January 2021

NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

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This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

Synthetic Lethality

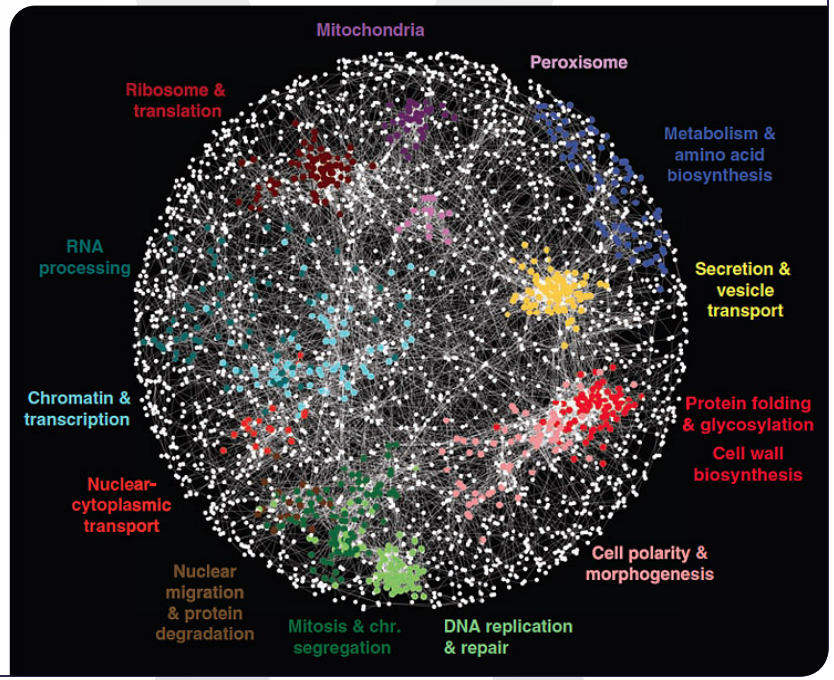
The Next Frontier in Precision Medicine Oncology

Synthetic Lethality provides a powerful approach to discover novel precision medicine therapies with patient biomarkers, including MTAP-deletion (~15% of solid tumors), BRCA/HRD (Breast, Prostate, Ovarian), and high-MSI (15% GI Cancers)

nature REVIEWS GENETICS

- **Synthetic lethality** occurs when the simultaneous perturbation of two genes results in cell death
- Synthetic lethal interactions with tumor-specific mutations (biomarker) may be exploited to develop anticancer therapies
- Large-scale screening for synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing)

Nature Reviews Genetics, Vol. 18, 2017, Hieter, et al



Reference: Charles Boone

IDEAYA Synthetic Lethality Platform

Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities

SL Target & Biomarker Discovery and Validation

Dual CRISPR, CRISPR, siRNA

Genetically Engineered Models

Bioinformatics, including AI Algorithms

- Synthetic Lethality Discovery Screening of broad-based cell libraries to identify SL interactions based on genetic alterations
- DECIPHER™ - Dual CRISPR SL Library in DDR in collaboration with UCSD
- PAGEO™ - Paralogous Gene Evaluation in Ovarian in collaboration with Broad Institute

Drug Discovery and Pharmacological Validation

Structure Based Drug Design

Small Molecule Chemistry

Protein Degrader Capabilities

- High-Throughput Screening approaches to identify biochemically active compounds
- Iterative chemistry / biology screening, including biochemical, cellular and *in vivo,* guided by structure-based-drug design, to evaluate SAR and advance Lead Series
- Pharmacological validation of SL interaction
- Preliminary tolerability of Lead Compounds
- Development Candidate Selection

Translational Research and Opportunity Expansion

Genomics – DNA and RNA Analysis

Proteomics – Protein Expression Profiling

Tissue (IHC, IF) and Liquid Biopsies Analysis

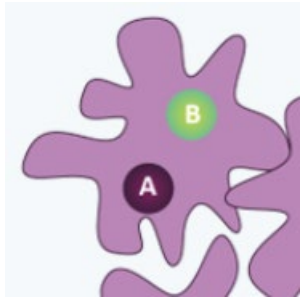
- Translational Research to define patient selection and pharmacodynamic biomarkers
- Opportunity Expansion through cell panel screening to evaluate Lead Compounds against human cancer cell lines across indications
- PD biomarker analysis to confirm target modulation and correlation with clinical activity

IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

Synthetic Lethality Discovery Screening

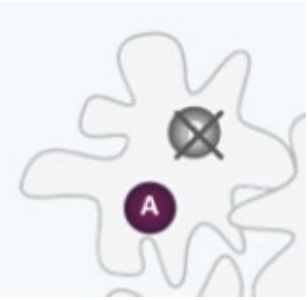
(1) Select Cancer-associated Genetic Alterations (Gene A)
(2) Select Genes encoding potential Drug Target (Gene B)



(3) Create DNA/RNA Libraries combining Cancer-associated Genetic Alterations (Gene A) with Genetic Knock-Out (CRISPR) or Knock-Down (RNAi) of Potential Drug Target (Gene B)

(4) Identify Synthetic Lethal relationships of paired Cancer-associated Genetic Alterations (Gene A) and Potential Drug Targets (Gene B)

(5) Experimentally Validate selected Drug Targets (Gene B) and associated Synthetic Lethal Biomarkers (Gene A)



DECIPHER™ (Dual-CRISPR Screening) screens curated cancer cell lines using CRISPR knock-out of cancer-associated genetic alterations (Gene A) and CRISPR knock-out of selected potential drug targets (Gene B) – IDEAYA Proprietary Database (UCSD Collaboration)

PAGEO™ (Paralog Screening) screens curated cancer cell lines using CRISPR knock-out and/or RNAi knock-down of functionally-redundant genes (Gene A1 and Gene A2) and of selected potential drug targets (Gene B) – IDEAYA Proprietary Database (Broad Institute Collaboration)

DepMap (Single-CRISPR Screening) screens curated cancer cell lines having selected cancer-associated endogenous genetic alterations (Gene A) against CRISPR knock-out of selected potential drug targets (Gene B) – Partnership Database (DepMap Consortium - Broad Institute)

IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

Target / Biomarker Identification and Validation Platform

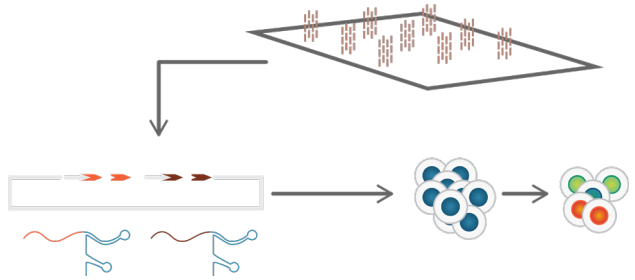
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

Bioinformatic analysis enables identification and validation of synthetic lethal target / biomarker interactions across vast datasets

Robust SL interactions validated genetically (Dual CRISPR, paralogues, isogenic pairs, CRISPR/siRNA), pharmacologically, & *in vivo*

DECIPHER™

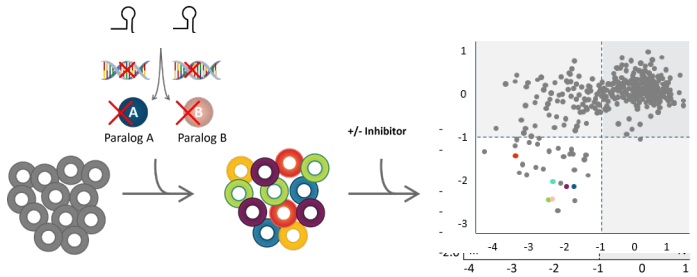
Dual CRISPR SL Library in DNA Damage Repair [2]



Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

PAGEO™

Paralogous Gene Evaluation in Ovarian Cancer [1]



Evaluation of SL targets in context of functionally redundant paralogous genes in ovarian cancer

Partnership Datasets

Cancer Dependency Map – Broad Institute

Foundation Insights™ – Foundation Medicine

depmap portal FOUNDATIONINSIGHTS™

Public Databases

IDEAYA data mining and analysis across data sets

PROJECTGENIE TCGA MSK-IMPACT™ Project Achilles BioPortal CCLE

[1, 2] IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute[1] and UC San Diego[2]

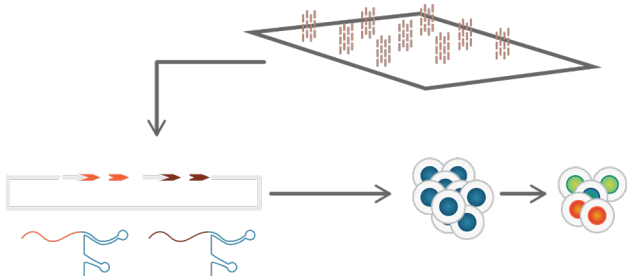
IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

DECIPHER™ Dual CRISPR Proprietary Synthetic Lethality Library

DECIPHER™

Dual CRISPR SL Library in DNA Damage Repair [1]



Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

DECIPHER™
DDR Library 1.0

~225 Non-Overlapped Genes

~12,000 Gene Pairs per Cell Line
67 TSG/OG's and 176 DDR Targets

Curated Breast / Lung Cell Lines

DECIPHER™ Genes

>20 Novel Drug Targets Identified

Target Validation Ongoing

[1] Developed in Collaboration with UCSD, Principal Investigator – Dr. Trey Ideker

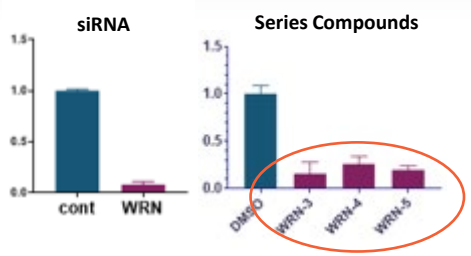
IDEAYA Synthetic Lethality Platform

Drug Discovery and Pharmacological Validation

Lead Compound Identification and Pharmacological Validation of SL Interaction

(1) Drug Discovery Research – to identify proprietary, novel, small molecule compounds as Lead Compounds / Development Candidate with composition-of-matter patent protection and freedom-to-operate

(2) Pharmacological Validation of Synthetic Lethality Interactions – to confirm biological response based on target inhibition with IDEAYA proprietary Lead Compound / Development



High-Throughput Screening approaches to identify compounds having biochemical activity against a Synthetic Lethality target, including HTS hit confirmation and validation of adjacent chemistry to identify Lead Series

Iterative Chemical Synthesis / Screening, including biochemical, cellular and *in vivo* screening, guided by structure-based-drug design and computational chemistry, to evaluate structure-activity-relationships (SAR) and advance Lead Series to identify Lead Compounds

Lead Optimization to evaluate and enhance selectivity, physical properties, and toxicological properties of Lead Compounds

Biomarker Optimization and Synthetic Lethality Validation, including functional genomics validation and pharmacological validation of Synthetic Lethality interaction using Lead Compounds

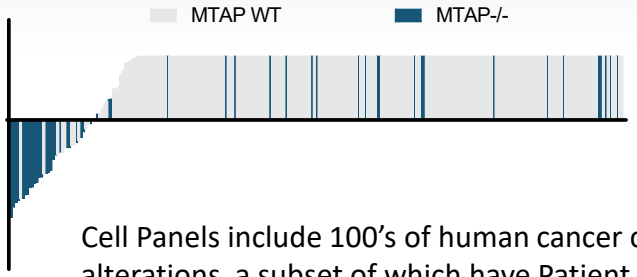
Development Candidate Selection based on comprehensive evaluation of Lead Compounds, including preliminary toxicology

IDEAYA Synthetic Lethality Platform

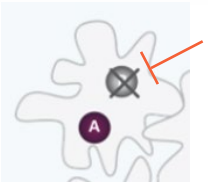
Translational Research and Opportunity Expansion

Synthetic Lethality Indication Expansion Screening

Broad Panel SL Screening for Opportunity Expansion – screen lead compounds / development candidate across broad cancer cell panels to inform patient selection and refine biological / tumor settings for clinical development with potential opportunity expansion (e.g., PRISM, Paralog)



Cell Panels include 100's of human cancer cells with endogenous genetic alterations, a subset of which have Patient Selection Biomarker (Gene A)



Cells are pharmacologically inhibited with lead compound / development candidate targeting Drug Target (Protein B)

Cell Panel Screening to evaluate proprietary lead compounds / development candidate activity against broad-scope panels of genomically-characterized human cancer cell lines representing a broad set of cancer lineages / indications (IDEAYA Selected Panels)

PRISM Screening high-throughput multiplexed screening to evaluate proprietary lead compounds / development candidate activity against a curated panel of more than 750 genomically-characterized human cancer cell lines representing > 45 lineages (Broad Institute Collaboration)

Paralog Lethality Screening high-throughput screening to evaluate proprietary lead compounds / development candidate activity against a panel of hundreds of engineered cell lines having CRISPR knock-out and/or RNAi knock-down of functionally-redundant genes (Broad Institute Collaboration)

IDEAYA is Advancing the Next Wave of Synthetic Lethality Therapies

IDEAYA Synthetic Lethality Pipeline

Strategic Focus on Potential First-in-Class Therapeutics

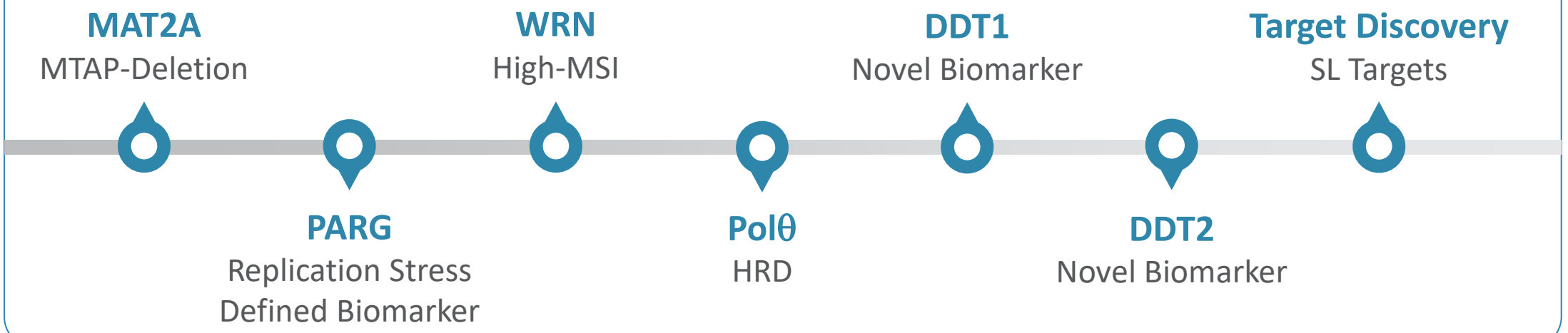
- Broad Portfolio of High-Value Synthetic Lethality Opportunities

IDE397 (MAT2A/MTAP) Lead SL Program is Transitioning to Clinic

- Potential First-in-Class Monotherapy and First-in-Class / Best-in-Class Combination Therapies (e.g., Type I PRMT, Taxane)

Deep Pipeline of Next Generation Synthetic Lethality Targets

- PARG, Werner Helicase, Pol Theta, DNA Damage Targets, and SL Target Discovery Platform



HRD = Homologous Recombination Deficiency, MSI = Microsatellite Instability