Augmenting and Accelerating Drug Discovery using Artificial Intelligence

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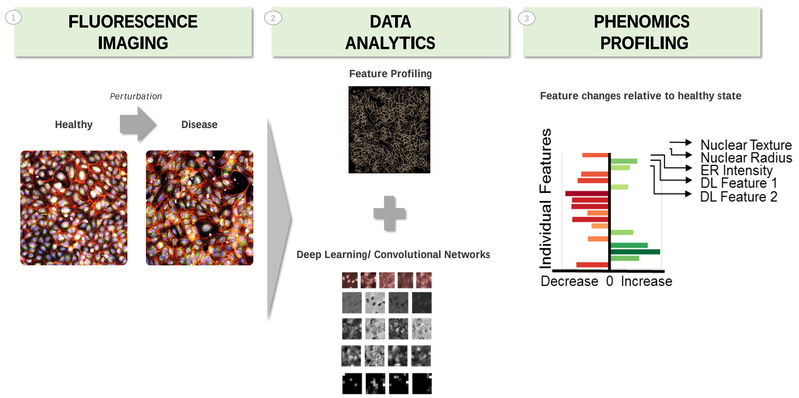
RECURSION pharmaceuticals

At Recursion, we are augmenting phenotypic screening with artificial intelligence to dramatically improve the power of screens, the pace of discovery, and the ability to identify worrisome signals early in the R&D process. The basis of our approach is to broadly probe both disease biology, and the effect of drugs on disease biology, across 1000+ dimensions of cellular morphology in an inexpensive, unbiased, and generalizable image-based assay. While this systems-based approach already affords us high confidence in the translatability of our hits, our application of artificial intelligence methods to our data further increases the power of our approach - allowing us to predict toxicity signatures, novel mechanisms of action, and even hits for diseases that were never tested in the same experiment. Our AI methods are also uniquely advantaged by a massive in-house dataset, which is constantly growing at the rate of 2M cellular images per week, generated across hundreds of relatable experiments. We describe here selected applications of the Recursion technology, which has generated a pipeline of 30+ rare genetic disease programs in ~2 years, rediscovered late-stage clinical assets for multiple conditions at a fraction of the cost, generated new targets in areas such as Immuno-Oncology, and increased screening efficiency by maximizing biological diversity of compound libraries. These data demonstrate Recursion's early progress towards our mission of decoding cellular biology to radically improve lives.

Recursion Approach

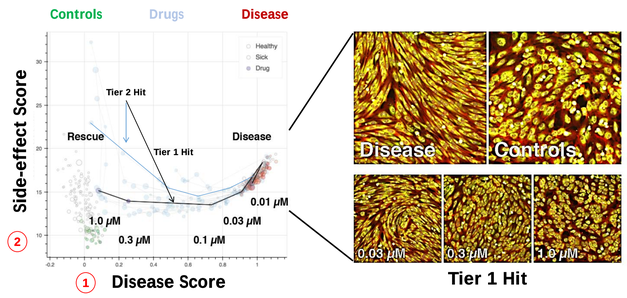
We extract image-based disease phenotypes using computer vision and AI

Cellular structural and functional changes revealed by our biology platform encode robust disease phenotypes



We leverage high-dimensional disease phenotypes in drug screens to find new treatments

Shown is a 2-D graphical representation of high-dimensional phenotypes extracted from control cells, disease cells, and drug treated disease cells. Highlighted is a hit that causes a dose-dependent rescue of the Hereditary Hemorrhagic Telangiectasia cellular phenotype.



Each glyph represents an individual well. The color and size of the dots represent our confidence in the measurements.

We have established an internal pipeline of 30+ programs in just 2 years

HITS SELECTED

- TUBEROUS SCLEROSIS COMPLEX (TSC1)
- CHARCOT-MARIE-TOOTH (MFN2)
- HEREDITARY HEMORRHAGIC TELANGIECTASIA (ACVRL1)
- RETINITIS PIGMENTOSA (MULTIPLE)
- RUBINSTEIN-TAYBI SYNDROME (CREBBP)
- CYSTINOSIS (CTNS)
- EMERY-DREIFUSS MUSCULAR DYSTROPHY/PROGERIA (LMNA)

IN VITRO

- NEUROFIBROMATOSIS TYPE 2 (NF2)
- PEUTZ-JEGHERS SYNDROME (STK11)
- USP7- ULTRA-RARE DISEASE
- LIMB-GIRDLE MUSCULAR DYSTROPHY (POMT1)
- COFFIN-LOWRY SYNDROME (RPS6KA3)
- DARIER DISEASE (ATP2A2)
- HEREDITARY MULTIPLE OSTEOCHONDROMAS (EXT1, EXT2)
- CEREBRAL CAVERNOUS MALFORMATION (KRIT1)
- JP / HEREDITARY HEMORRHAGIC TELANGIECTASIA (SMAD4)
- UNDISCLOSED PARTNER INDICATION PARTNER 1, PROGRAM 1
- UNDISCLOSED PARTNER INDICATION PARTNER 1, PROGRAM 2
- UNDISCLOSED PARTNER INDICATION PARTNER 1, PROGRAM 3
- UNDISCLOSED PARTNER INDICATION PARTNER 1, PROGRAM 4
- UNDISCLOSED PARTNER INDICATION PARTNER 1, PROGRAM 5
- UNDISCLOSED PARTNER INDICATION PARTNER 2, PROGRAM 1

IN VIVO

- SPINAL MUSCULAR ATROPHY (SMN) PROGRAM 1
- SPINAL MUSCULAR ATROPHY (SMN) PROGRAM 2
- DIAMOND BLACKFAN ANEMIA (RPS19)
- METACHROMIC LEUKODYSTROPHY/ATYPICAL GAUCHER DISEASE (PSAP)

PRE-IND

- CEREBRAL CAVERNOUS MALFORMATION PROGRAM 1 *(IND expected Q1, 2018)*
- ATAXIA-TELANGIECTASIA PROGRAM 1 *(IND expected Q1, 2018)*
- ATAXIA-TELANGIECTASIA PROGRAM 2

30+ PROGRAMS

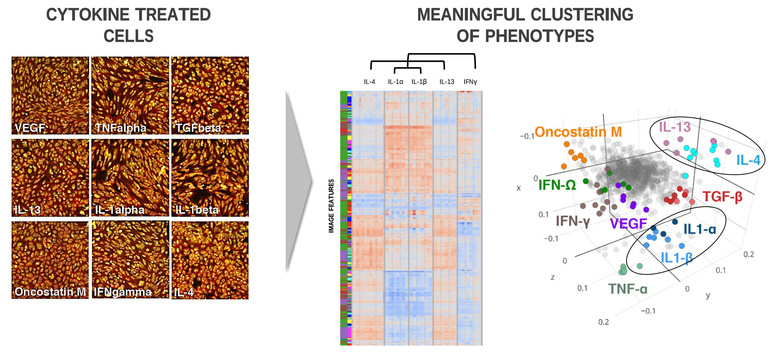
Disease Areas & Discovery Applications

We have developed 100s of unique cellular models of genetic disease

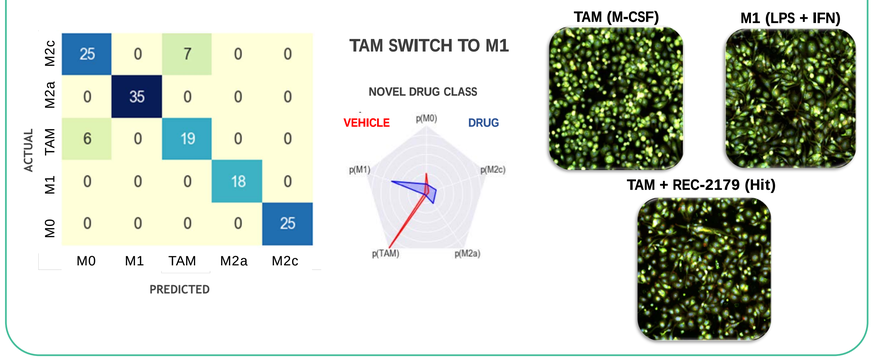
Gene	Disease
ANG	Familial Amyotrophic Lateral Sclerosis
APC	Adenomatous polyposis coli
ASPM	Primary autosomal recessive microcephaly
ATM	Ataxia Telangiectasia
ATP2A2	Brody Myopathy
ATP8B1	Cholestasis
DNAAF3	Ciliary Dyskinesia
CEP290	Leber congenital amaurosis, Joubert, Senior-Loken
CCM2	Cerebral Cavernous Malformation
CNGA3	Achromatopsia-2
CREBBP	Rubinstein-Taybi Syndrome
DHCR7	Smith-Lemli-Optiz Syndrome
DMPK	Myotonic Dystrophy
DNAH5	Primary Ciliary Dyskinesia
DSP	Familial Cardiomyopathy
EFHC1	Juvenile Epilepsy
EXT1	Hereditary multiple exostoses, Langer-Giedion
EXT2	Potocki-Shaffer Syndrome
FAM161A	Retinitis Pigmentosa
GALNS	Mucopolysaccharidosis Type IV (Morquio)
HFE	Hemochromatosis
KMT2D	Kabuki syndrome
KRIT1	Cerebral Cavernous Malformation
LCA5	Leber congenital amaurosis
LRRK2	Inherited Parkinson disease

Gene	Disease
MANBA	Mannosidosis Beta
MFN2	Charcot-Marie-Tooth
MID1	Opitz GBBB syndrome, Type 1
MTM1	Myotubular myopathy, X-linked
NBN	Aplastic Anemia, ALL, Nijmegen breakage syndrome
NF2	Neurofibromatosis Type II
NIPBL	Cornelia de Lange Syndrome
PABPN1	Oculopharyngeal muscular dystrophy
PEX13	Zellweger syndrome
PKHD1	Polycystic Kidney / Hepatic Disease
PRPF31	Retinitis Pigmentosa
PSAP	Combined SAP, Atypical Gaucher, Krabbe Disease
RPS10	Diamond Blackfan Anemia
RPS19	Diamond Blackfan Anemia
RPS6KA3	Coffin-Lowry Syndrome
SCN8A	Cognitive impairment with or without cerebellar ataxia
SMAD4	Hereditary Hemorrhagic Telangiectasia
SMARCB1	Coffin-Siris Syndrome
SMN1	Spinal Muscular Atrophy
STK11	Peutz-Jeghers Syndrome
STX11	Hemophagocytic Lymphohistiocytosis
TCOF1	Treacher Collins Syndrome
TP53	Cancers (various)
TSC2	Lymphangioleiomyomatosis
UBA1	Spinal Muscular Atrophy

We have over 40 cytokine phenotypes for novel inflammation, auto-immunity, and oncology drug discovery

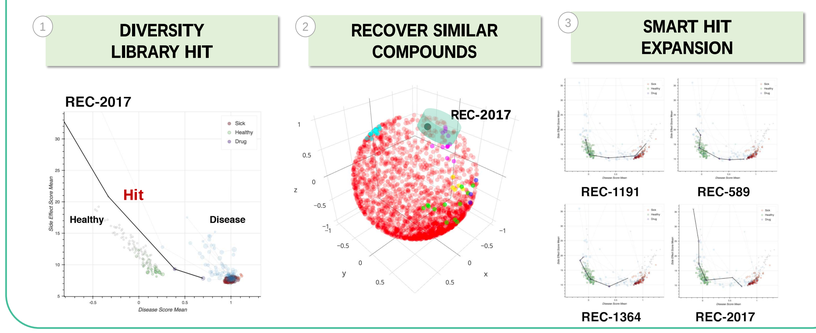


We are applying ML to complex macrophage phenotypic states and discovering novel IO targets



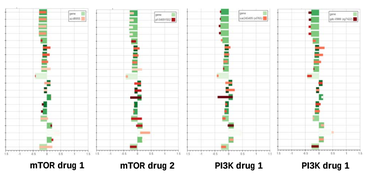
We can generate efficient smart libraries with phenotypic profiling

We can shrink the size of a parent library by 80% or more by maximizing for biological diversity after phenotypic profiling.



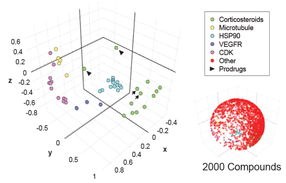
We can predict targets and MoA using AI

HIGH-DIMENSIONAL PHENOTYPES RECAPITULATE MECHANISMS



Compounds with similar MOA have similar impact on individual disease phenotypes. Shown here are different PI3K family inhibitors that differ in selectivity and show corresponding differences in top 4 features.

CLUSTERING OF HIGH-DIMENSIONAL PHENOTYPES:



Machine learning techniques enable clustering of phenotypes to reveal compound MOA or pathways. Note corticosteroids cluster tightly from phenotypic data with compounds that are not bioactive in cell based assays (prodrugs) clustering separately.

SHORT TERM

RARE GENETIC DISEASE

100+ repurposed or rare genetic disease treatments by 2025

INTERMEDIATE TERM

NEW INDICATIONS

Expand the search space:
1) New therapeutic areas
2) New chemical entities

VISION

SYSTEMS BIOLOGY

Leverage technology to map human cellular biology