SARS-CoV-2의 단백질 구조 예측

Get information from PDB & JSON file – view 3D structure



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

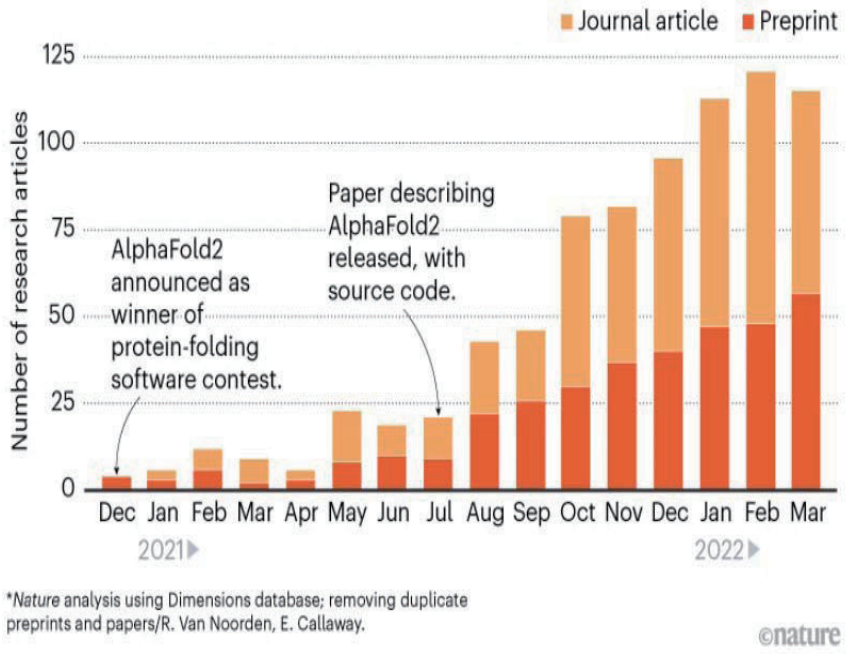
Contents

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

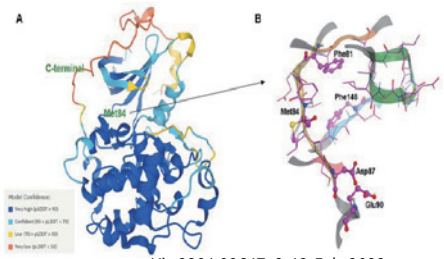
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

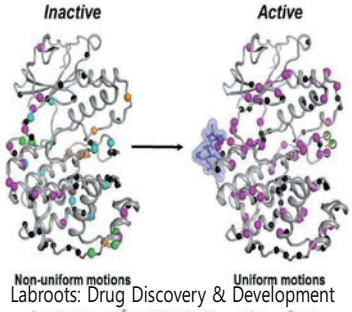


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

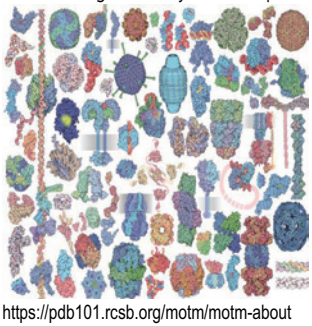


arXiv:2201.09647v2 13 Feb 2022



Labroots: Drug Discovery & Development

② Moving parts

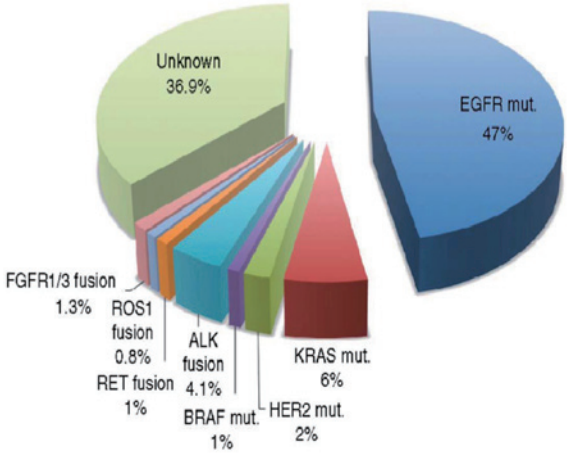


https://pdb101.rcsb.org/motm/motm-about

③ The longer wish list

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측



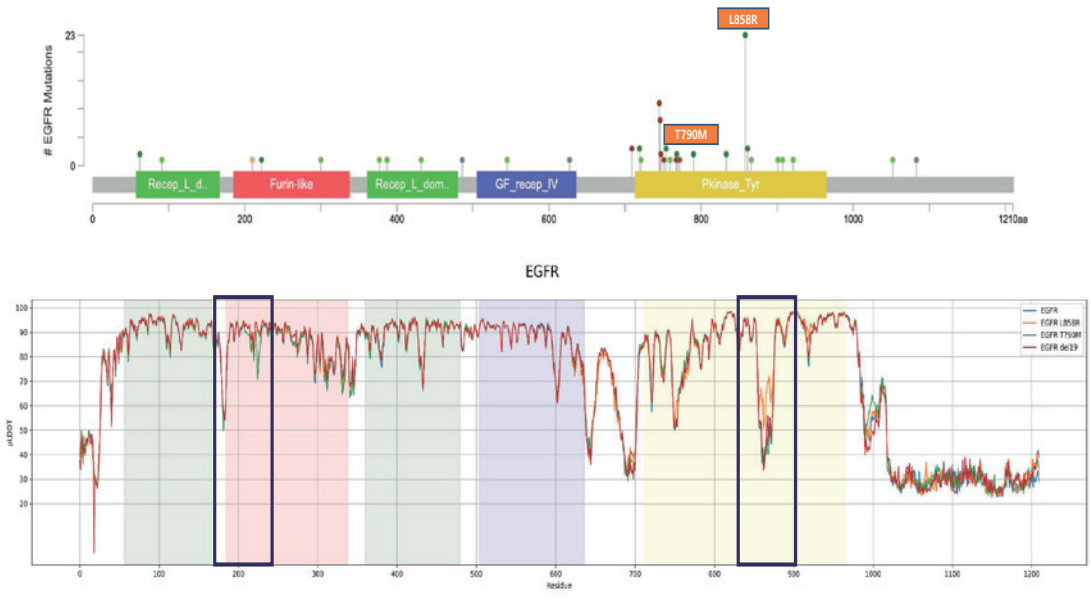
Cancer drugs

- Vemurafenib and trametinib
  BRAF V600E mutations in melanoma
- Erlotibin and osimertinib
  EGFR mutations in NSCLC; L858R, Del (19), T790M
- Pembrolizumab (immune checkpoint inhibitor): FDA approved
  SOLID tumors from any tissue type
  Mismatch repair deficiency (dMMR)
- Nivolumab, ipilimumab and atezolizumab
  High tumor mutation burden

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

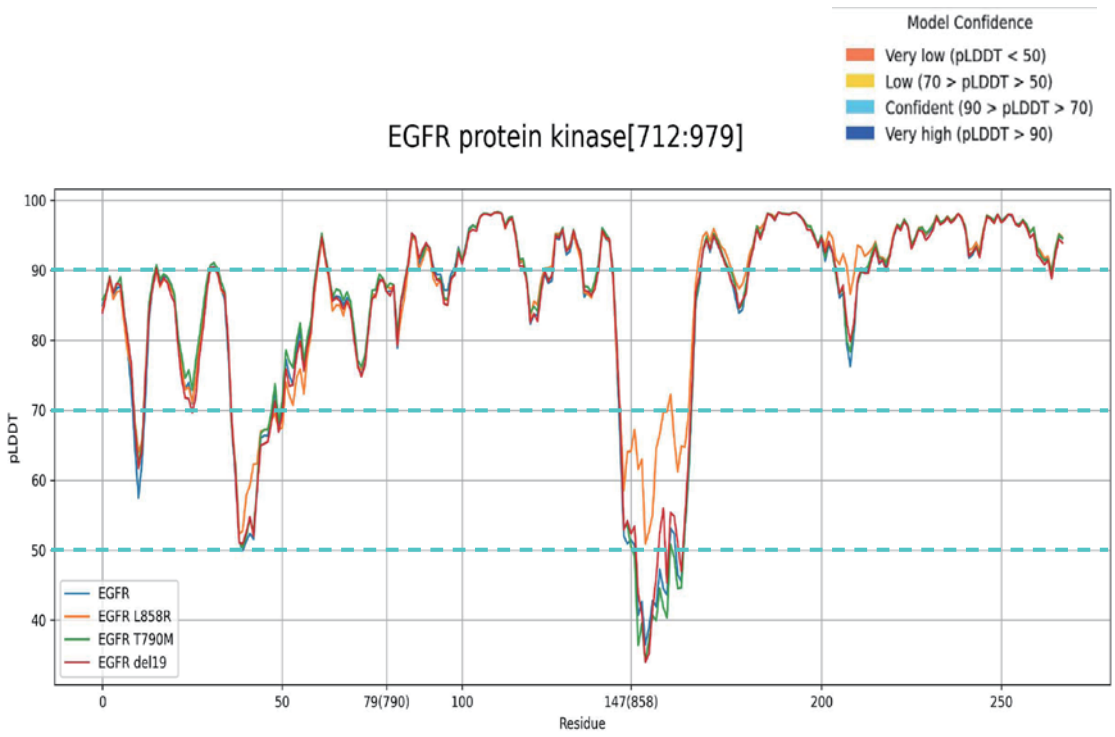
1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

Lung Adenocarcinoma
(TCGA, PanCancer Atlas, 566 patients; EGFR is altered in 12% of patients



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

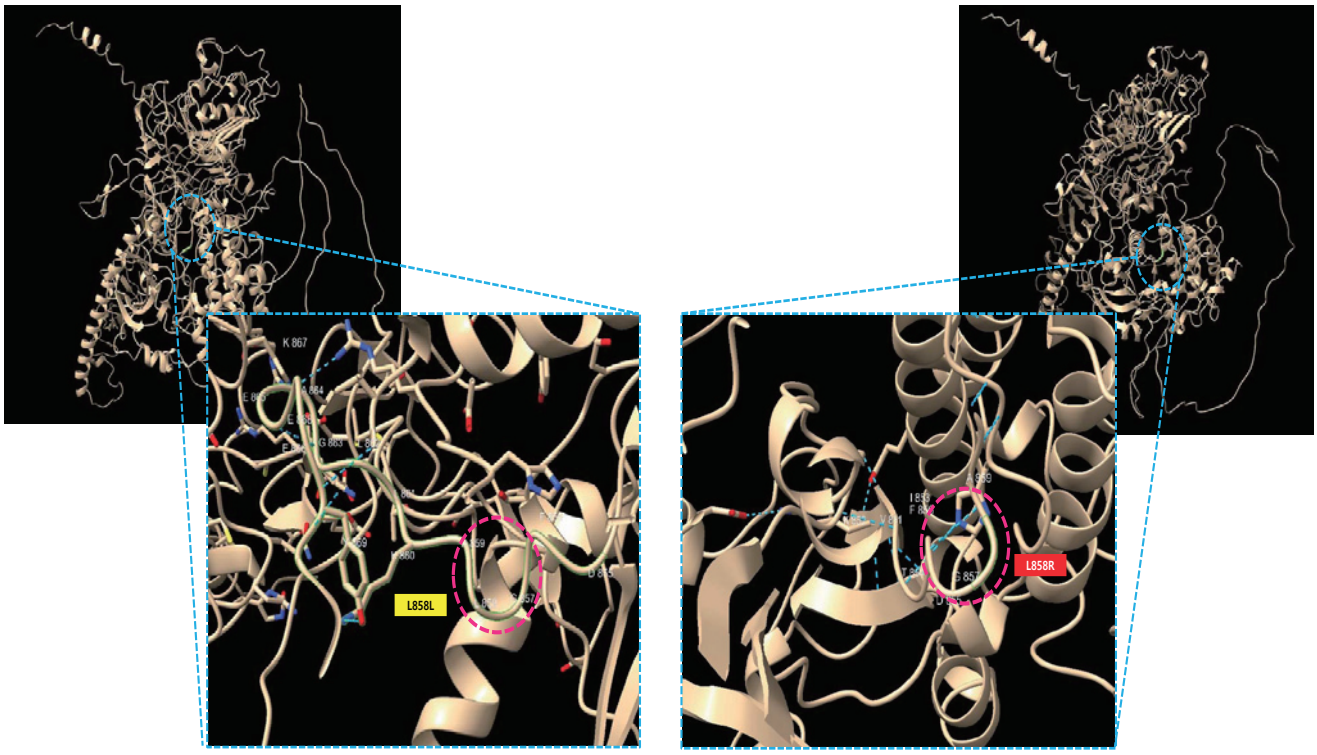


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

1 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

EGFR_Wild

EGFR_L858R



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 AlphaFold를 이용한 Protein- target 간의 상호작용의 친화도 측정 방법

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

Article | Open Access | Published: 10 March 2022

Improved prediction of protein-protein interactions using AlphaFold2

Patrick Bryant, Gabriele Pozzati & Arne Elofsson

Nature Communications **13**, Article number: 1265 (2022) | Cite this article

32k Accesses | **31** Citations | **48** Altmetric | Metrics

FoldDock

This repository contains the simultaneous folding and docking protocol **FoldDock**.

The protocol has been developed on 216 heterodimeric complexes from Dockground and tested on 1481 heterodimeric complexes extracted from the PDB.

The protocol uses the recently published state-of-the-art end-to-end protein structure predictor AlphaFold2 to predict the structure of heterodimeric complexes.
AlphaFold2 is available under the Apache License, Version 2.0 and so is FoldDock, which is a derivative thereof.
The AlphaFold2 parameters are made available under the terms of the CC BY 4.0 license and have not been modified.

You may not use these files except in compliance with the licenses.

The success rate of the final protocol is 63% on the test set. By analyzing the predicted interfaces, we are able to distinguish accurate models with an AUC of 0.94 on the test set. For more information on this pipeline and its performance see Improved prediction of protein-protein interactions using AlphaFold2 and extended multiple-sequence alignments

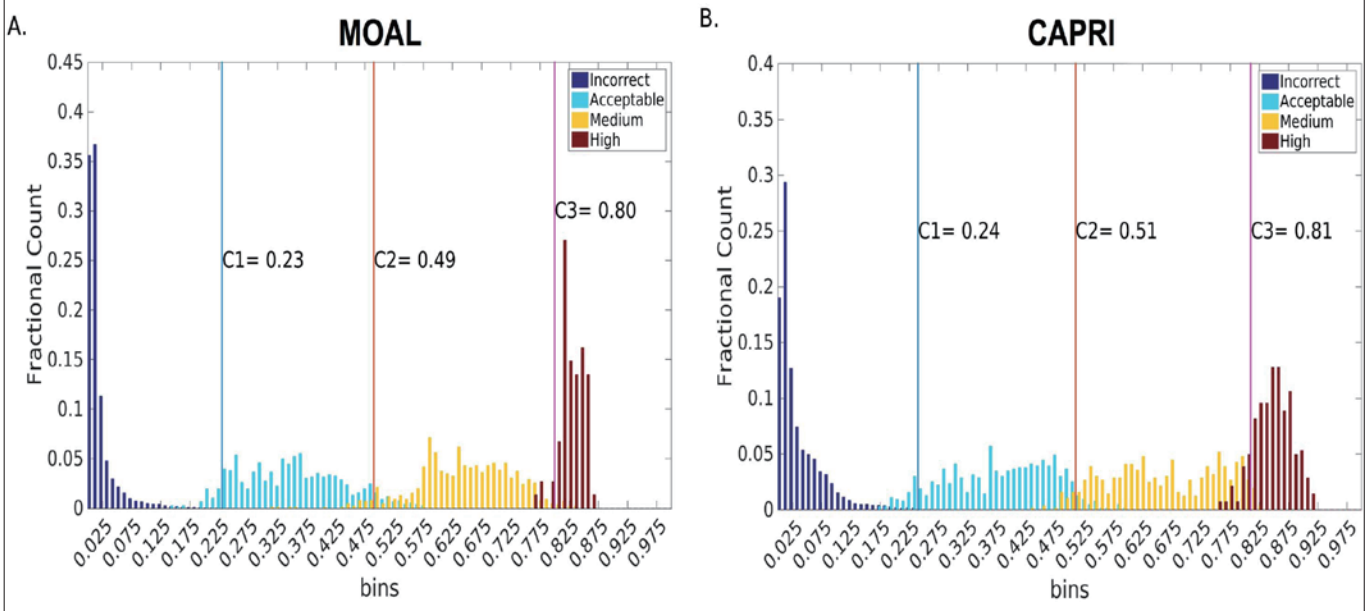
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측

```
[1]  !git clone https://gitlab.com/ElofssonLab/FoldDock.git

Cloning into 'FoldDock'...
remote: Enumerating objects: 30083, done.
remote: Counting objects: 100% (198/198), done.
remote: Compressing objects: 100% (190/190), done.
remote: Total 30083 (delta 89), reused 61 (delta 8), pack-reused 29885
Receiving objects: 100% (30083/30083), 2.94 GiB | 18.00 MiB/s, done.
Resolving deltas: 100% (5586/5586), done.
Checking out files: 100% (19182/19182), done.

!python3 /content/FoldDock/src/pdockq.py --pdbfile /content/selected_prediction.pdb

pDockQ = 0.154 for /content/selected_prediction.pdb
This corresponds to a PPV of at least 0.71391784
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

2 Cancer에서 AlphaFold를 이용한 protein 3차원 구조 예측



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3

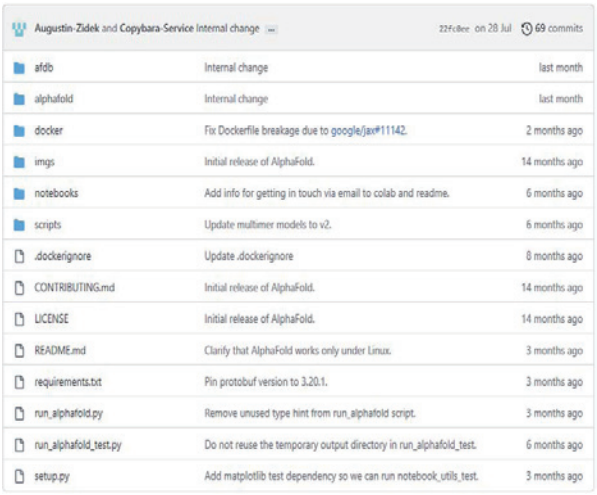
Local computer에서 AlphaFold 사용 방법

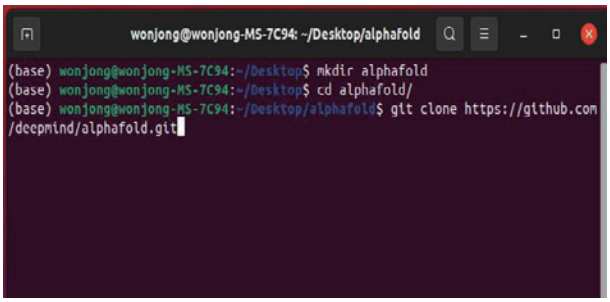
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Use alphafold in local PC – download alphafold

● Downloaded file list



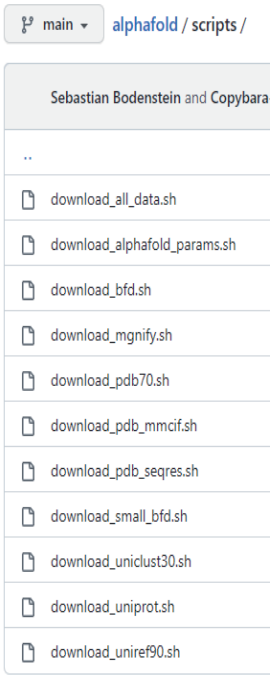


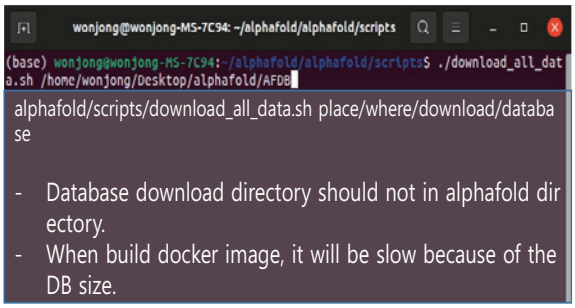
https://github.com/deepmind/alphafold

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Download alphafold Database





alphafold/scripts/download_all_data.sh place/where/download/database

- Database download directory should not in alphafold directory.
- When build docker image, it will be slow because of the DB size.

3 Local computer에서 AlphaFold 사용 방법

Install docker

#update advance packaging tool(apt) list
$ sudo apt update

#install apt-transport-https, ca-certificates, curl, gnupg, and lsb-release to setting docker repository
$ sudo apt install apt-transport-https ca-certificates curl gnupg lsb-release

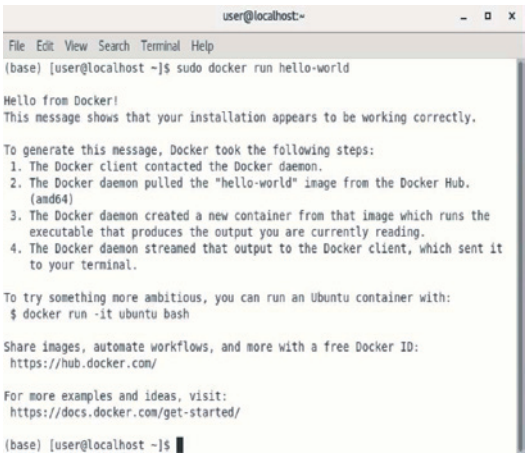
#generate docker GPG(GNU Privacy Guard) key
$ curl -fsSL https://download.docker.com/linux/ubuntu/gpg | sudo gpg --dearmor -o /usr/share/keyrings/docker-archive-keyring.gpg

#setting docker repository to install docker. Arch=amd64 or arm64 (users env)
$ echo "deb [arch=amd64 signed-by=/usr/share/keyrings/docker-archive-keyring.gpg]
https://download.docker.com/linux/ubuntu $(lsb_release -cs) stable" | sudo tee /etc/apt/sources.list.d/docker.list > /dev/null

#update apt list
$ sudo apt update

# install docker-ce, docker-ce-cli, and containerd.io
$ sudo apt install docker-ce docker-ce-cli containerd.io

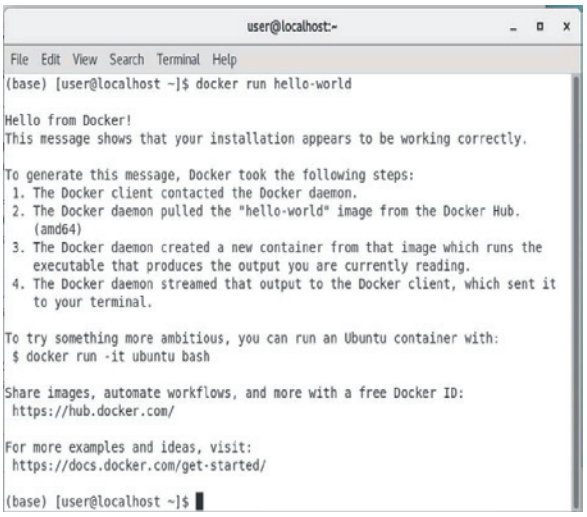
#test docker
$ sudo docker run hello-world



3 Local computer에서 AlphaFold 사용 방법

Install docker – add user

```
# add docker user group
$ sudo groupadd docker

#add user in docker user group
$ sudo usermod -aG docker $USERNAME

#update group infomation
$ newgrp docker

#test docker
$ docker run hello-world
```

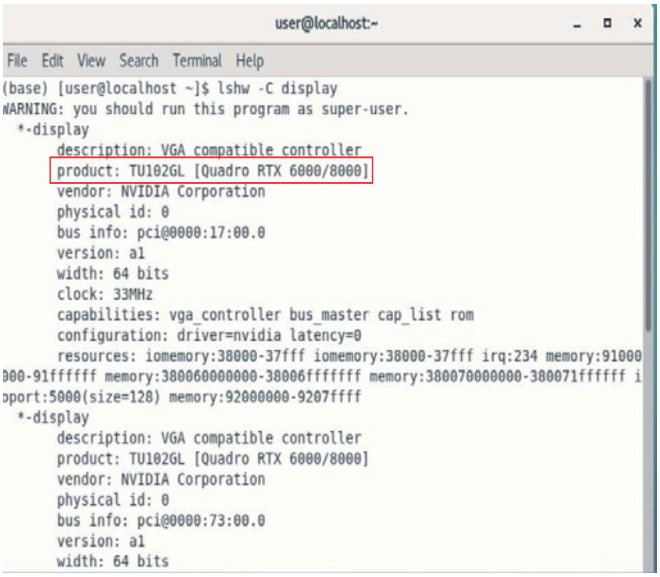


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Install GPU driver

```
#check PC GPU product
$ lshw –C display
```

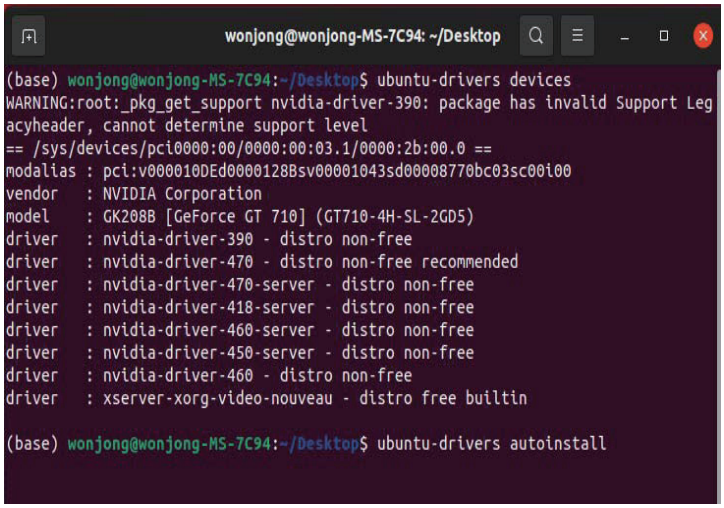


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Install GPU driver

#in ubuntu environment, ubuntu can check and auto install recommended GPU driver
$ ubuntu-drivers devices
$ ubuntu-drivers autoinstall

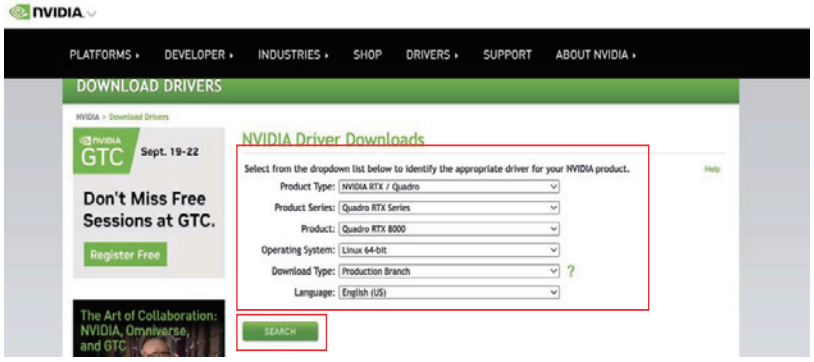


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

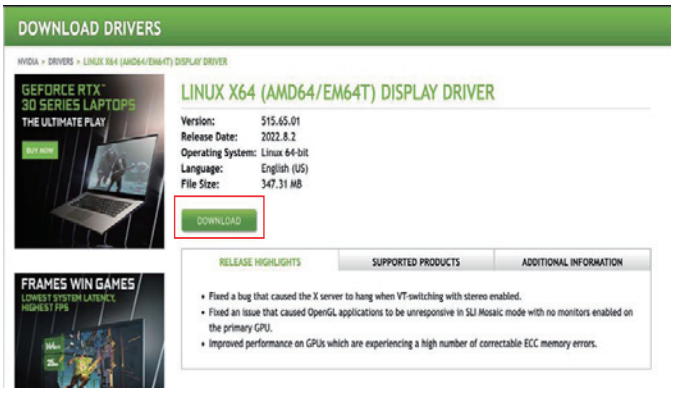
3 Local server에서 AlphaFold 사용 방법

Install GPU driver from nvidia driver download page

Step ①



Step ②



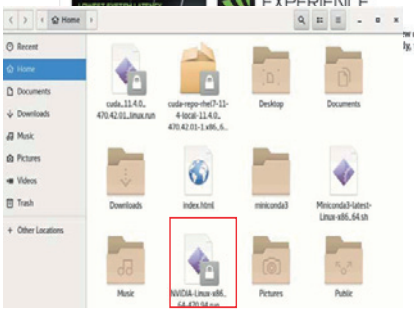
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Install GPU driver from nvidia driver download page

Step ③

Step ④



Step ⑤

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Install Nvidia container toolkit for using gpu in docker container

Install nvidia container toolkit

```
$ distribution=$(. /etc/os-release;echo $ID$VERSION_ID) && ₩
curl -s -L https://nvidia.github.io/nvidia-docker/gpgkey | sudo apt-key add - && ₩
curl -s -L https://nvidia.github.io/nvidia-docker/$distribution/nvidia-docker.list | sudo tee /etc/apt/sources.list.d/nvidia-docker.list
$ curl -s -L https://nvidia.github.io/nvidia-container-runtime/experimental/$distribution/nvidia-container-runtime.list | sudo tee /etc/apt/sources.list.d/nvidia-container-runtime.list
$ sudo apt update
$ sudo apt install -y nvidia-docker2
$ sudo service docker restart
$ docker run --rm --gpus all nvidia/cuda:11.1-base nvidia-smi
```

```
(base) [user@localhost ~]$ docker run --runtime=nvidia --rm nvidia/cuda:11.4.0-devel-centos8 nvidia-smi
Thu Sep  8 00:02:50 2022
+-----------------------------------------------------------------------------+
| NVIDIA-SMI 470.94       Driver Version: 470.94       CUDA Version: 11.4     |
|-------------------------------+----------------------+----------------------+
| GPU  Name        Persistence-M| Bus-Id        Disp.A | Volatile Uncorr. ECC |
| Fan  Temp  Perf  Pwr:Usage/Cap|         Memory-Usage | GPU-Util  Compute M. |
|                               |                      |               MIG M. |
|===============================+======================+======================|
|   0  Quadro RTX 8000     Off  | 00000000:17:00.0 Off |                  Off |
| 33%   34C    P8    20W / 260W |   3912MiB / 48601MiB |      0%      Default |
|                               |                      |                  N/A |
+-------------------------------+----------------------+----------------------+
|   1  Quadro RTX 8000     Off  | 00000000:73:00.0  On |                  Off |
| 33%   38C    P8    17W / 260W |    572MiB / 48592MiB |      5%      Default |
|                               |                      |                  N/A |
+-------------------------------+----------------------+----------------------+
|   2  Quadro RTX 8000     Off  | 00000000:A6:00.0 Off |                  Off |
| 33%   33C    P8     9W / 260W |   2120MiB / 48601MiB |      0%      Default |
|                               |                      |                  N/A |
+-------------------------------+----------------------+----------------------+

+-----------------------------------------------------------------------------+
| Processes:                                                                  |
|  GPU   GI   CI        PID   Type   Process name                  GPU Memory |
|        ID   ID                                                   Usage      |
|=============================================================================|
+-----------------------------------------------------------------------------+
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

Build docker image

Build docker image and install docker require packages

#docker build –f (use dockerfile) –t (docker image name)
$ docker build -f docker/Dockerfile -t alphafold .
#install requirement packages to use alpafold
$ pip3 install -r docker/requirements.txt
#check installed docker image
$ docker images


```
(base) [user@localhost docker]$ docker images
REPOSITORY    TAG                 IMAGE ID       CREATED
 SIZE
alphafold     latest              e8d8550291c8   13 hours ago
 12.6GB
```

3 Local computer에서 AlphaFold 사용 방법

Running alphafold in local pc

Running alphafold code

python3 /data/AF/alphafold/docker/run_docker.py
  --fasta_paths=input_fasta_path_path ₩
  --max_template_date=used_template_date ₩
  --model_preset=(monomer/monomer_tpm/multimer) ₩
  --num_multimer_predictions_per_model=num_of_seeds_per_model (only multimer, default = 5) ₩
  --data_dir=Database_path ₩
  --db_preset=reduced_dbs (if use reduced database) ₩
  --docker_user=0 ₩
  --gpu_devices=id_of_using_gpu ₩
  --output_dir=result_saved_path

-> result file = .pdb/.pkl file

3 Local computer에서 AlphaFold 사용 방법

Running alphafold in local pc

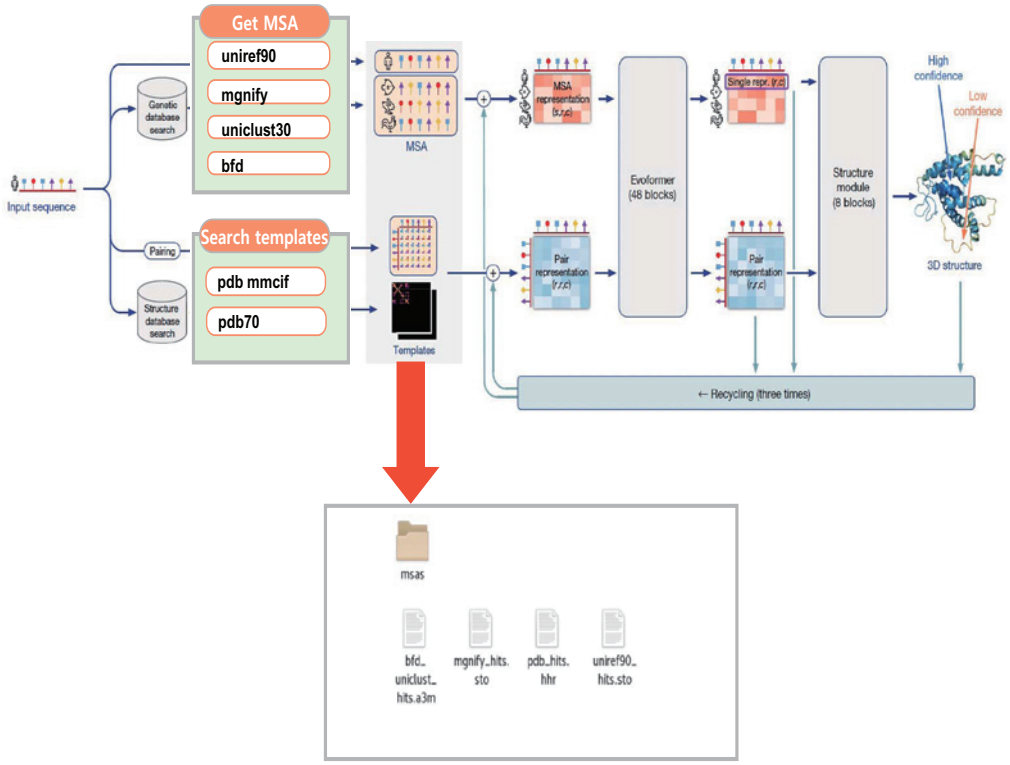
Input file : monomer seq fasta file & multimer seq fasta file

Example Monomer file
>sars-cov-2 ace2 receptor bind domain
NSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSKPCNGVEGFNCYFPLQSYGFQPTNGVGYQPY

Example Multimer file
> sars-cov-2 ace2 receptor bind domain
NSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSKPCNGVEGFNCYFPLQSYGFQPTNGVGYQPY
>sp|Q9BYF1|ACE2_HUMAN Angiotensin-converting enzyme 2
MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNYNTNITEENVQNMNNAGDKWSAFLKEQSTLA
QMYPLQEIQNLTVKL...

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

bfd_uniclust_hits.a3m

format of bfd_uniclust_hits.a3m

Input AA sequence

```
>sp|P00533|EGFR_HUMAN Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNMYYENSYALAVLSNYDANKTGLKELPMRNLQEILHGAVRFSNNPALCNVESIQWRDIVSSDFLSNM
SMDFQNHLGSCQKCDPSCPNGSCWGAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESDCLVCRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYVVTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFK
DSLSINATNIKHFKNCTSISGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKEITGFLLIQAWPENRTDLHAFENLEIIRGRTKQHGQFSLAVVSLNITSLGLRSLKEISDGDVIISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCKATGQVCHALCSPEGCWGPEPRDCVSCR
NVSRGRECVDKCNLLEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGVMGENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPTNGPKIPSIATGMVGALLLLLVVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPNQ
ALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREATSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVREHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQHVKITDFGLAKLLGAEEKEYHAEGGKVPIKW
MALESILHRIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVACIDRNGLQS
CPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA
```

MSA

```
>tr|A0A218UMP6|A0A218UMP6_9PASE Receptor protein-tyrosine kinase OS=Lonchura striata domestica OX=299123 GN=ERBB2 PE=3 SV=1
----------AAAEVCTGTDMKLLRPSSPESHYETLRHLYQGCQVVQGNLELTYLPADADTSFLKDIKEVQGYVLIAENQVSGLELQSLRIIRGTQLFQDRYALAVVGNAGpT-gTPGLRQLGMRHLTEILKGGVRIERNPELCFQETILWSDILH----
RQNEFRAEiqvesarsrsc------PDCRALCAEGHCWGEGKQDCQTLTNSICH-GC-
PRCKGTKPTDCCHEQCAAGCTGPKHSDCLACLNFNRSGICELHCPPLVVYNSDTFESMPNPDGRYTFGASCVSQCPYNYLATEVGSCTLVCPQNSQEVTVNNVQKCEKCSKPCPEVCYGLGVDFLKGVRAVNASNIQHFSGCTKIFGSLAFLPETFAGDPSTNTPPLDPKLLRIF
ESLEELTGFLYIAAWPPDMKDLGVFQNLRVIRGRVLHNGAYSLTLREI-
AVQALGLRALQEISSGMVLVHHNPQLCFLQKVPWHSIFRNPRQRLFQTHNKPPEQCESEGLVCFHLCAQGHCWGPGPTQCVACERFLRGQECVASCNLLDGAVREHANGTRCLPCHPECQPQngt---
ETCFGSDPDQCVACAHYKDAQQCVRRCPSGVKADAsFVPVWKYPDEFGVCQLCPTNCTHSCTIRDEDGCPVDQkpSQVTSIIAGVVGALLVIVLLIIVICVKRRRQQERKHTMRRLLQETELVEPLTPSGALPNQAQMRILKETELKKVKVLGSGAFGTVYKGIWIPDGESVKIPV
AIKVLRENTSPKANKEILDEAYVMAGVGSPYVSRLLGICLTSTVQLVTQLMPYGCLLDYVRENKDRIGSQDLLNWCVQIAKGMSYLEEVRLVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFTHQSDVWSYGVTVWELMTFGAKPYDG
IPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWMIDSECRPKFRELVTEFSRMARDPQRFVVIQNDLVGLPGS-MDSTFYRALLDEEDMDDLVDAEEYLVPHHGFFSTDTSTTYRSRISSMRSTAEsPaKVE-egeglaafsfpaqglaegpegpvpevpdgdkVA--LQSPP-
GREPGTLPRYSEDPTGLTA-kdgedpecFTVPAPHSAMPEYVNQAGE---RPPRAPPSPPDKPKGHQgknglIKDPKNSFPGPFghA--VENPEYLAPHGA--P----------APFSQAFDNPYYWNQDPAK--aggPEGGPGTTPTAENPEYLGLAGPDTTAV--
>tr|A0A0F7Z597|A0A0F7Z597_CROAD Receptor protein-tyrosine kinase OS=Crotalus adamanteus OX=8729 PE=2 SV=1
----------STTEVCTGTDMKLQQPSSPENHPDTLRRLYEYCQVVQGNLEITYLPADVDTSFLKDIREVQGYVLIAKNHMHHLHLNSLLIIRGTQLYEEKYALAVLDNADsS-gDVGLQELGMLKLTEILKGSVIIERNPQLCFQETIHWEAIFHKYNW-----
QKYteissrrrnc------PDCSQICPHnNHCWGEAKGSCQILTSTICASSC-
PRCKGGHPTDCCHEQCAAGCTGPKHSDCLACLHFNHSGICELHCPPLMNYNPDTFEIMHNPNGRYTFGASCVPHCPYNYLAAEVGSCTLVCPQNSQEVSIGAMQKCEKCDSSCPEVCYGLGMDFLKGVRAVNASNIHHFTGCTKIFGSLAFLKETFAGDPATNTPPLQLEQLE
VFVHLKDLTGFLYIESWPETLLDLSPFQNLQVIRGRALYNGAYSLMLQNI-
NISSLGLRSLQEISSGMVLIHHNPNLCFIQNVPWDDIFRNPRQKLFHNDNNSPEQCDLQGQVCYSLCSQGHCWGPGKSQCVSCSGFLRGKECIENCNVLDGDIREYVNGTHCFPCHPECMPQngt---
ESCYGSEADQCIACAHYKDGLSCVERCPSGVKLDGsFIPVWKYPDEDNVCQLCPVNCTLSCALRDEFGCPVDQkpSHASSIIAGVVSAALALLLLLTVICINRRKQQERKHTMRRLLQETELVEPLTPSGALPNQAQMRILKETELKKVKVLGSGAFGTVYKGVWIPDGENVKIPVA
IKVLRENTSPKANKEILDEAYVMAGVGSPYVSRLLGICLTSTVQLVTQLMPYGCLLDYVRENKDRIGSQDLLNWCVQIAKGMSYLEDVRLVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFTHQSDVWSYGVTVWELMTFGAKPYDGI
PAREIPDLLEKGERLPQPPICTIDVYMIMVKCWMIDSECRPKFRELVTEFTRMARDPQRFVVIQNDEKMGLASPIDSTFYRTLLEEEDMQDLVDAEEYLVPHQGFFSGETSADYRSRISSTRNAIEtQmDAG-
eteespqypylgpslseesesitsdlreedyTASKaVQNSAPLQaPDCSLQRYSEDPTSASLNekenpdnksYTTPLTLAVPEYINQPENNL-ppnKNLRLQGSTLEKQKRHMgkngliKEPKNAFYTSFtsA--VENPEYLTPCSVPAS----------
SPLPQAFDNLYYWNQENPKCNpaeffatsivppaATNGFPPTPTAENLEYLGLSEPVTCSKDF
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

bfd_uniclust_hits.a3m

bfd_uniclust_hits.a3m의 format

>**db**|UniqueIdentifier|EntryName ProteinName **OS**=OrganismName **OX**=OrganismIdentifier [**GN**=GeneName]**PE**=ProteinExistence **SV**=SequenceVersion

db : sp = UniProtKB/Swiss-Prot | tr = UniProtKB/TrEMBL
UniqueIdentifier : uniprot ID /accession number
EntryName ProteinName : entry name of the UniProtKB entry
OS : scientific name of the organism of the UniProtKB entry(생물명)
OX : unique identifier of the source organism, assigned by the NCBI(생물 식별번호)
GN : gene name

PE : numerical value describing the evidence for the existence of the protein [1:5]
1. Experimental evidence at protein level : The value 'Experimental evidence at protein level' indicates that there is clear experimental evidence for the existence of the protein. The criteria include partial or complete Edman sequencing, clear identification by mass spectrometry, X-ray or NMR structure, good quality protein-protein interaction or detection of the protein by antibodies.
2. Experimental evidence at transcript level : The value 'Experimental evidence at transcript level' indicates that the existence of a protein has not been strictly proven but that expression data (such as existence of cDNA(s), RT-PCR or Northern blots) indicate the existence of a transcript.
3. Protein inferred from homology : The value 'Protein inferred by homology' indicates that the existence of a protein is probable because clear orthologs exist in closely related species.
4. Protein predicted : The value 'Protein predicted' is used for entries without evidence at protein, transcript, or homology levels.
5. Protein uncertain : The value 'Protein uncertain' indicates that the existence of the protein is unsure.

SV : sequence version

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

mgnify_hits.sto


```
# STOCKHOLM 1.0

#=GS sp|P00533|EGFR_HUMAN       DE Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
#=GS MGYP000983186742/226-829   DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
#=GS MGYP000983186742/1016-1366 DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
#=GS MGYP001020618282/199-789   DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
                                                                                .
                                                                                .
                                                                                .
                                                                                .
                                                                                .
sp|P00533|EGFR_HUMAN          MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGT-FEDHFLSLQRMFNNCEVVLGNLEITYVQ-----R-----N------Y----DLSF-LKT-------IQEVAGY-VLI-ALNTVE--RIP--LENLQIIRG-NMYY------E-----N---SYAL
MGYP000983186742/226-829      ----------------------------LEKICIGTSNRMSGQHN-KTDHYQNLAERYRNCTYVIGNLEITWLD-----KAASGEQ-----V----DLSF-LES-------IREITGY-LLI-AYVEVE--RIR--MPNLQIIRG-RDLF------K----LN---SDQKEEF---AL
MGYP000983186742/1016-1366    ----------------------------------------------------------------------------------------------------------------------------------------------------
MGYP001020618282/199-789      ----------------------------EKICIGTANRMSGQHN-KTDHYQNLAERYRNCTYVIGNLEITWLE-----K------GPDNKPV----DLTF-LES-------IREITGY-LLI-AYVEVE--KIR--MPNLQIIRG-RDLF------R----LN---NGQKEEF---AI
MGYP001020618282/983-1329     ----------------------------------------------------------------------------------------------------------------------------------------------------
```

uniref90_hits.sto


```
# STOCKHOLM 1.0

#=GS sp|P00533|EGFR_HUMAN          DE Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
#=GS UniRef90_P00533/1-1210        DE [subseq from] Epidermal growth factor receptor n=96 Tax=Boreoeutheria TaxID=1437010 RepID=EGFR_HUMAN
#=GS UniRef90_A0A2I3GX32/20-1206   DE [subseq from] Receptor protein-tyrosine kinase n=3 Tax=Nomascus leucogenys TaxID=61853 RepID=A0A2I3GX32_NOMLE
#=GS UniRef90_A0A2R9CTL6/11-1201   DE [subseq from] Receptor protein-tyrosine kinase n=4 Tax=Pan TaxID=9596 RepID=A0A2R9CTL6_PANPA
                                                                                .
                                                                                .
                                                                                .
                                                                                .
                                                                                .
sp|P00533|EGFR_HUMAN          MRPSG-TAG-A-A-L-L----A-L--L----A--A--L----C---P--A----S-------R---A-----L----E----E---K--K--V-CQG---T--S--N-K----L-T-Q---L---G--TF--E--D--HFLS-L--Q------R-MF-N---NCEVVL----G--NLEI
UniRef90_P00533/1-1210        MRPSG-TAG-A-A-L-L----A-L--L----A--A--L----C---P--A----S-------R---A-----L----E----E---K--K--V-CQG---T--S--N-K----L-T-Q---L---G--TF--E--D--HFLS-L--Q------R-MF-N---NCEVVL----G--NLEI-
UniRef90_A0A2I3GX32/20-1206   ----------------------------------------------------------------------------P--V-CQG---T--S--N-K----L-T-Q---L---G--TF--E--D--HFLS-L--Q------R-MF-N---NCEVVL----G--NLEI-------T--
UniRef90_A0A2R9CTL6/11-1201   --------------L-L----S-Q--I----S--L--L----C---P--L----V-------R---I-----------------------F-CQG---T--S--N-K----L-T-Q---L---G--TF--E--D--HFLS-L--Q------R-MF-N---NCEVVL----G--NLEI-------
UniRef90_A0A8B7H412/1-1208    MRPSG-TAA-A-A-L-L----V-L--L----A--A--L----V---Q--A----S-------R---A-----L----E----E---K--K--V-CQG---T--S--N-K----L-T-Q---L---G--TF--E--D--HFLS-L--Q------R-MF-N---NCEVVL----G--NL
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

mgnify_hits.sto의 format


```
# STOCKHOLM 1.0

#=GS sp|P00533|EGFR_HUMAN       DE Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
#=GS MGYP000983186742/226-829   DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
#=GS MGYP000983186742/1016-1366 DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
#=GS MGYP001020618282/199-789   DE [subseq from] PL=00 UP=0 BIOMES=0000000100000
```

uniref90_hits.sto의 format


```
# STOCKHOLM 1.0

#=GS sp|P00533|EGFR_HUMAN          DE Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
#=GS UniRef90_P00533/1-1210        DE [subseq from] Epidermal growth factor receptor n=96 Tax=Boreoeutheria TaxID=1437010 RepID=EGFR_HUMAN
#=GS UniRef90_A0A2I3GX32/20-1206   DE [subseq from] Receptor protein-tyrosine kinase n=3 Tax=Nomascus leucogenys TaxID=61853 RepID=A0A2I3GX32_NOMLE
#=GS UniRef90_A0A2R9CTL6/11-1201   DE [subseq from] Receptor protein-tyrosine kinase n=4 Tax=Pan TaxID=9596 RepID=A0A2R9CTL6_PANPA
```

#=GS : Metadata make-up line. Data relating to a specific sequence in the multiple sequence alignment. Starts with #=GS followed by the sequence name followed by a feature name and data relating to the feature. Typically comes after GF metadata in a Stockholm file.
taxId : NCBI taxonomy ID currently attached to the AnnotationDb objects database.

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

pdb_hits.hhr

pdb_hits.
hhr

```
Query         sp|P00533|EGFR_HUMAN Epidermal growth factor receptor OS=Homo sapiens OX=9606 GN=EGFR PE=1 SV=2
Match_columns 1210
No_of_seqs    605 out of 8826
Neff          6.32692
Searched_HMMs 80799
Date          Wed Oct 26 16:16:13 2022
Command       /usr/bin/hhsearch -i /tmp/tmp0pc346f3/query.a3m -o /tmp/tmp0pc346f3/output.hhr -maxseq 1000000 -d /mnt/pdb70_database_path/pdb70

 No Hit                             Prob E-value P-value  Score    SS Cols Query HMM  Template HMM
  1 3QWQ_A Epidermal growth factor 100.0   8E-93 9.9E-98  888.9   0.0  641    1-641     1-641 (648)
  2 5MY6_A Receptor tyrosine-prote 100.0 2.9E-87 3.6E-92  834.9   0.0  608   29-637     1-620 (622)
  3 6JK8_A Insulin-like growth fac 100.0 1.1E-86 1.4E-91  894.3   0.0  876   53-974    47-1272(1367)
  4 1MOX_B Epidermal Growth Factor 100.0 2.2E-85 2.7E-90  798.5   0.0  500   26-525     2-501 (501)
  5 6PXV_A Insulin receptor (E.C.2 100.0   3E-85 3.7E-90  881.5   0.0  906   27-975     4-1258(1354)
  6 3P11_A Fab DL11 heavy chain, F 100.0 3.3E-85   4E-90  800.9   0.0  507   25-538     4-513 (522)

No 1
>3QWQ_A Epidermal growth factor receptor (E.C.2.7.10.1); CELL SURFACE RECEPTOR, TYROSINE KINASE; HET: BMA, FUC, MAN, NAG; 2.75A {Homo sapiens}
Probab=100.00  E-value=8e-93  Score=888.93  Aligned_cols=641  Identities=100%  Similarity=1.644  Sum_probs=547.3  Template_Neff=9.000

Q sp|P00533|EGFR    1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (1210)
Q Consensus         1 ~~~~~~~~~~~|~||~~~~~~~~~~~~~~~vC~Gt~~~|~~~~~~~~~y~~|~~~y~nCtvV~GnLeIt~|~~~~dlsFl~   80 (1210)
                      |||+.+++|++|++++++.....+.+||.|++++++.+++++|+.++++|+||++|.|+|+|+.+...++++|+
T Consensus         1 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~C~g~~~~~~~~~~~~~~~~~~~~~Ct~|~G~|~|~~~~~~~~~~|~   80 (648)
T 3QWQ_A            1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (648)
T ss_dssp           ------------------------CCCCEEECCBCCTTCEEESSHHHHHHHHHHHHHTTCSEESSBEEEECCCTTCCCGGGG
T ss_pred           CCCcHHHHHHHHHHHHHHchhccccccCceeeccCCCcccCCChHHHHHHHHHHHhCCCCEEeCCEEEEEeecCCCCchhhc
Confidence          899999999999999999999999999999999999999999999999999999999999999999999887778899999
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

pdb_hits.hhr 의 format ①

No Hit	Prob	E-value	P-value	Score	SS	Cols	Query HMM	Template HMM

No: the index of the datbase match.

Hit: the first 30 characters of the name line.

Prob: the Probability of template to be a true positive. For the probability of being a true positive, the secondary structure score in column SS is taken into account, together with the r aw score in column Score. True positives are defined to be either globally homologous or they are at least homologous in parts, and thereby locally similar in structure.

E-value: The E-value gives the average number of false positives ('wrong hits') with a score better than the one for the template when scanning the database. It is a measure of reliabilit y: E-values near to 0 signify a very reliable hit, an E-value of 10 means about 10 wrong hits are expected to be found in the database with a score at least this good. Note that E-value and P-value are calculated without taking the secondary structure into account!

P-value: The P-value is the E-value divided by the number of sequences in the database. It is the probability that in a pairwise comparison a wrong hit will score at least this good.

Score: the raw score is computed by the Viterbi HMM-HMM alignment excluding the secondary structure score. It is the sum of similarities of the aligned profile columns minus the pos ition-specific gap penalties in bits. The column similarity score is the log-sum-of-odds score (base 2). The gap penalties are the log2 of the state transition probabilities, e.g. from match state to insert or delete to match state.

SS: the secondary structure score. This score tells you how well the PSIPRED-predicted (3-state) or actual DSSP-determined (8-state) secondary structure sequences agree with each othe r. PSIPRED confidence values are used in the scoring, low confidences getting less statistical weight.

Cols: the number of aligned Match columns in the HMM-HMM alignment.

Query HMM: the range of aligned match states from the query HMM.

Template HMM: the range of aligned match states from the database/template HMM and, in parenthesis, the number of match states in the database HMM.

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

```
No 1
>3QWQ_A Epidermal growth factor receptor (E.C.2.7.10.1); CELL SURFACE RECEPTOR, TYROSINE KINASE; HET: BMA, FUC, MAN, NAG; 2.75A {Homo sapiens}  ①
Probab=100.00  E-value=8e-93  Score=888.93  Aligned_cols=641  Identities=100%  Similarity=1.644  Sum_probs=547.3  Template_Neff=9.000  ②

Q sp|P00533|EGFR    1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (1210)
Q Consensus         1 ~~~~~~~~~~~|~||~~~~~~~~~~~~~~~vC~Gt~~~|~~~~~~~~~y~~|~~~y~nCtvV~GnLeIt~i~~~~dlsFl~   80 (1210)
                      |||.|.+++|+|++|++++++.....+.+||.|++++++.+++++++|+.++++|+||++|.|+|+|+.+....++++|+
T Consensus         1 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~C~g~~~~~~~~~~~~~~~~~~~Ct~i~G~|~i~~~~~~~~~~|~   80 (648)
T 3QWQ_A            1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (648)
T ss_dssp           ------------------------CCCCEECCBCCTTCEESSHHHHHHHHHHHHHTTCSEESSBEEEECCCTTCCCGGGG
T ss_pred           CCCcHHHHHHHHHHHHHHchhccccccCceeeccCCCcccCCChHHHHHHHHHHHhCCCCEEeCCEEEEeecCCCCchhhc
Confidence           899999999999999999999999999999999999999999999999999999999999999999999887778899999
```

① The first line, which begins with with a >, contains the name and description line of the template/database HMM. (We use "template HMM" and "matched database HMM" synonymously.)

② The next line summarizes the main statistics for the alignment: The probability for the query and template HMMs to be homologous (Probab)

③ The Sum_probs value is the sum over the posterior probabilities of all aligned pairs of match states. These probabilities are calculated by the Forward-Backward algorithm.

- Dssp : method for assigning secondary structure to the amino acids of a protein, given the atomic-resolution coordinates of the protein.

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

```
No 1
>3QWQ_A Epidermal growth factor receptor (E.C.2.7.10.1); CELL SURFACE RECEPTOR, TYROSINE KINASE; HET: BMA, FUC, MAN, NAG; 2.75A {Homo sapiens}
Probab=100.00  E-value=8e-93  Score=888.93  Aligned_cols=641  Identities=100%  Similarity=1.644  Sum_probs=547.3  Template_Neff=9.000

Q sp|P00533|EGFR    1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (1210)
Q Consensus         1 ~~~~~~~~~~~|~||~~~~~~~~~~~~~~~vC~Gt~~~|~~~~~~~~~y~~|~~~y~nCtvV~GnLeIt~i~~~~dlsFl~   80 (1210)
                      |||.|.+++|+|++|++++++.....+.+||.|++++++.+++++++|+.++++|+||++|.|+|+|+.+....++++|+
T Consensus         1 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~C~g~~~~~~~~~~~~~~~~~~~Ct~i~G~|~i~~~~~~~~~~|~   80 (648)
T 3QWQ_A            1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (648)
T ss_dssp           ------------------------CCCCEECCBCCTTCEESSHHHHHHHHHHHHHTTCSEESSBEEEECCCTTCCCGGGG
T ss_pred           CCCcHHHHHHHHHHHHHHchhccccccCceeeccCCCcccCCChHHHHHHHHHHHhCCCCEEeCCEEEEeecCCCCchhhc
Confidence           899999999999999999999999999999999999999999999999999999999999999999999887778899999
```

The line in the middle shows the column score between the query and template amino acid distributions. It gives a valuable indication for the alignment quality.

```
= : column score below -1.5
- : column score between -1.5 and -0.5
. : column score between -0.5 and +0.5
+ : column score between +0.5 and +1.5
| : column score above   +1.5
```

```
T Consensus:    the template alignment consensus sequence
T <T_name>:     the template domain sequence
T ss_dssp:      the template secondary structure as determined by DSSP (when available)
T ss_pred:      the template secondary structure as predicted by PSIPRED (when available)
```

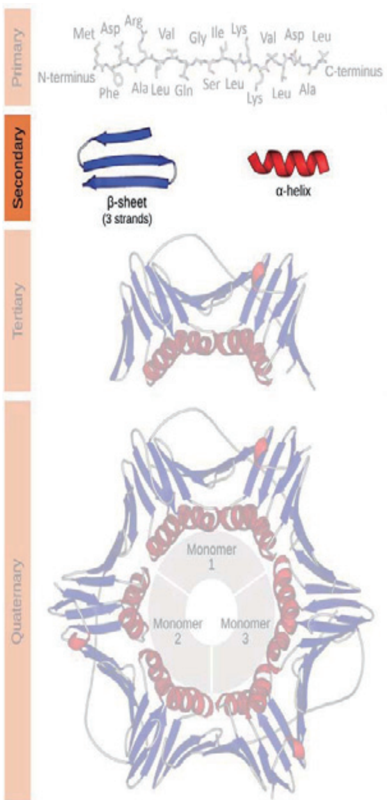
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local computer에서 AlphaFold 사용 방법

```
No 1
>3QWQ_A Epidermal growth factor receptor (E.C.2.7.10.1); CELL SURFACE RECEPTOR, TYROSINE KINASE; HET: BMA, FUC, MAN, NAG; 2.75A {Homo sapiens}
Probab=100.00  E-value=8e-93  Score=888.93  Aligned_cols=641  Identities=100%  Similarity=1.644  Sum_probs=547.3  Template_Neff=9.000

Q sp|P00533|EGFR     1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (1210)
Q Consensus          1 ~~~~~~~~~~~~|~||~~~~~~~~~~~~~~~vC~Gt~~~|~~~~~~~~~~~~y~~|~~~y~nCtvV~GnLeIt~i~~~~dlsFl~   80 (1210)
                       |||.|.+++|+|++|++++++.....+.+||.|++++++.+++++++|+.++++|+||++|.|+|+|+.+....++++|+
T Consensus          1 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~C~g~~~~~~~~~~~~~~~~~~~~~~~~Ct~i~G~l~i~~~~~~~~~~~~~~|~   80 (648)
T 3QWQ_A             1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (648)
T ss_dssp            -------------------------CCCCEECCBCCTTCEESSHHHHHHHHHHHHHTTCSEESSBEEEECCCTTCCCGGGG
T ss_pred            CCCcHHHHHHHHHHHHHHchhccccccCceeeccCCCcccCCChHHHHHHHHHHHhCCCCEEeCCEEEEeecCCCCchhhc
Confidence          899999999999999999999999999999999999999999999999999999999999999999887778899999
```

```
T Consensus:    the template alignment consensus sequence
T <T_name>:     the template domain sequence
T ss_dssp:      the template secondary structure as determined by DSSP (when available)
T ss_pred:      the template secondary structure as predicted by PSIPRED (when available)
```

3 Local computer에서 AlphaFold 사용 방법



Dssp algorithm
(hydrogen bond estimation algorithm)

3 Local computer에서 AlphaFold 사용 방법

```
No 1
>3QWQ_A Epidermal growth factor receptor (E.C.2.7.10.1); CELL SURFACE RECEPTOR, TYROSINE KINASE; HET: BMA, FUC, MAN, NAG; 2.75A {Homo sapiens}
Probab=100.00  E-value=8e-93  Score=888.93  Aligned_cols=641  Identities=100%  Similarity=1.644  Sum_probs=547.3  Template_Neff=9.000

Q sp|P00533|EGFR    1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (1210)
Q Consensus         1 ~~~~~~~~~~~~l~||~~~~~~~~~~~~~~~~vC~Gt~~~l~~~~~~~~~~~~~y~~l~~~y~nCtyV~GnLeIt~i~~~~dlsFl~   80 (1210)
                      |||.|.+++|+|++|++++++....+.+||.|++++++.+++++++|+.++++|+||++|.|+|+|+.+....++++|+
T Consensus         1 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~C~g~~~~~~~~~~~~~~~~~~~~~~~~~~Ct~i~G~l~i~~~~~~~~~~~~~~l~   80 (648)
T 3QWQ_A            1 MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLK   80 (648)
T ss_dssp             ------------------------CCCCEECCBCCTTCEESSHHHHHHHHHHHHHTTCSEESSBEEEECCCTTCCCGGGG
T ss_pred             CCCcHHHHHHHHHHHHHHHchhccccccCceeeccCCCcccCCChHHHHHHHHHHHhCCCCEEeCCEEEEeecCCCCchhhc
Confidence          89999999999999999999999999999999999999999999999999999999999999999999988777889999
```

The first line, which begins with with a >, contains the name and description line of the template/database HMM. (We use "template HMM" and "matched database HMM" synonymously.)

The next line summarizes the main statistics for the alignment: The probability for the query and template HMMs to be homologous (Probab

The Sum_probs value is the sum over the posterior probabilities of all aligned pairs of match states. These probabilities are calculated by the Forward-Backward algorithm.

Dssp : method for assigning secondary structure to the amino acids of a protein, given the atomic-resolution coordinates of the protein.

The line in the middle shows the column score between the query and template amino acid distributions. It gives a valuable indication for the alignment quality.

```
= : column score below -1.5
- : column score between -1.5 and -0.5
. : column score between -0.5 and +0.5
+ : column score between +0.5 and +1.5
| : column score above   +1.5
```

```
T Consensus:   the template alignment consensus sequence
T <T_name>:    the template domain sequence
T ss_dssp:     the template secondary structure as determined by DSSP (when available)
T ss_pred:     the template secondary structure as predicted by PSIPRED (when available)
```

가톨릭대학교
THE CATHOLIC UNIVERSITY OF KOREA

3 Local server에서 AlphaFold 사용 방법

Get information from Pkl file

Ranking_debug.json file에서 각 모델의 평균 plddt값으로 매겨진 rank 정보를 가져와서 각 rank의 pkl file정보를 얻는다

ranking_debug.json - Windows 메모장
파일(F) 편집(E) 서식(O) 보기(V) 도움말(H)


```
{
    "plddts": {
        "model_1_ptm_pred_0": 94.41104130504127,
        "model_2_ptm_pred_0": 93.75401871735953,
        "model_3_ptm_pred_0": 54.51199709165903,
        "model_4_ptm_pred_0": 48.86862857508933,
        "model_5_ptm_pred_0": 51.993447355271364
    },
    "order": [
        "model_1_ptm_pred_0",
        "model_2_ptm_pred_0",
        "model_3_ptm_pred_0",
        "model_5_ptm_pred_0",
        "model_4_ptm_pred_0"
    ]
}
```


```
[2] import pickle
    import json
    import pandas as pd
    import numpy as np
    from matplotlib import pyplot as plt
    import seaborn as sns
    #from Bio import SeqIO
```

```
[3] with open('/content/WT/ranking_debug.json', 'r') as rank:
      WT_rank = json.load(rank)
    for i in range(0,5):
      rank = WT_rank['order'][i]
      with open('/content/WT/result_'+rank+'.pkl', 'rb') as f:
        globals()['WT_ranking'+str(i)] = pickle.load(f)
```

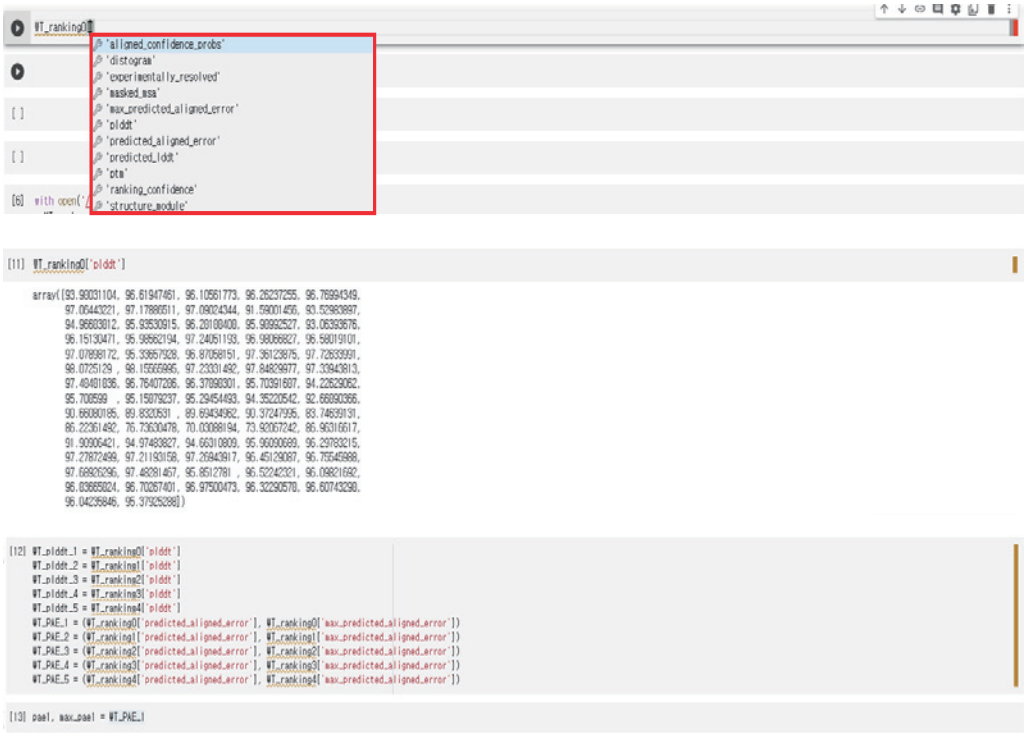
PKl file에 저장된 data key list

```
[9] WT_ranking0.keys()

dict_keys(['distogram', 'experimentally_resolved', 'masked_msa', 'predicted_aligned_error', 'predicted_lddt', 'structure_module', 'plddt', 'aligned_confidence_probs', 'max_predicted_aligned_error', 'ptm',
'ranking_confidence'])
```

가톨릭대학교
THE CATHOLIC UNIVERSITY OF KOREA

3 Local server에서 AlphaFold 사용 방법

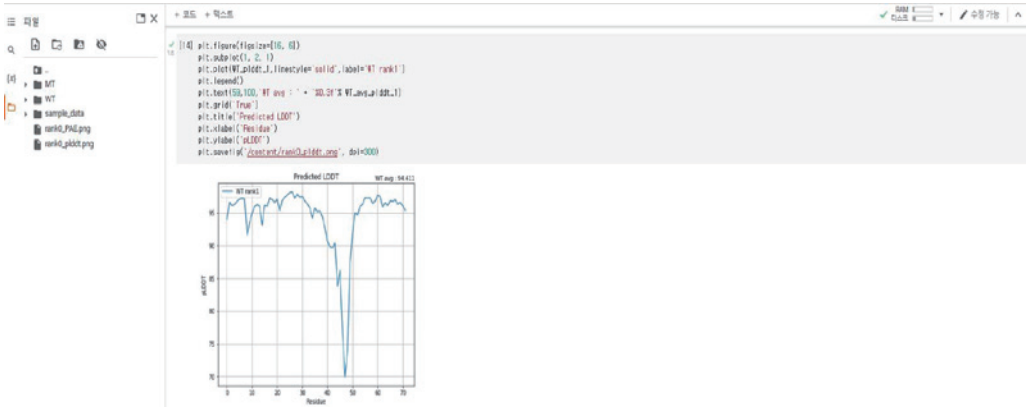
Get information from Pkl file

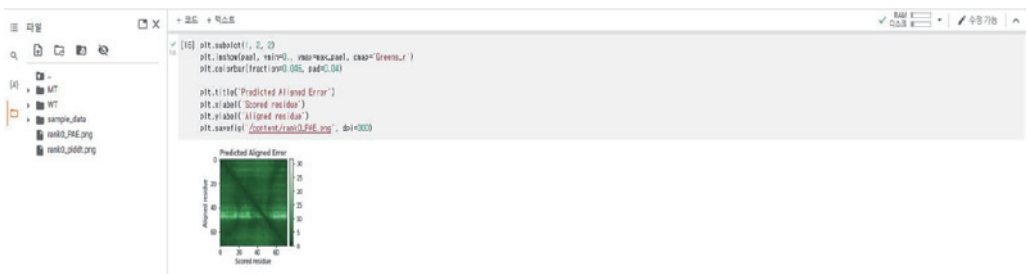


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local server에서 AlphaFold 사용 방법

Get information from Pkl file – draw pLDDT & PAE





가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local server에서 AlphaFold 사용 방법

Compare other predictions - local

```
[ ] with open('/content/WT/ranking_debug.json', 'r') as rank:
      WT_rank = json.load(rank)
    for i in range(0,5):
      rank = WT_rank['order'][i]
      with open('/content/WT/result_'+rank+'.pkl', 'rb') as f:
        globals()['WT_ranking'+str(i)] = pickle.load(f)
```

```
[ ] with open('/content/MT/ranking_debug.json', 'r') as rank:
      MT_rank = json.load(rank)
    for i in range(0,5):
      rank = MT_rank['order'][i]
      with open('/content/MT/result_'+rank+'.pkl', 'rb') as f:
        globals()['MT_ranking'+str(i)] = pickle.load(f)
```

```
[ ] WT_plddt_1 = WT_ranking0['plddt']
    WT_plddt_2 = WT_ranking1['plddt']
    WT_plddt_3 = WT_ranking2['plddt']
    WT_plddt_4 = WT_ranking3['plddt']
    WT_plddt_5 = WT_ranking4['plddt']
    WT_PAE_1 = (WT_ranking0['predicted_aligned_error'], WT_ranking0['max_predicted_aligned_error'])
    WT_PAE_2 = (WT_ranking1['predicted_aligned_error'], WT_ranking1['max_predicted_aligned_error'])
    WT_PAE_3 = (WT_ranking2['predicted_aligned_error'], WT_ranking2['max_predicted_aligned_error'])
    WT_PAE_4 = (WT_ranking3['predicted_aligned_error'], WT_ranking3['max_predicted_aligned_error'])
    WT_PAE_5 = (WT_ranking4['predicted_aligned_error'], WT_ranking4['max_predicted_aligned_error'])
    WT_avg_plddt_1 = WT_ranking0['ranking_confidence']
    WT_avg_plddt_2 = WT_ranking1['ranking_confidence']
    WT_avg_plddt_3 = WT_ranking2['ranking_confidence']
    WT_avg_plddt_4 = WT_ranking3['ranking_confidence']
    WT_avg_plddt_5 = WT_ranking4['ranking_confidence']
```

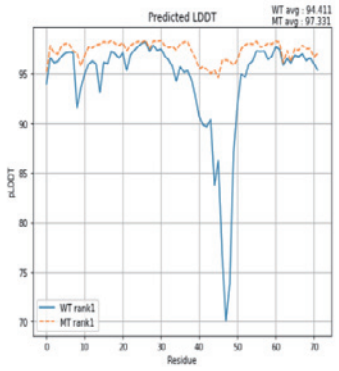
```
[ ] MT_plddt_1 = MT_ranking0['plddt']
    MT_plddt_2 = MT_ranking1['plddt']
    MT_plddt_3 = MT_ranking2['plddt']
    MT_plddt_4 = MT_ranking3['plddt']
    MT_plddt_5 = MT_ranking4['plddt']
    MT_PAE_1 = (MT_ranking0['predicted_aligned_error'], MT_ranking0['max_predicted_aligned_error'])
    MT_PAE_2 = (MT_ranking1['predicted_aligned_error'], MT_ranking1['max_predicted_aligned_error'])
    MT_PAE_3 = (MT_ranking2['predicted_aligned_error'], MT_ranking2['max_predicted_aligned_error'])
    MT_PAE_4 = (MT_ranking3['predicted_aligned_error'], MT_ranking3['max_predicted_aligned_error'])
    MT_PAE_5 = (MT_ranking4['predicted_aligned_error'], MT_ranking4['max_predicted_aligned_error'])
    MT_avg_plddt_1 = MT_ranking0['ranking_confidence']
    MT_avg_plddt_2 = MT_ranking1['ranking_confidence']
    MT_avg_plddt_3 = MT_ranking2['ranking_confidence']
    MT_avg_plddt_4 = MT_ranking3['ranking_confidence']
    MT_avg_plddt_5 = MT_ranking4['ranking_confidence']
```

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

3 Local server에서 AlphaFold 사용 방법

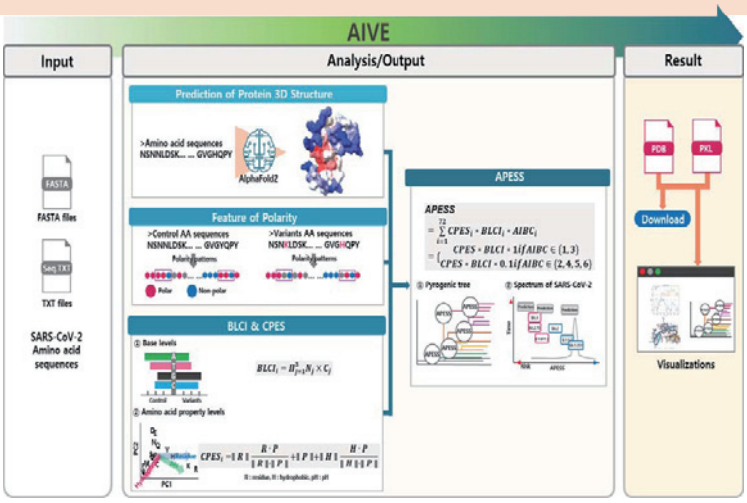
Compare other predictions - local

```
[ ] plt.figure(figsize=[16, 6])
    plt.subplot(1, 2, 1)
    plt.plot(WT_plddt_1,linestyle='solid',label='WT rank1')
    plt.plot(MT_plddt_1,linestyle='dashed',label='MT rank1')
    plt.legend()
    plt.text(59,100,'WT avg : ' + '%0.3f'%WT_avg_plddt_1 + 'WnMT avg : ' + '%0.3f'%MT_avg_plddt_1)
    plt.grid('True')
    plt.title('Predicted LDDT')
    plt.xlabel('Residue')
    plt.ylabel('pLDDT')
    plt.savefig('/content/11.png', dpi=300)
```



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명



The information and analysis tools we provide are the following:

A. Protein structure prediction from viral sequences using learning models
Prediction of folding and docking from viral mutations
Comparison of folding and docking scores

B. Polarity changes in protein sequences
Measurement of repeated polarity changes

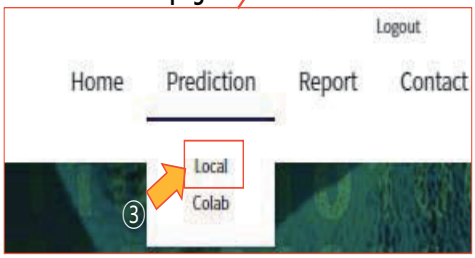
C. Mathematical models based on base and amino acid property levels (BLCI & CPES)
Scoring of rate of change in base levels
Scoring of rate of change amino acid property(residue, hydrophobicity, and pH levels)

D. Comprehensive mathematical analysis model: Protein structure prediction and base/amino acid property levels (APESS)

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

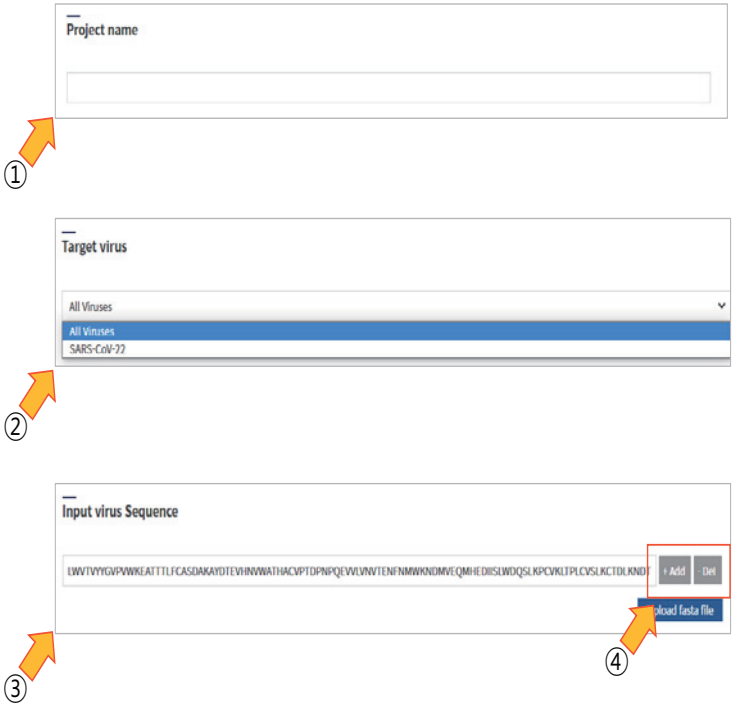
4 AIVE 사용 설명

Local Prediction page



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명

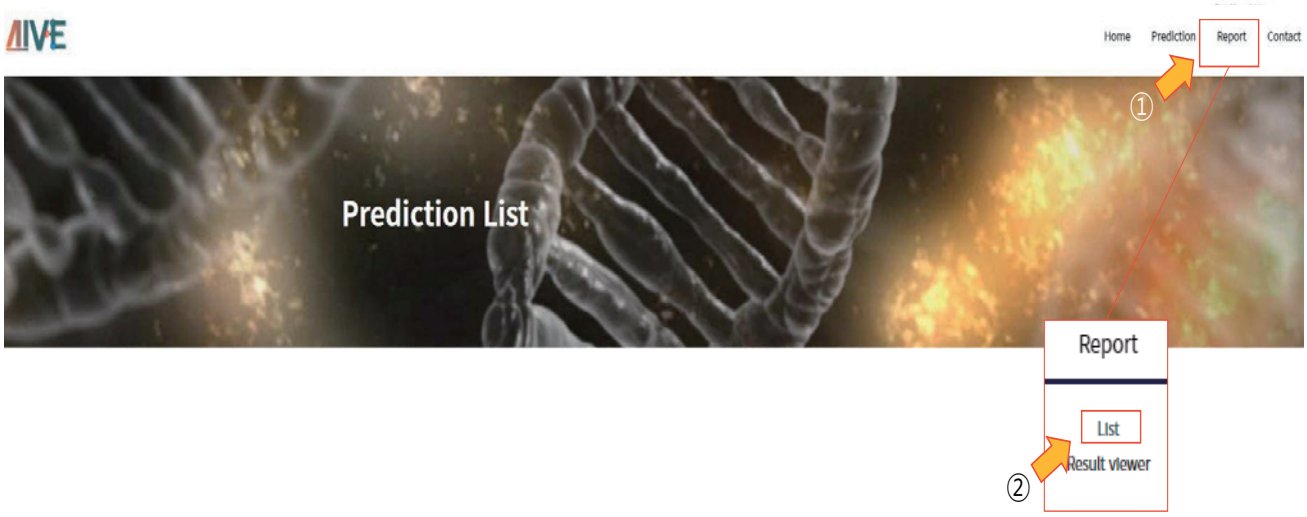


가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명

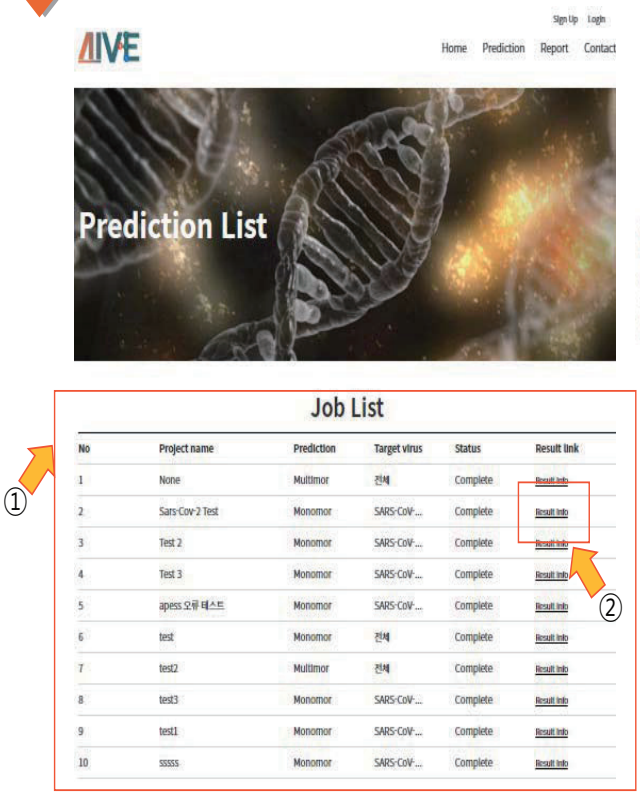
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명



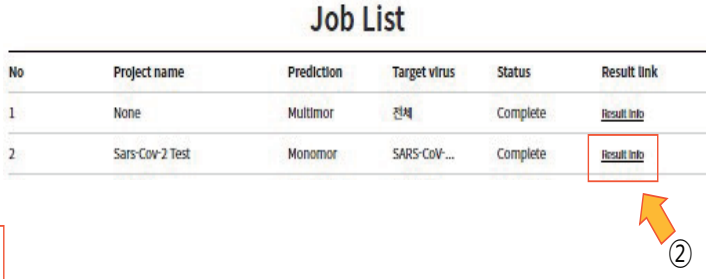
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명



No	Project name	Prediction	Target virus	Status	Result link
1	None	Multimor	전체	Complete	Result Info
2	Sars-Cov-2 Test	Monomor	SARS-CoV-...	Complete	Result Info
3	Test 2	Monomor	SARS-CoV-...	Complete	Result Info
4	Test 3	Monomor	SARS-CoV-...	Complete	Result Info
5	apess 오류 테스트	Monomor	SARS-CoV-...	Complete	Result Info
6	test	Monomor	전체	Complete	Result Info
7	test2	Multimor	전체	Complete	Result Info
8	test3	Monomor	SARS-CoV-...	Complete	Result Info
9	test1	Monomor	SARS-CoV-...	Complete	Result Info
10	sssss	Monomor	SARS-CoV-...	Complete	Result Info

<< < 1 2 > >>

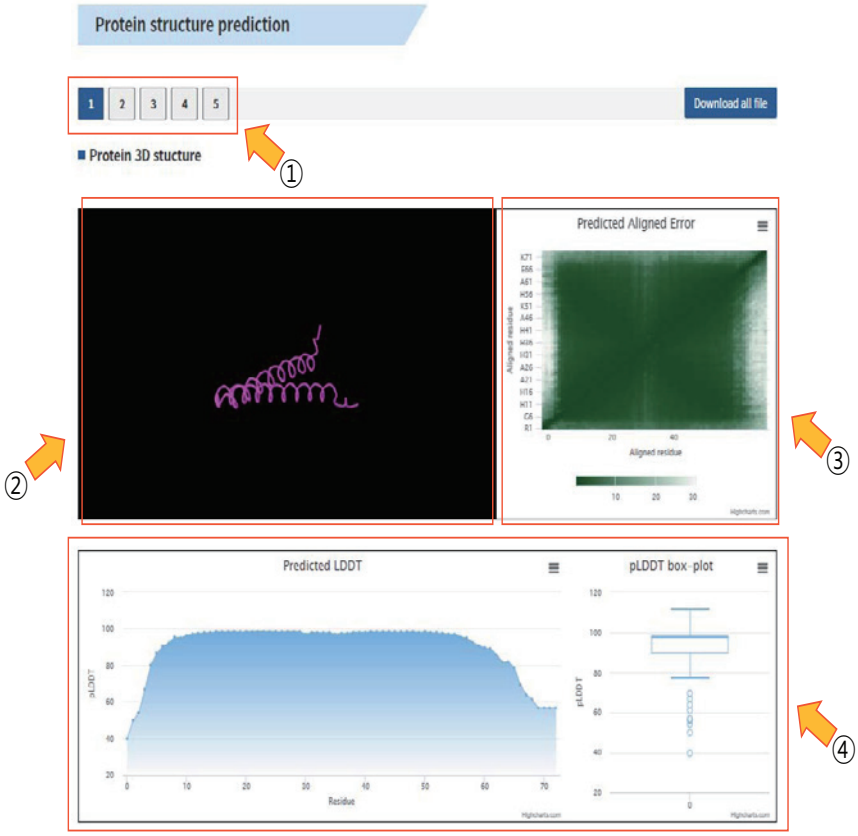


No	Project name	Prediction	Target virus	Status	Result link
1	None	Multimor	전체	Complete	Result Info
2	Sars-Cov-2 Test	Monomor	SARS-CoV-...	Complete	Result Info

②

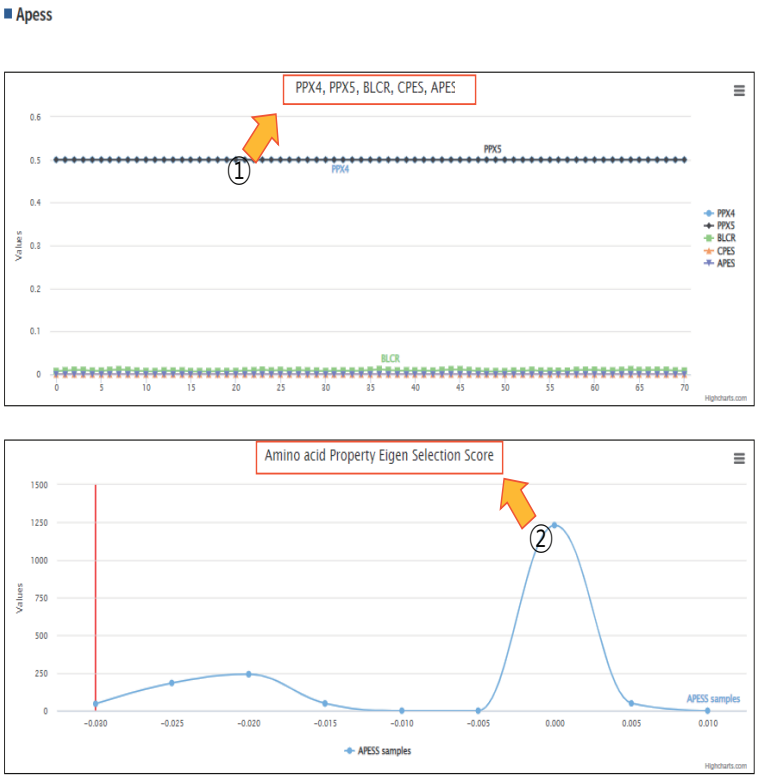
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명 : 결과 설명



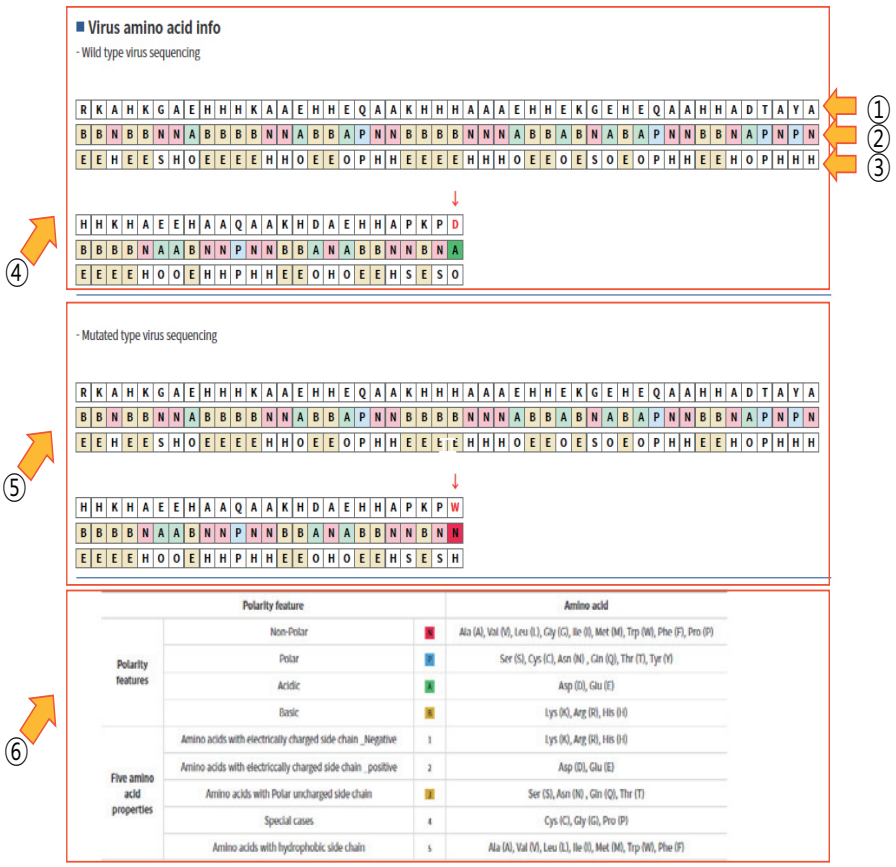
가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명 : 결과 설명



가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

4 AIVE 사용 설명 : 결과 설명

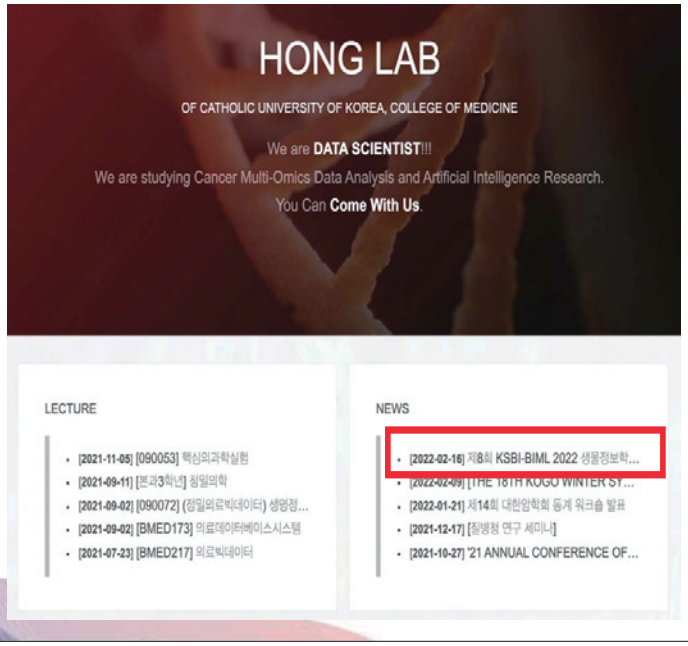


	Polarity feature		Amino acid
Polarity features	Non-Polar	N	Ala (A), Val (V), Leu (L), Gly (G), Ile (I), Met (M), Trp (W), Phe (F), Pro (P)
	Polar	P	Ser (S), Cys (C), Asn (N) , Gln (Q), Thr (T), Tyr (Y)
	Acidic	A	Asp (D), Glu (E)
	Basic	B	Lys (K), Arg (R), His (H)
Five amino acid properties	Amino acids with electrically charged side chain _Negative	1	Lys (K), Arg (R), His (H)
	Amino acids with electriccally charged side chain _positive	2	Asp (D), Glu (E)
	Amino acids with Polar uncharged side chain	3	Ser (S), Asn (N) , Gln (Q), Thr (T)
	Special cases	4	Cys (C), Gly (G), Pro (P)
	Amino acids with hydrophobic side chain	5	Ala (A), Val (V), Leu (L), Ile (I), Met (M), Trp (W), Phe (F)

가톨릭대학교 THE CATHOLIC UNIVERSITY OF KOREA

QUIZ

- http://honglab.catholic.ac.kr 의 NEWS 링크를 참조하세요.
(실습 데이터, 향후 솔루션을 제공합니다)



Q1.

- Mutalisk를 수행 후 확인할 수 있는 결과입니다. 돌연변이가 한 곳에 집중적으로 모여 있는 현상을 무엇이라고 합니까?

Q2.

- Mutalisk 웹 사이트 (http://mutalisk.org)에서 제공하는 melanoma 환자의 돌연변이 데이터 (sample_melanoma.vcf)를 다운로드 받아서 분석을 진행하고 다음 물음에 답하시오.

- Version 2와 Version 3을 이용한 시그니처 분석 후 1st, 2nd signature번호 (타입)는 각각 무엇인가?

- Replication timing에서 돌연변이가 가장 많은 구간과 유의미한 돌연변이는 무엇인가? (Version 2, 3 각각에 대해 답하시오.)

Q3.

- AlphaFoldI에서는 (.) 방식을 이용하여 구조를 예측하고, AlphaFoldII에서는 ( ) 방식을 예측하게 된다. 이로 인하여 단백질 구조 예측 개수에서 약 1,000배 가까운 성능 향상을 보이게 되었다.

Q4.

- 오미크론 세부 계통 변이 BQ 1.1의 pLDDT와 PAE를 제시하고, Alpha 변이와 어느 정도의 위험도 (전파도) 차이를 보이는지? 보이시오.

Q5.

- BRAF 유전자 V600E 변이에 대해서 Vemurafenib의 표적 치료를 할 수 있다. AlphaFold를 이용하여 변이 유/무에 따른 구조 차이를 보이시오.

경청해 주셔서 고맙습니다.

Big Data Analysis Lab. (http://honglab.catholic.ac.kr)
교수: 홍동완 (dwhong@catholic.ac.kr, 02-3147-8424)
연구실: 가톨릭 성의교정 옴니버스파크 의과대학 7113호

연구 주제

- **Cancer Multi-Omics (WGS, WES, Panel, RNA-Seq, Proteome, Hi-C 등) 분석**
- **분석 소프트웨어 및 통합 데이터베이스 개발**
- **인공 지능 기반 약물반응성, 적정 치료제, 치료법 개발**
- **빅데이터 분석 알고리즘 개발**
- **NFT & Metaverse**

I Dear CMC I #2. 유전자? 내 손안에 있소이다! I 홍동완 교수
조회수 577회 · 2주 전
가톨릭대학교 산학협력단

이런 연구를 하고 있습니다!

https://www.youtube.com/watch?v=H9fFnAwEcyQ

'구독'과 '좋아요'는 생계형.과학자에게 도움이 됩니다