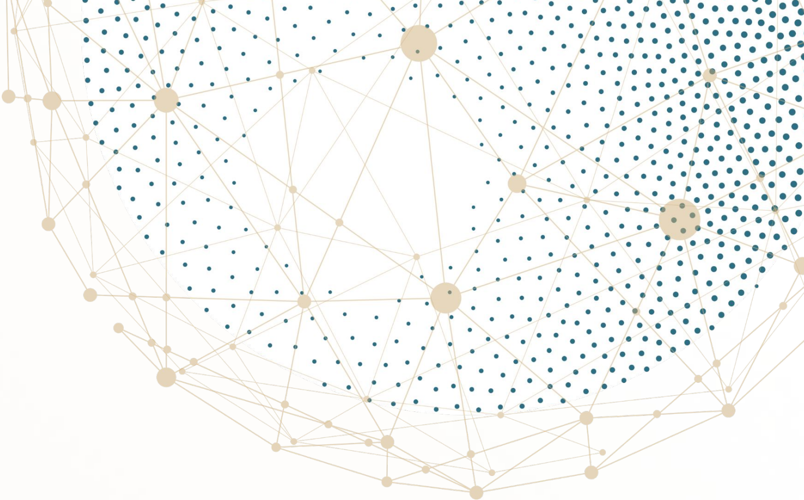


AI Research at Genialis

Luka Ausec, Chief Discovery Officer, Genialis
October 8, 2024

NON-CONFIDENTIAL

Genialis Co-founders and Senior Leadership

Rafael Rosengarten, PhD

Co-founder, Chief Executive Officer

Co-founder, Board Director | Alliance for AI in Healthcare | Baylor College of Medicine, Lawrence Berkeley Labs, Yale University

Miha Štajdohar, PhD

Co-founder, Chief Technology Officer

Research Fellow | Baylor College of Medicine | 20+ years in artificial intelligence for biomedical discovery

Tjaša Krisper Kutin

Chief Operating Officer,
Head of People & Culture

Founder | Naymit, Primeris | 15+ years in leading startup business operations, finance, people operations, and compliance.

Luka Ausec, PhD

Chief Product Officer

Research Fellow | University of Ljubljana | 15+ years in computational biology and AI driven drug discovery

Krista McKerracher, MBA

Chairperson, Board of Directors

VP Oncology Global Development | Novartis
Exec Director Ortho Diagnostics | J&J
25+ years in big Pharma product development

Ines Hikl

Head of Regulatory, Quality & Compliance

Technical manager | Bureau Veritas
20+ years in quality management, information security and social responsibility

Aditya Pai, MBA

Head of Business Development

VP of Corp and Business Dev | Medgenome
VP of Sales | Genuity | IBM Watson
25+ years in genomics / life sciences

Mark Uhlik, PhD

VP of Biomarker Development

VP, Head of Biomarker Discovery | OncXerna
VP of Translational Oncology | HiberCell, Biothera
Principal Research Scientist | Eli Lilly & Co.,
20+ years in oncology translational development

Team Highlights

- 38 team members globally
- 14 PhDs, including 2 MD/PhD

Company Highlights

- Globally diverse data catalog approaching 1M harmonized transcriptomics samples
- Commercialization lead for the Xerna™ TME Panel
- Founding member of the Alliance for Artificial Intelligence in Healthcare

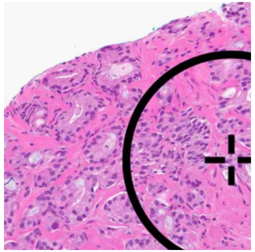
Biomarkers are key to precision medicine

Bi·o·mark·er /ˈbīōˌmärkər/

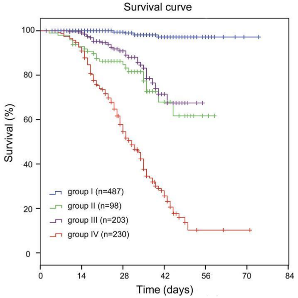
noun

A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

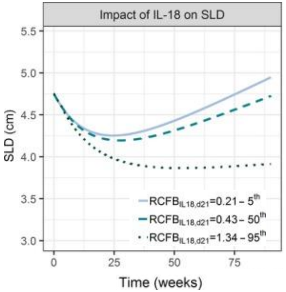
Disease/normal



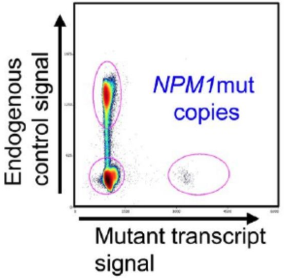
Prognosis



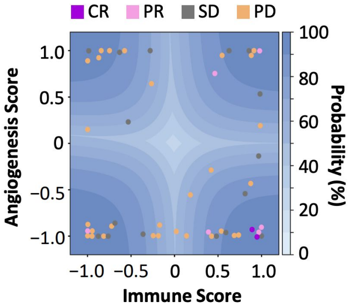
Pharmacology



Monitoring

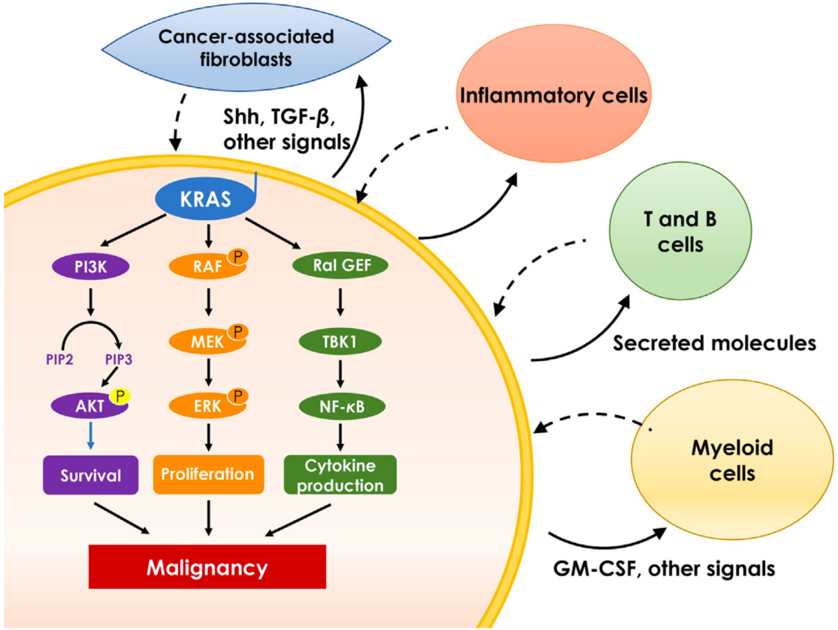


Prediction

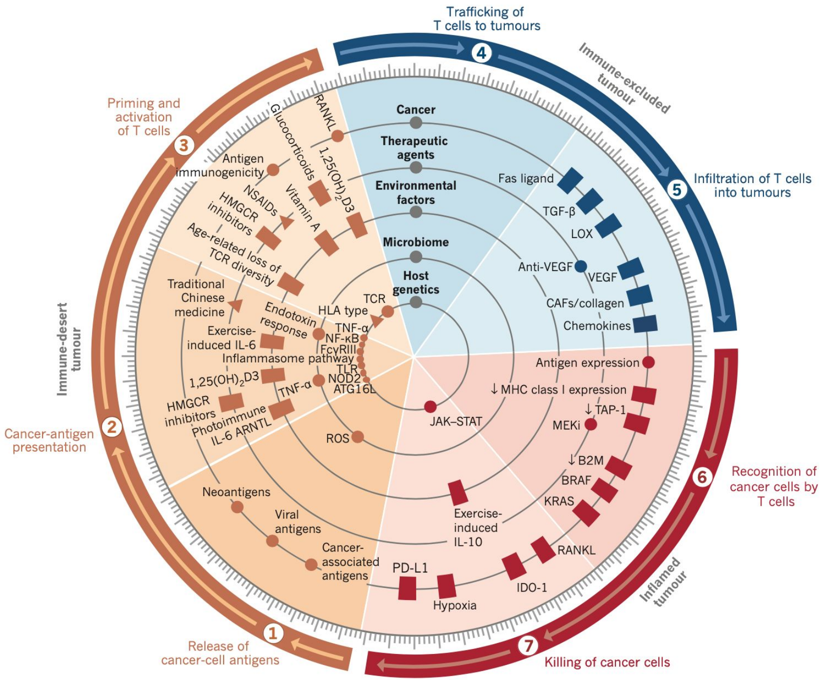


Genialis is the RNA biomarker company.

Biology is too complex to rely on a single mutation



https://doi.org/10.1016/j.apsb.2019.03.002



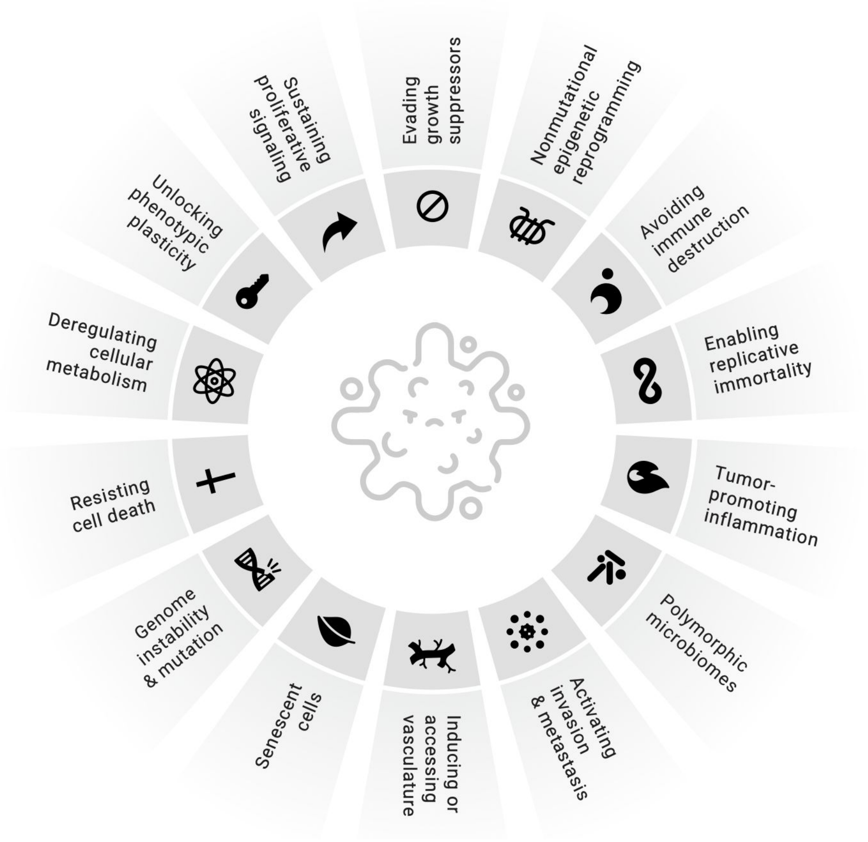
Chen & Mellman. Nature Vol 541, 2017

We abstract biological complexity as a set of measurable phenotypes

Hallmark biologies can be represented as multi-gene signatures, measured by gene expression.

RNA-sequencing is clinically robust and yields high dimensional data that can indicate cancer subtype.

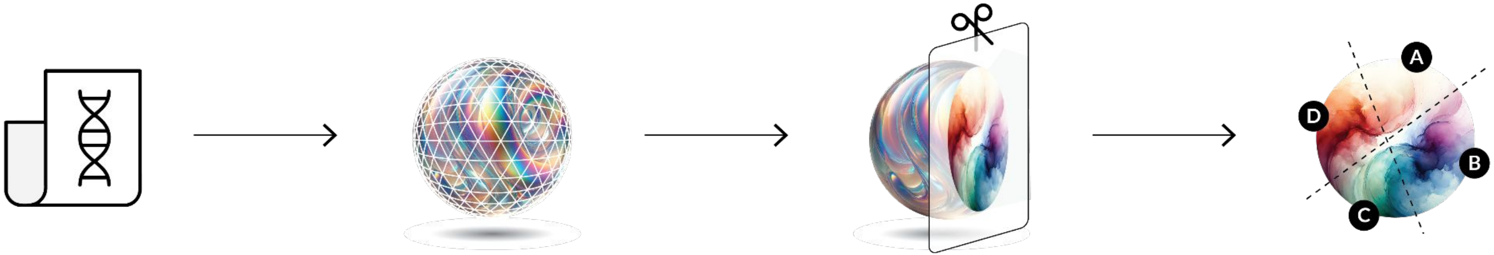
Genialis has a library of over 100 distinct, validated **biomodules for modeling cancer-related biologies**



Genialis ResponderID™

Biology-first approach to guide therapy for all cancer patients

ResponderID uses Genialis Foundation Model to predict patient response to therapy. Hallmark biologies are learned from nearly ~1M harmonized transcriptomic records.



RNA SEQUENCING

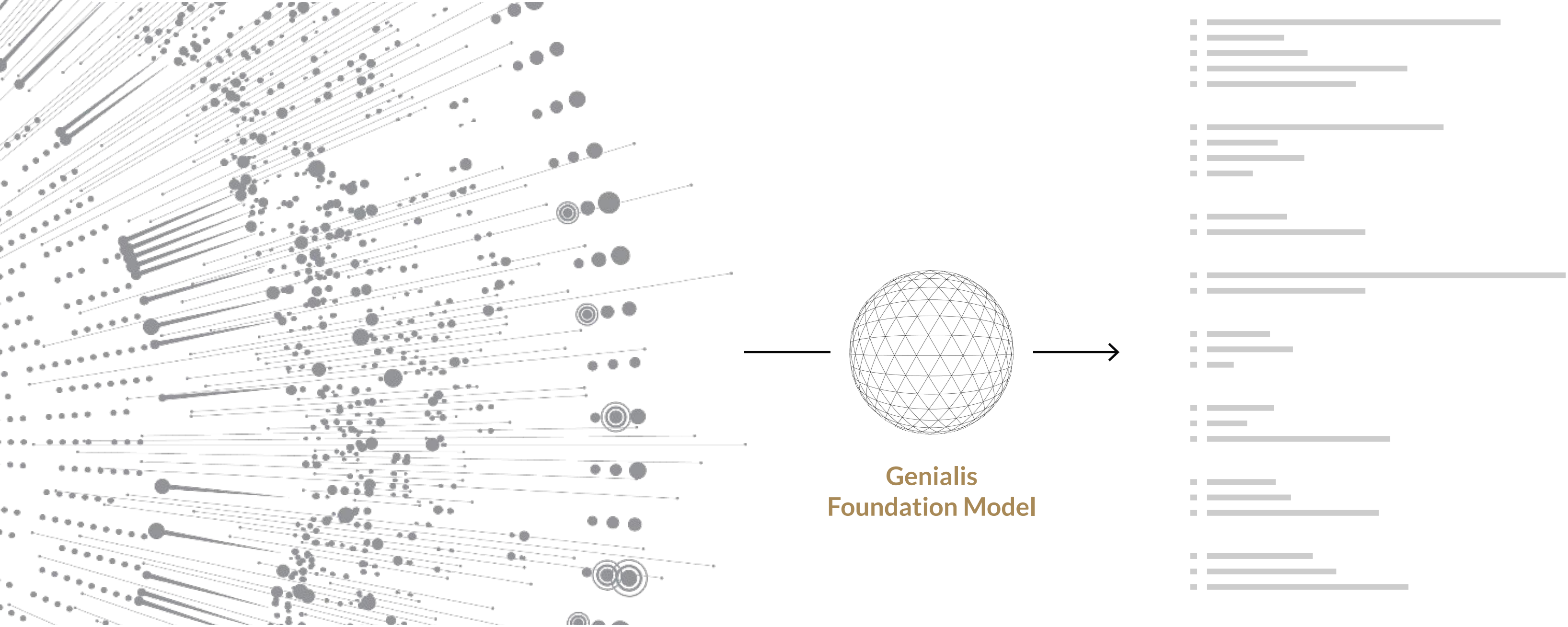
GENIALIS FOUNDATION MODEL

BIOLOGY-INFORMED FILTERS

CLINICALLY RELEVANT SUBTYPES

(Thresholds, Correlation with response)

Genialis Foundation Model maps RNA-seq data into cancer biology space



Genialis Foundation Model

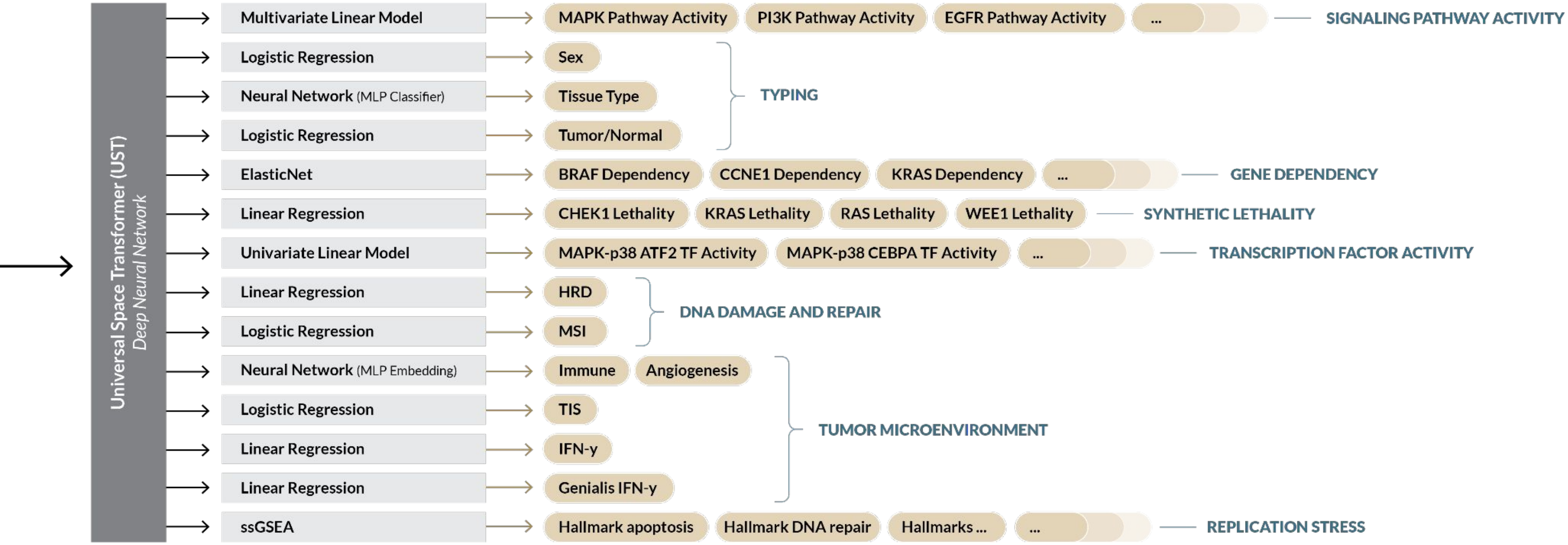
RNA-Seq Assay (Gene Expression Profile)

4,200 oncogenes, 60,000 RNA variants

Cancer Biology Space

128 validated signatures

Genialis Foundation Model integrates specialized AI/ML models, each capturing distinct biological mechanisms



Universal Space Transformer (UST)
Deep Neural Network

Multivariate Linear Model → MAPK Pathway Activity | PI3K Pathway Activity | EGFR Pathway Activity | ... — **SIGNALING PATHWAY ACTIVITY**

Logistic Regression → Sex
Neural Network (MLP Classifier) → Tissue Type
Logistic Regression → Tumor/Normal
TYPING

ElasticNet → BRAF Dependency | CCNE1 Dependency | KRAS Dependency | ... — **GENE DEPENDENCY**

Linear Regression → CHEK1 Lethality | KRAS Lethality | RAS Lethality | WEE1 Lethality — **SYNTHETIC LETHALITY**

Univariate Linear Model → MAPK-p38 ATF2 TF Activity | MAPK-p38 CEBPA TF Activity | ... — **TRANSCRIPTION FACTOR ACTIVITY**

Linear Regression → HRD
Logistic Regression → MSI
DNA DAMAGE AND REPAIR

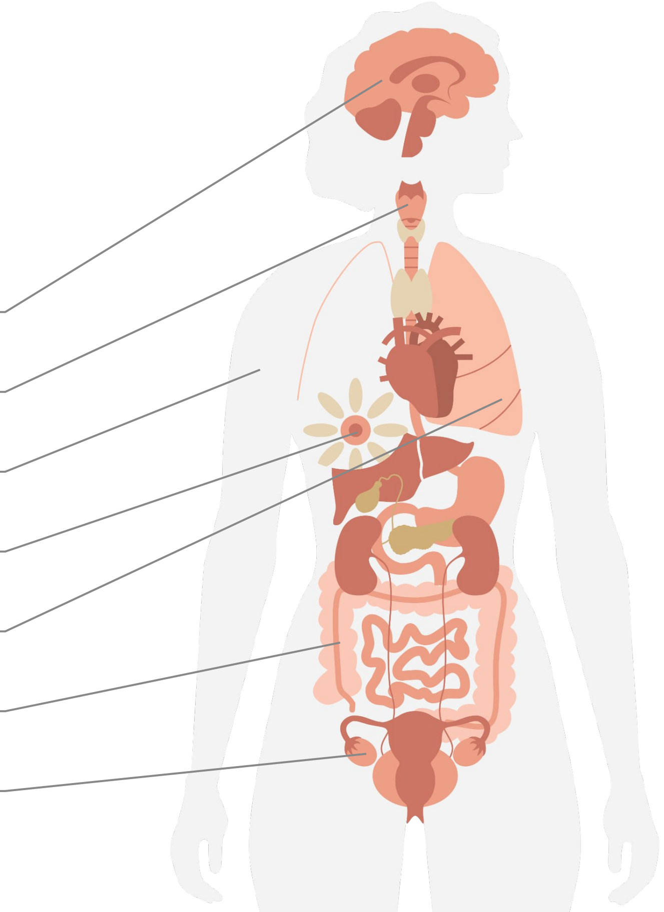
Neural Network (MLP Embedding) → Immune | Angiogenesis
Logistic Regression → TIS
Linear Regression → IFN-y
Linear Regression → Genialis IFN-y
TUMOR MICROENVIRONMENT

ssGSEA → Hallmark apoptosis | Hallmark DNA repair | Hallmarks ... | ... — **REPLICATION STRESS**

Genialis Foundation Model was trained on ~1M harmonized transcriptomic records

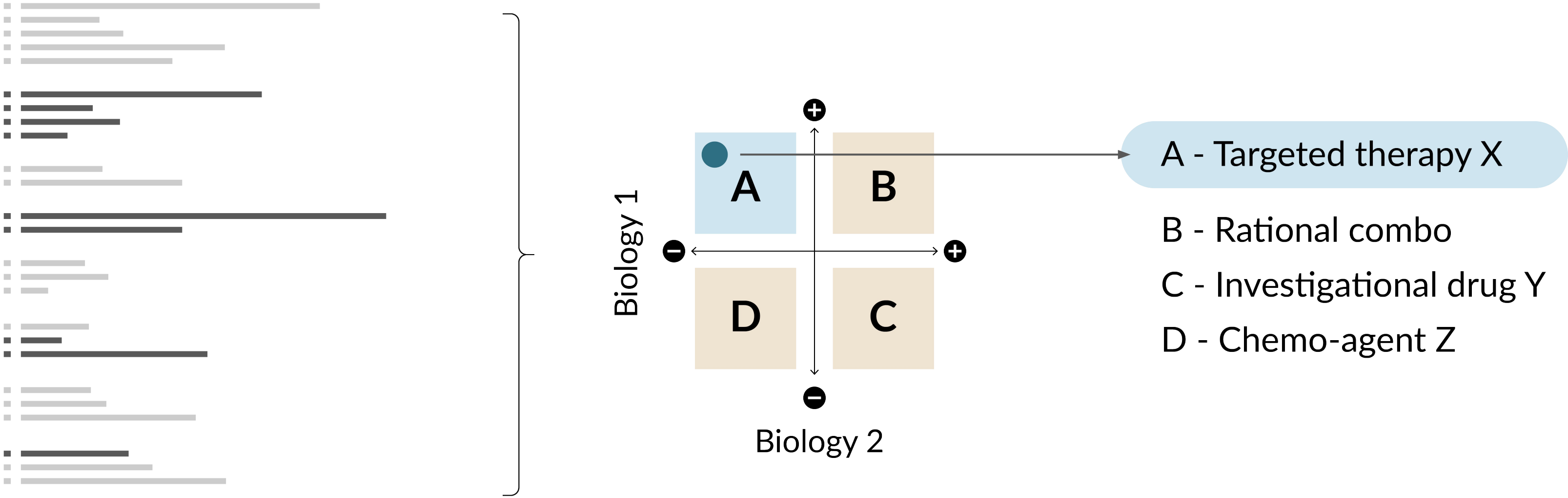
Sourced from 25k datasets across 30 tissue types, blending diverse biological and clinical data

	All: Stages I, II, III, IV | Treatment info
Brain	2,100 datasets | 80,000 Samples | T, N, M Samples
Head and neck	360 datasets | 30,000 Samples | T, N, M Samples
Skin	2,300 datasets | 90,000 Samples | T, N, M Samples
Breast	1,500 datasets | 50,000 Samples | T, N, M Samples
Lung	3,400 datasets | 90,000 Samples | T, N, M Samples
Gastrointestinal	5,600 datasets | 160,000 Samples | T, N Samples
Reproductive	2,300 datasets | 70,000 Samples | T, N, M Samples



Patient stratification is achieved by defining phenotypes from combinations of signatures, then assigning therapies to phenotypes

Fine-tuning the decision model to patient outcomes



A - Targeted therapy X

B - Rational combo

C - Investigational drug Y

D - Chemo-agent Z

Cancer Biology Space

Disease phenotypes

Treatment Decision

Genialis^{TM} krasID predicts clinical benefit consistent with real world & clinical findings

Real World Data

Patients stratified as krasID-HIGH vs. krasID-LOW demonstrate dramatically different time on treatment

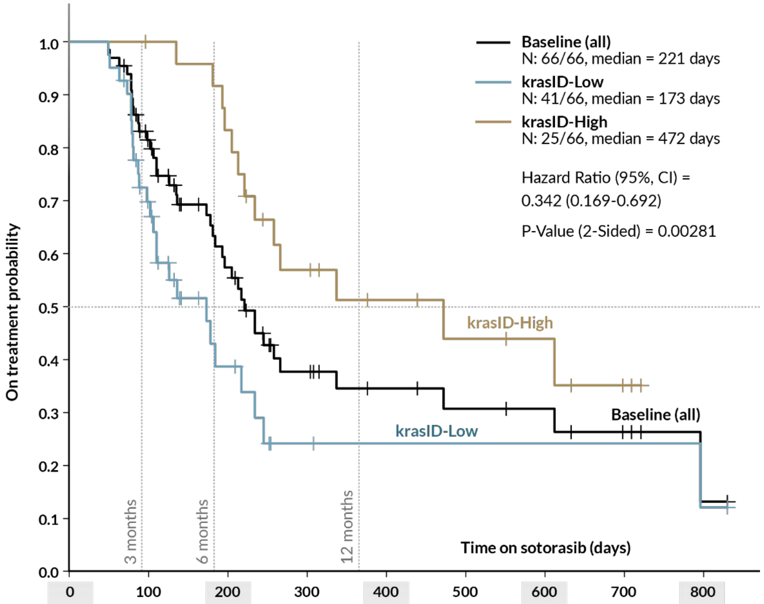
Clinical Trial

Cohort characteristics and response results align closely with CodeBreak100/200 clinical trial observations, demonstrating accuracy in forecasting outcomes in clinical trial settings.

Time on Treatment

krasID-High patients stayed on sotorasib nearly 50% longer than G12C-selected patients and 2.5x longer than krasID-LOW patients

▶ **KM plot of predicted benefit to sotorasib in a NSCLC RWE cohort**



At risk:	0	200	400	600	800
Baseline (all)	66	29	10	7	1
krasID-Low	41	9	2	2	1
krasID-High	25	20	8	5	0

Genialis™ krasID outperforms current Standard of Care Biomarkers, which are limited to mutational status

Historical Approach

- Limited to **presence or absence of DNA mutation**
- **Insufficient to predict efficacy** (mutation selected ORR ~ 30-40%)
- **Cannot inform time on treatment** or combination strategies

VS

Genialis Advantage

- Integrates signal from **KRAS biology** with surrounding **tumor milieu** using RNA-seq & ML
- **>84%** precision in real world patients
- Stratifies patients based on **time on treatment/ survival**
- **Reads-out actionable changes** to other relevant biologies

Want to learn more?

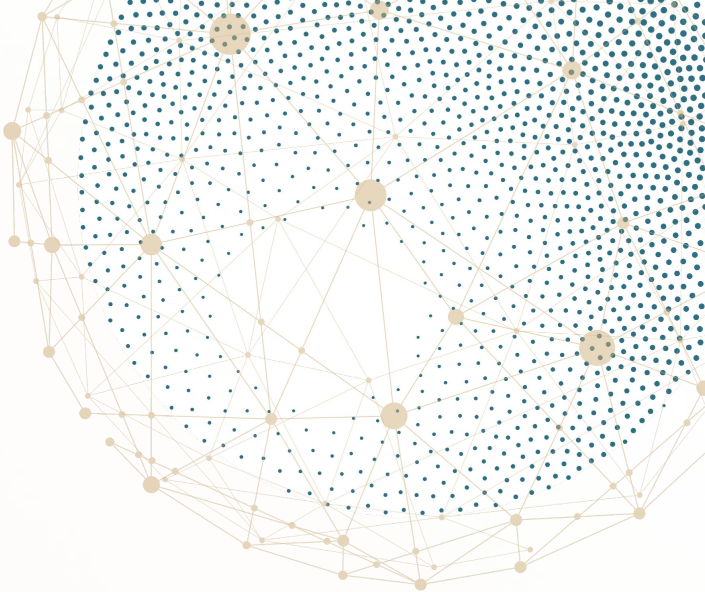
Corporate website

- **https://www.genialis.com/category/scientific-publications/**

Internship program

- **Duration, remuneration:** 2-3 month paid internship
- **Work arrangement:** fully remote, flexible hours, access to Genialis infrastructure
- **Research focus:** High-risk, low-admin research projects
- **Mentorship:** MD PhD & Data Scientist

Genialis



Q&A

lukaa@genalis.com