AURON THERAPEUTICS

[Changing Cancer Cell States to Change the Future for People living with Cancer]

Non-confidential deck

October 2023

Auron™

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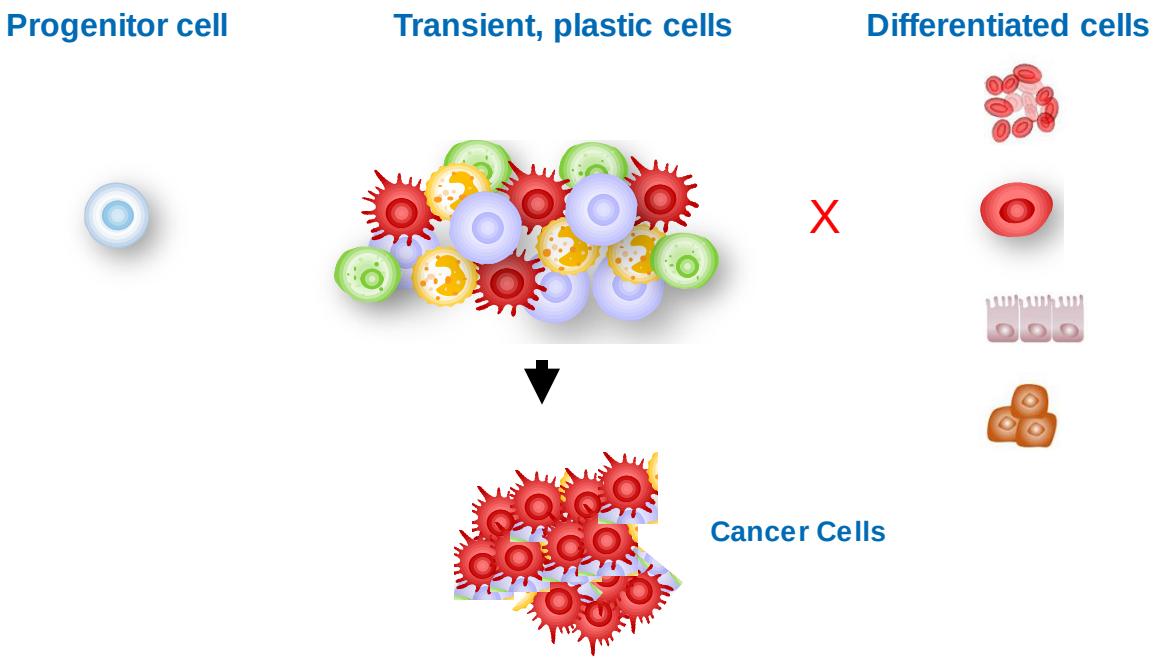
Platform-based, product-driven company that uses artificial intelligence (AI) to target the plastic cell states of cancer

Disruption of normal cell differentiation induces cell state plasticity and proliferation of cancer cells



Drivers of cell state plasticity offer new therapeutic targets for oncology

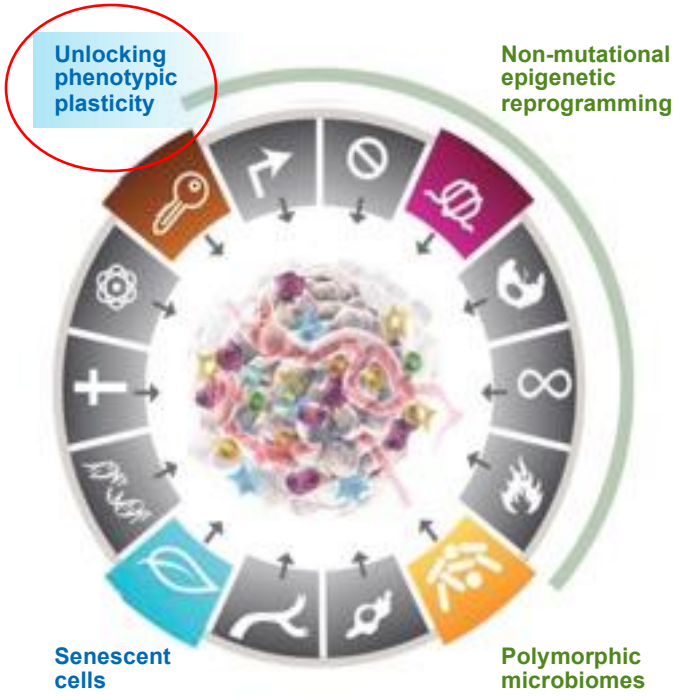
- AI algorithms identify targets with higher probability of biological validation and higher probability of success (PoS) in the clinic
- Platform already has delivered two validated programs with a third in validation

Better, faster, cheaper drug development with higher PoS

Citation

The scientific community is focused on targeting plastic cell states, which are a 'hallmark of cancer'

Hanahan, Cancer Discovery 2022; A Missing Hallmark of Cancer



Growing enthusiasm in the scientific and medical community

nature cancer

Review article https://doi.org/10.1038/s43018-023-00595-y

Cancer cell plasticity during tumor progression, metastasis and response to therapy

Unraveling the dangerous duet between cancer cell plasticity and drug resistance

Namrata Chatterjee[1] | Bhavana Pulipaka[2] | Ayalur Raghu Subbalakshmi[3] | Mohit Kumar Jolly[3] | Radhika Nair[4,5]

nature > signal transduction and targeted therapy > review articles > article

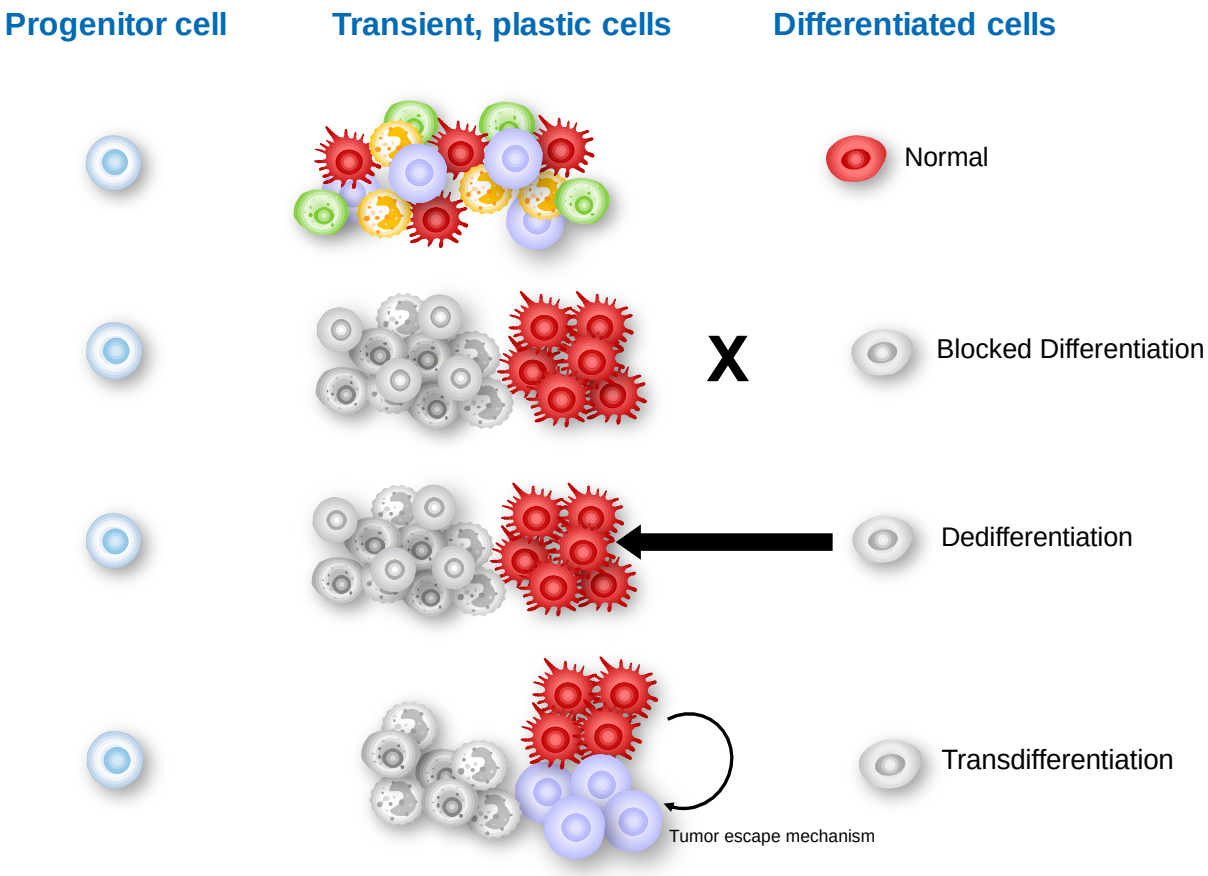
Review Article | Open Access | Published: 07 October 2020

Emerging role of tumor cell plasticity in modifying therapeutic response

The leader in the discovery and development of therapies targeting plastic cell states of cancer

Additonal citations on slide x

Plastic cell states arise when cancer cells disrupt normal developmental pathways



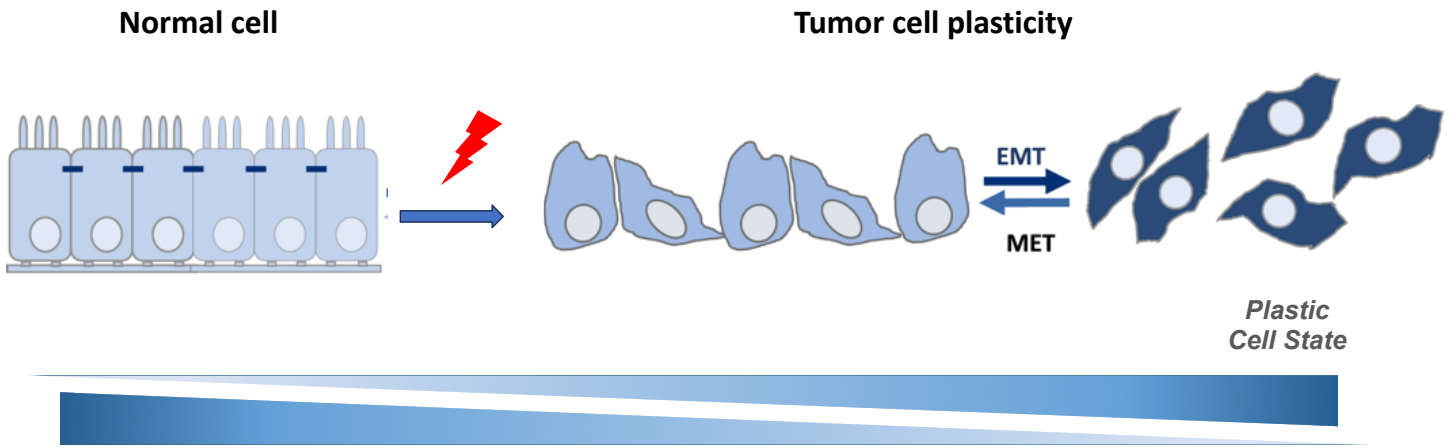
- During normal development, cells go through a plastic, proliferative state on their way to becoming mature, terminally differentiated stable cell
- Reprogramming of cancer cells prevents maturation and shifts the cells to a more plastic and proliferative cell state

Cancer cell plasticity causes significant clinical problems

Citation

Plastic cell states are a root cause of metastatic and drug-resistant tumors

Make cell figures consistent
with slides 2 and 4



- ***Metastatic (EMT Tumors)***
- ***Drug Resistant*** *(a**EGFR**,* a*AR*, a*SOC)*

Targeting pathways that regulate plastic cell states can combat metastases and drug-resistance

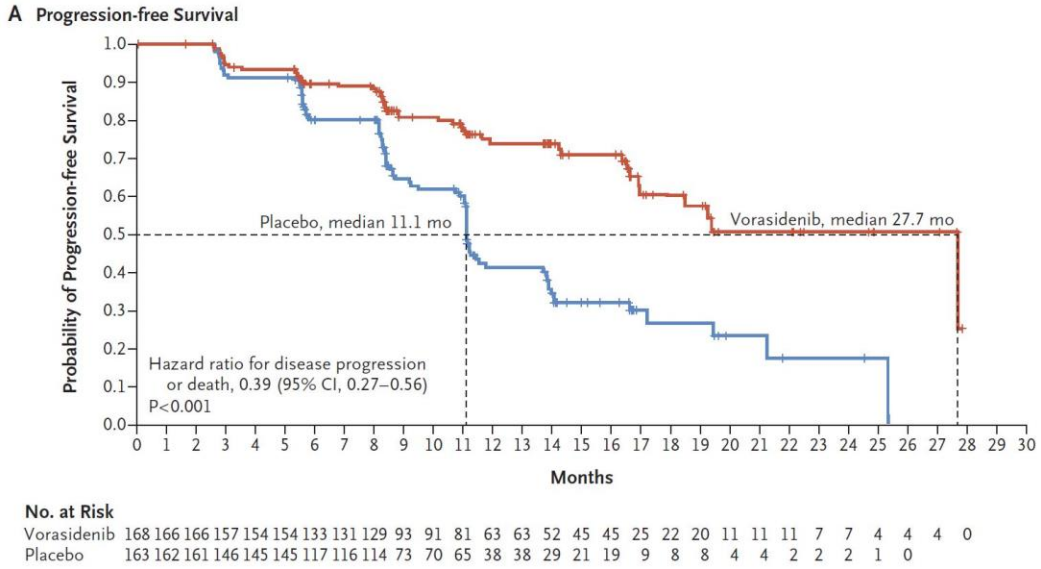
Citation

Shifting cell state is clinically validated in solid and heme tumors

Clinical validation from approved products and late-stage clinical development candidates

Therapy	Solid Tumors	Hematologic Tumors	FDA
VESANOID® Atra	neuroblastoma	APL	Approved
IDHIFA® Enasidenib		AML	Approved
TIBSOVO® Ivosidenib	cholangiocarcinoma	AML	Approved
Vorasidenib	low-grade glioma		Fast Track
Revumenib		AML	Fast Track

Vorasidenib's remarkable Phase 3 data presented in plenary session at ASCO 2023



Founders led discovery and development of three IDHm inhibitors targeting disrupted cell states in solid in heme tumors

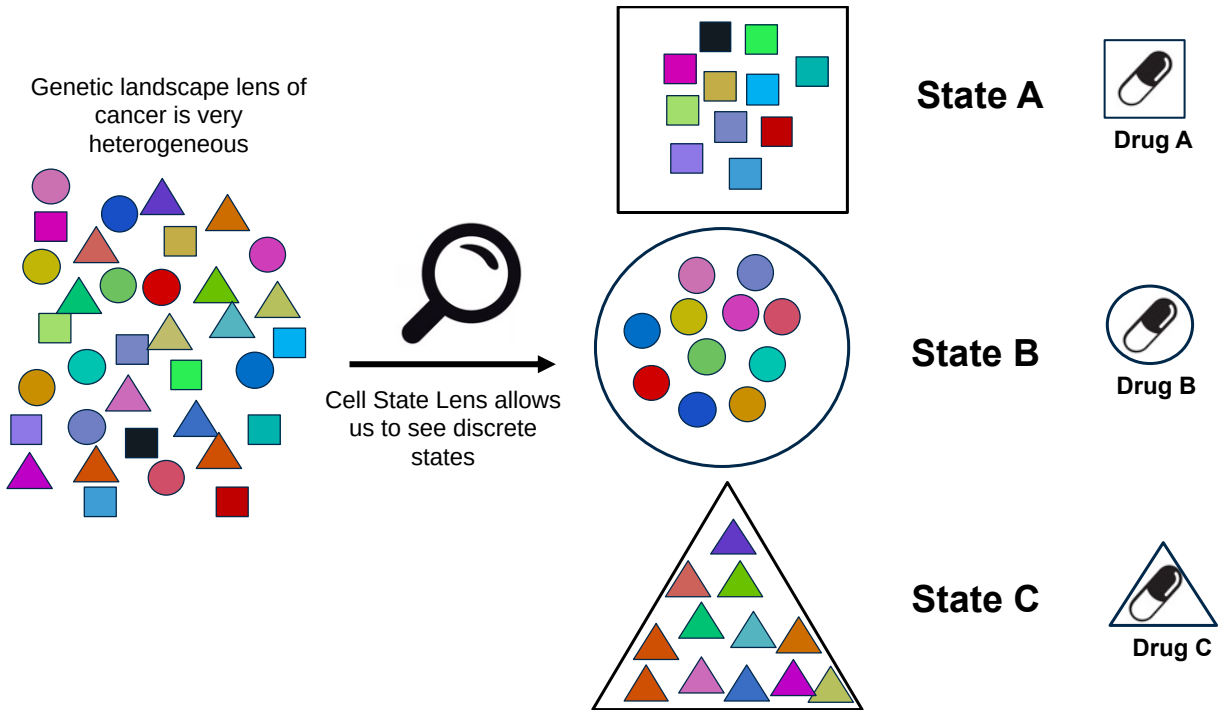
Mellinghoff, NEJM 2023

We have a *novel* approach to tackling a *known* clinical problem

We classify tumors based on developmental cell state vs. genetic mutation

The cell state lens is getting lost in this figure..

- Make simpler, less colors and shapes
- Go back to people



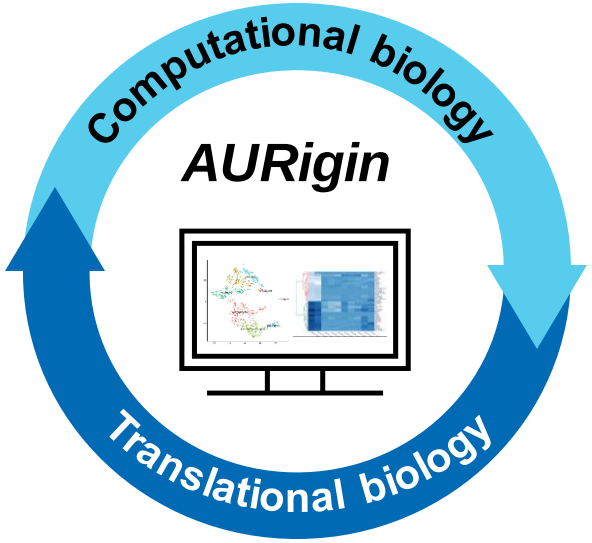
- Shapes represent gene mutations
- Colors?

Targeting cell state offers new opportunities to fight cancer heterogeneity, metastasis, and drug resistance

Citation

Our validated product engine delivers therapies that target plastic cell state

Our AI Platform, AURigin™, provides…



…efficient drug discovery and development

- Rapid identification of targets that drive cell state
- High success rate of target validation in relevant cell state cancer models
- Cell state biomarkers for patient selection
- Efficacy biomarkers

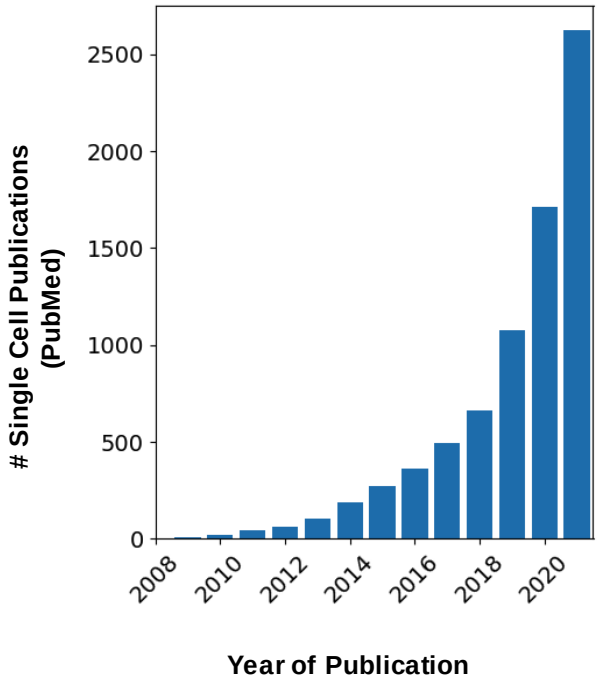
Higher PoS in discovery and higher PoS in clinical development

Citation

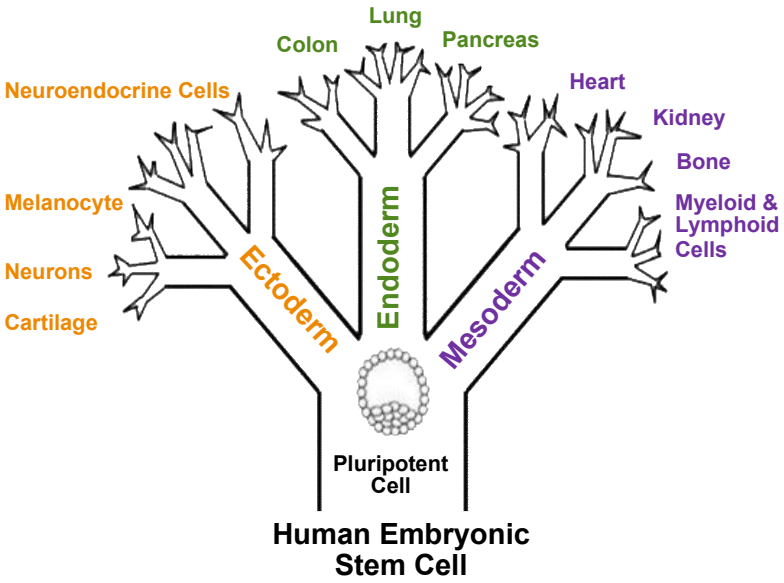
AURigin

We use AURigin to identify the drivers of plastic cell states in tumors

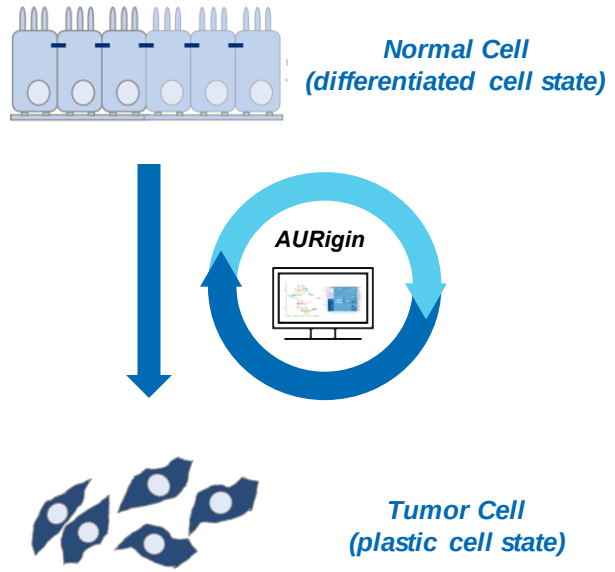
Explosion of single cell-omics datatsets…



…allows us to build a high resolution map of normal human development…



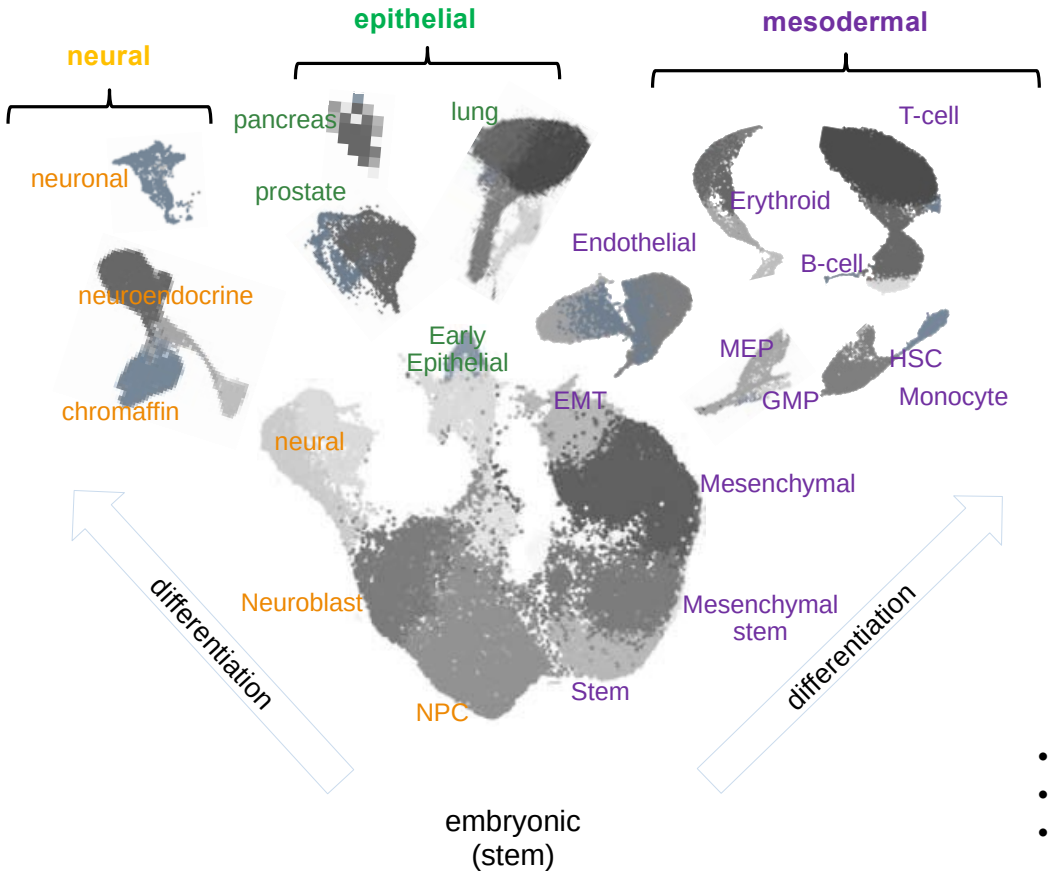
…and define an AI/ML paradigm to identify drivers of plastic cell state in tumors



Significant first mover advantage in newest frontier for oncology drug development

Put in tree reference if we do not redraw with graphic artist

First, we build an atlas of human cell development to define normal cell states



Proprietary AI algorithms used to create a map of normal cell states

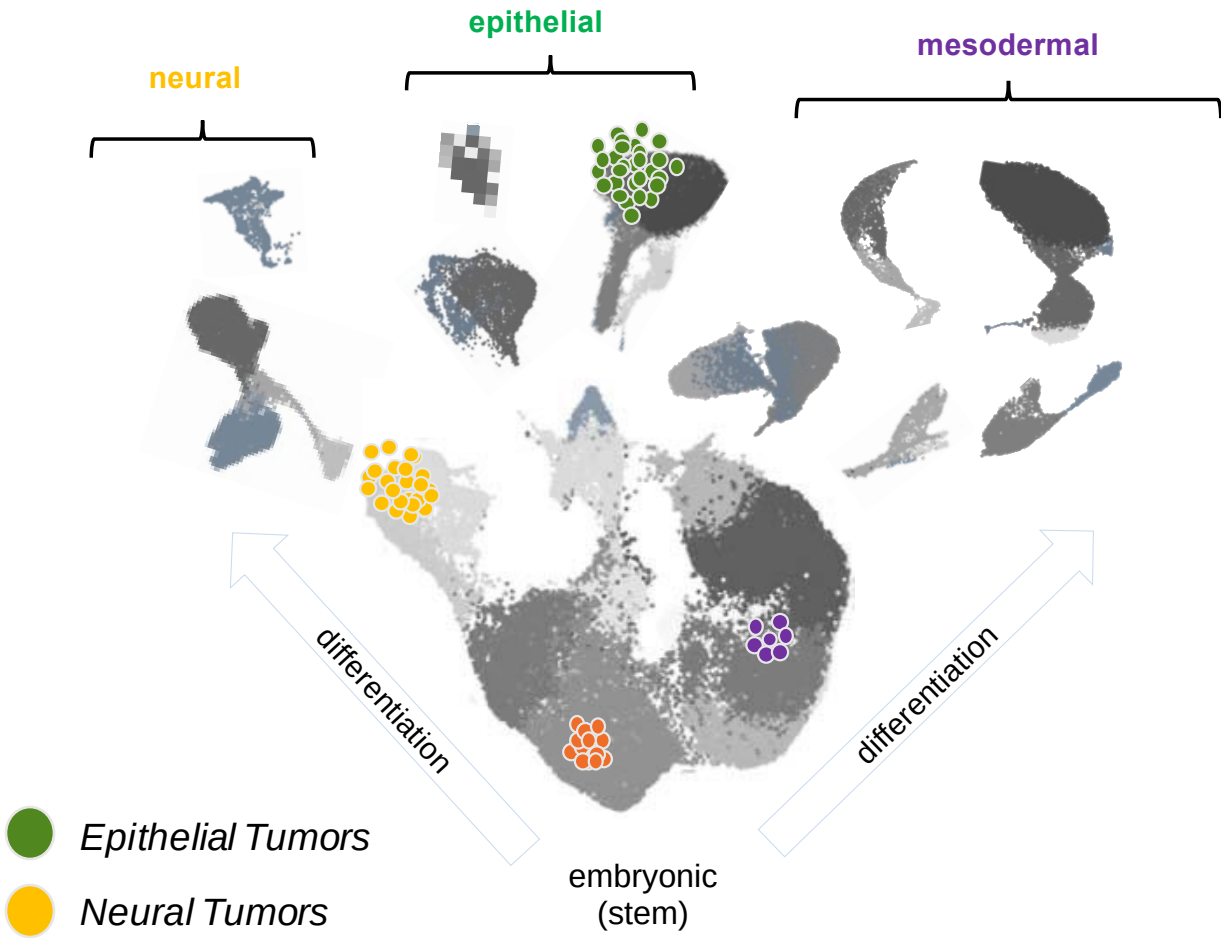
- Define the normal states of human development using single cell -omics data
- Train ML classifiers to define developmental cell states of a tumor sample

- Proprietary ***Normal Cell State Classifiers***
- Currently >200 normal states mapped
- Comprising > 1000 donors

The most comprehensive proprietary atlas of normal human development

Citation

Second, we map tumors to our atlas to define their disrupted cell state



- Use proprietary cell state classifiers to define the cell state of primary patient tumors
- AURigin enables an understanding of inter- and intra-tumor heterogeneity of patient samples
- We have integrated data from thousands of public and private primary patient tumor samples

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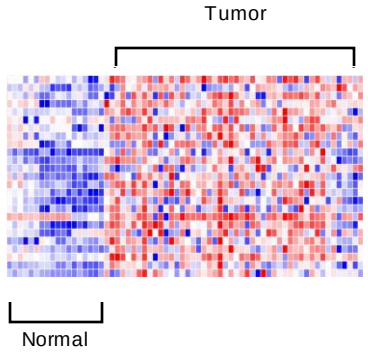
Third, we computationally compare normal and tumor cells to identify master regulators driving plastic cell state

Differential expression between tumor and normal reference cell state

Target ID: Drivers of plasticity and differentiation



AURigin-DRIVE$_{REG}$
AURigin-DRIVE$_{PATH}$

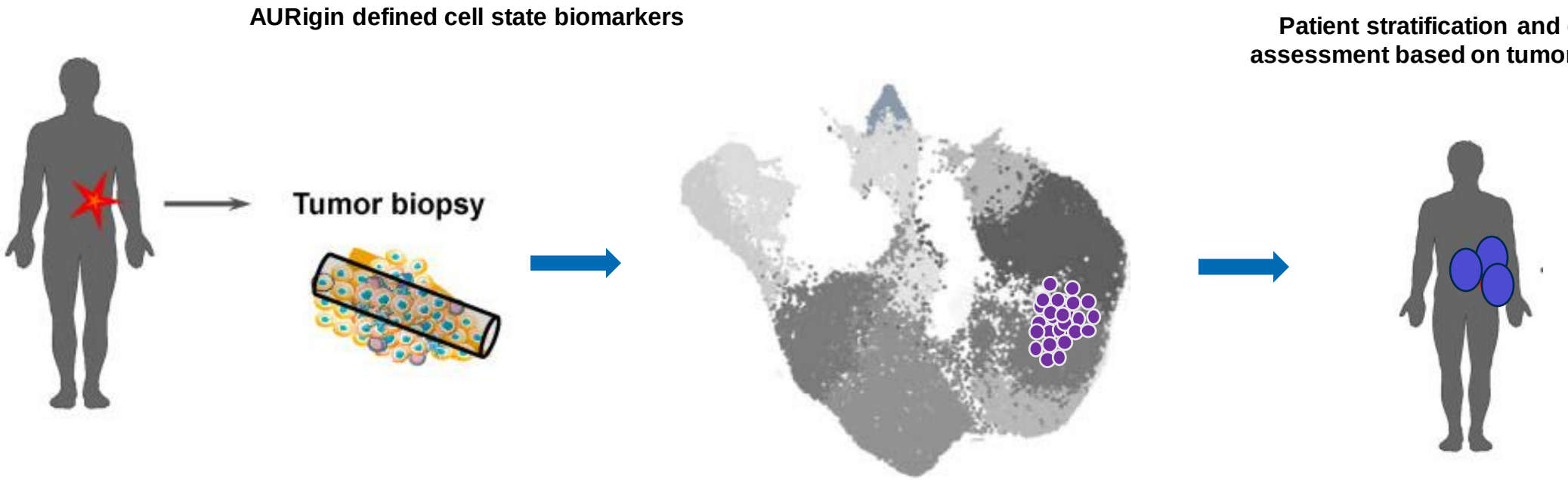
Compare normal versus tumor state

Apply our proprietary ML algorithms to prioritize the master regulators driving cell state

Triage targets for biological validation

Finally, we pair drug targets with cell state response and efficacy biomarkers

AURigin identifies unique cell state biomarkers that are used to select patients and assess efficacy



We know which patients we want to treat based on cell state

Finally, we pair drug targets with cell state response and efficacy biomarkers

AURigin defined cell state biomarkers

Patient stratification and efficacy assessment based on tumor cell state

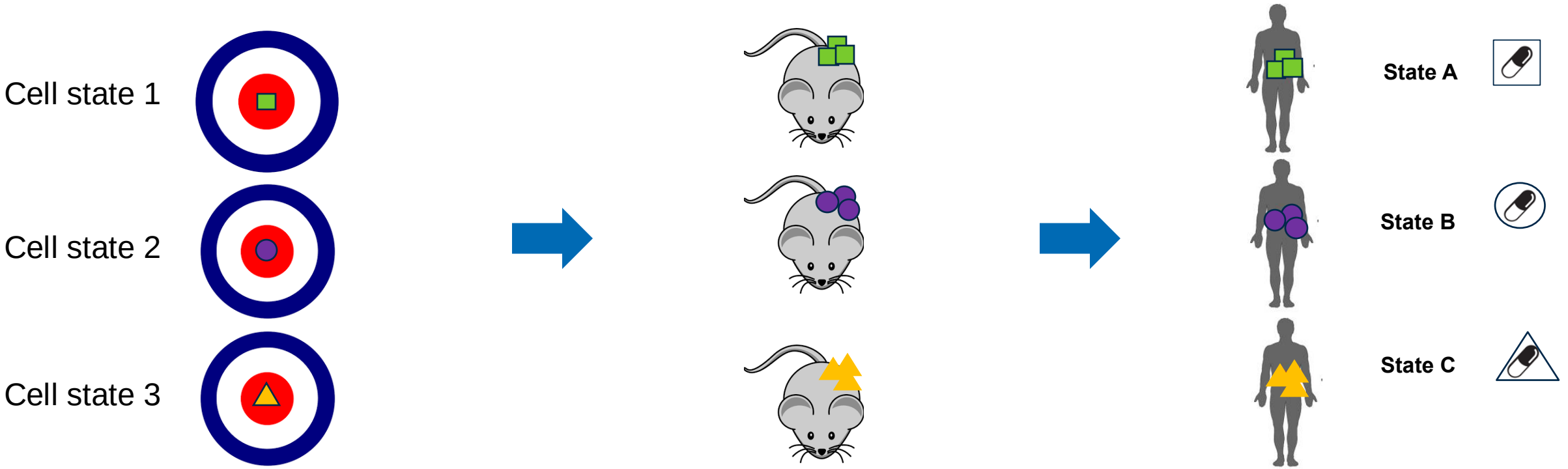
We know which patients we want to treat based on cell state

AURigin accelerates drug discovery and increases PoS in the clinic

Cell state specific ML derived high-quality targets

Cell state specific models for target validation

Cell state specific biomarkers for patient selection and efficacy assessment



Focus on cell state to identify the right targets, the right models, and the right patients

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Therapies targeting cell state are well suited for single agent activity and for use in combination

TIBSOVO®
ivosidenib tablets 250mg

IDHIFA®
(enasidenib) tablets
100mg • 50mg

AUGMENT-101

INDIGO | INVESTIGATING VORASIDENIB IN GLIOMA

- Therapies targeting cell state have been shown to work as monotherapy in relapsed/refractory patient populations
- Targeting the cell state can be combined with other therapeutic mechanisms in the frontline:
  - additive/synergistic to standard of care therapies
  - sensitization/resensitization to standard of care therapies

Fast approval as monotherapy in late line and expand rapidly with combination in frontline

Citation

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Platform-Generated Pipeline

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Platform-generated portfolio addresses large market opportunities to treat both solid tumors and hematological malignancies

Program	U.S. Patient Population	Targeted Subset	Target ID	Target Validation	Lead Discovery	Lead Optimization	Development Candidate	IND	FPI	Clinical PoC
Lead							Q1 '24	Q4 '24	Q1 '25	[2026]
• SCLC	30K/yr	70%								
• NEPC	50K/yr	[___]								
• AML	20K/yr	25%								
2nd						2024	2025	TBD	TBD	TBD
• SCLC	30K/yr	[___]								
• Colorectal	[___]	[___]								
3rd				2024	2024	2025	TBD	TBD	TBD	TBD
• EMT tumors	[___]	TBD								

Clinical PoC in solid tumors and hematological malignancies in [2026]

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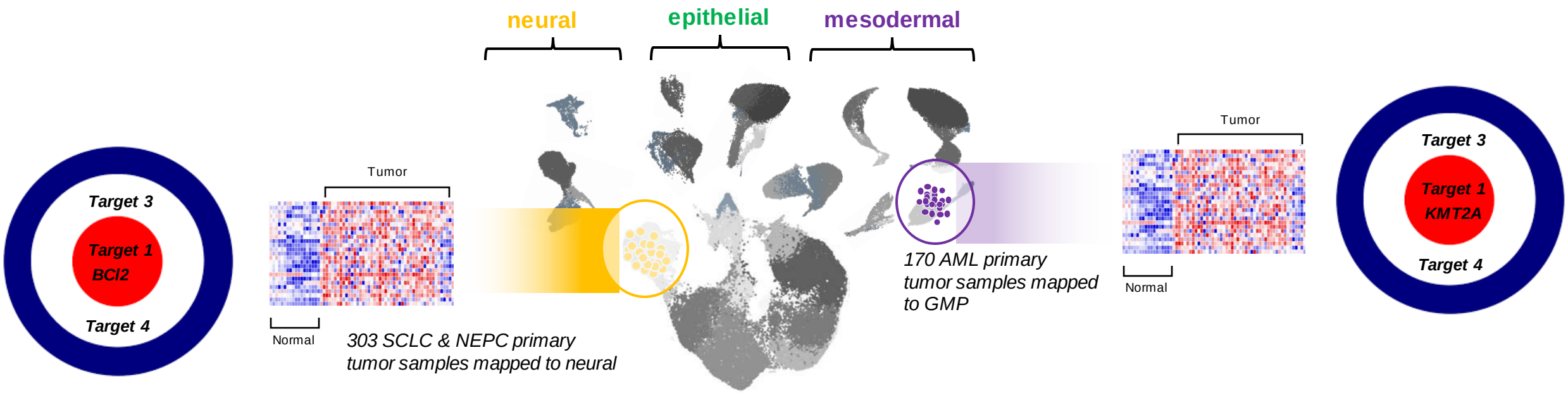
Our lead program was derived from our platform and is validated in 3 indications

Target 1 was identified in two cell states alongside other known, clinical targets, validating the platform



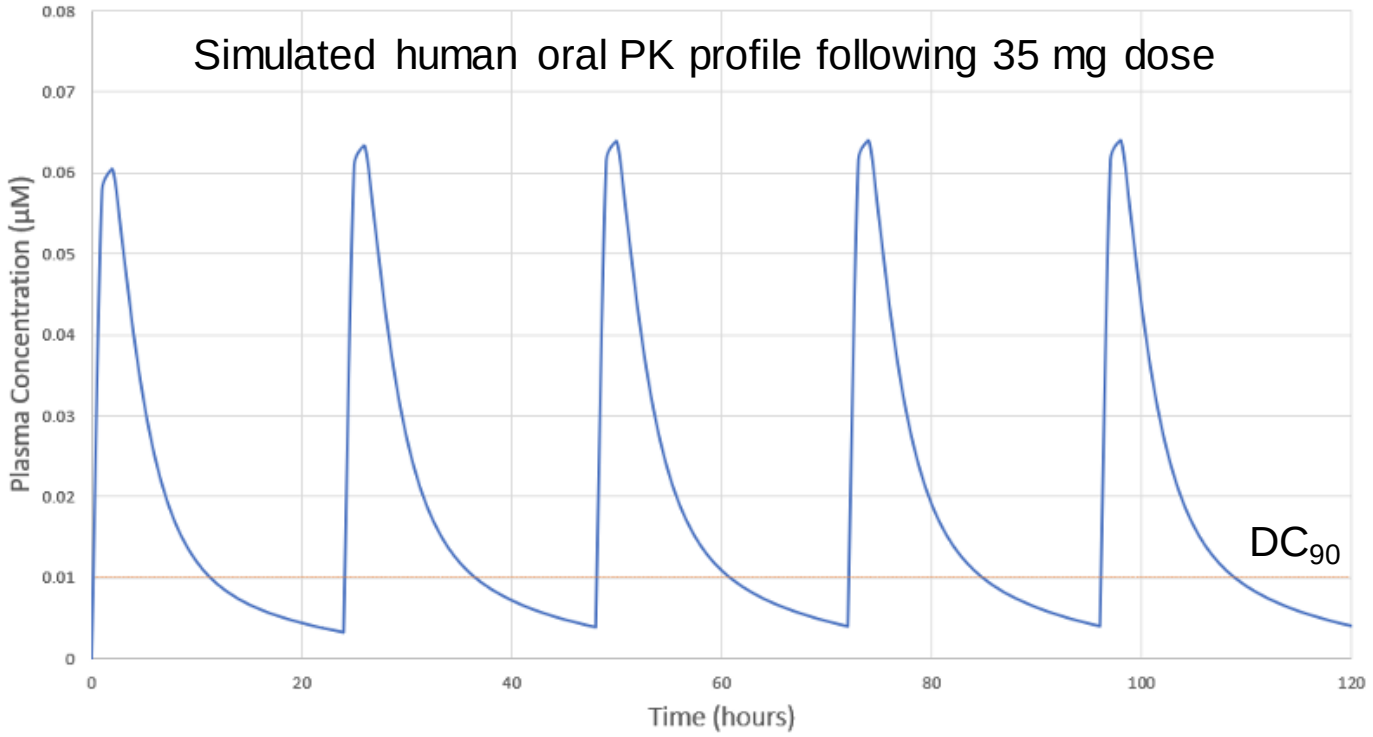
Validated in SCLC, NEPC, and AML with additional opportunities in tumors with neural and mesenchymal cell states

Citation

We have developed a novel orally bioavailable degrader to Target 1 that is entering non-GLP Tox: AUR1959

DC Criteria	AUR1959
Highly Potent & Selective	✓
Solubility & drug-like properties	✓
Oral bioavailability	✓
Low drug-drug interaction potential	✓
TI ≥ 1 (preclinical models)	✓
Low developability risk (DCS)	✓
Non-GLP Tox	Pending

AUR1959 is a potent and orally bioavailable degrader with a low predicted human dose

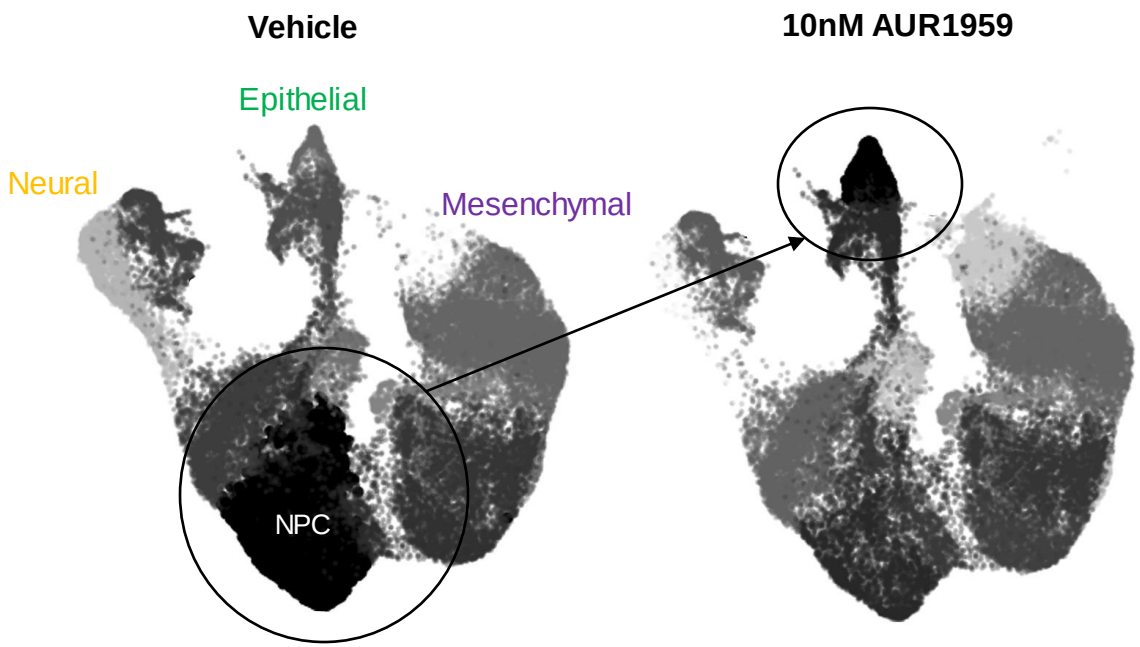


Development candidate nomination in Q1 2024

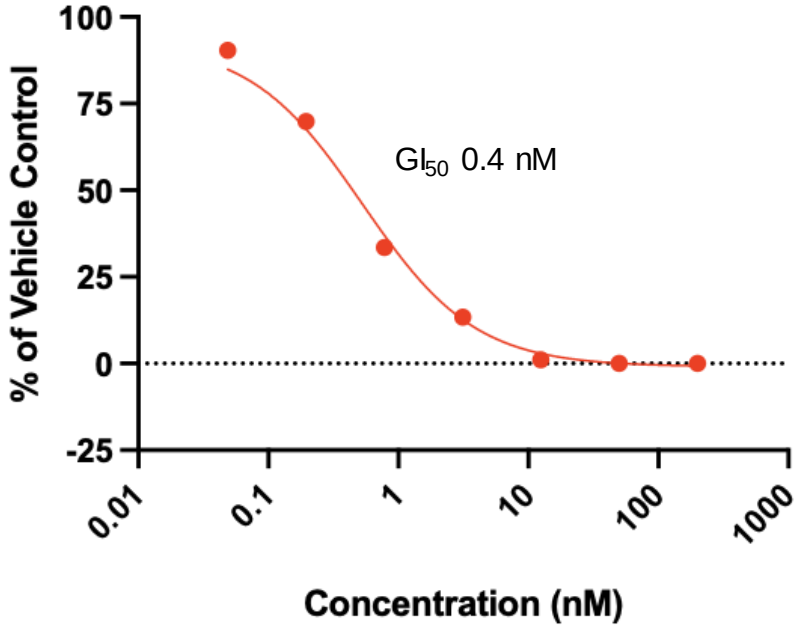
*Additional data available

In SCLC, degrading Target 1 shifts cell state, leading to growth arrest

AUR1959 induces cell state switch from neural progenitor (NPC) to adult epithelial*



AUR1959 induces potent growth effects in patient derived organoid models of SCLC

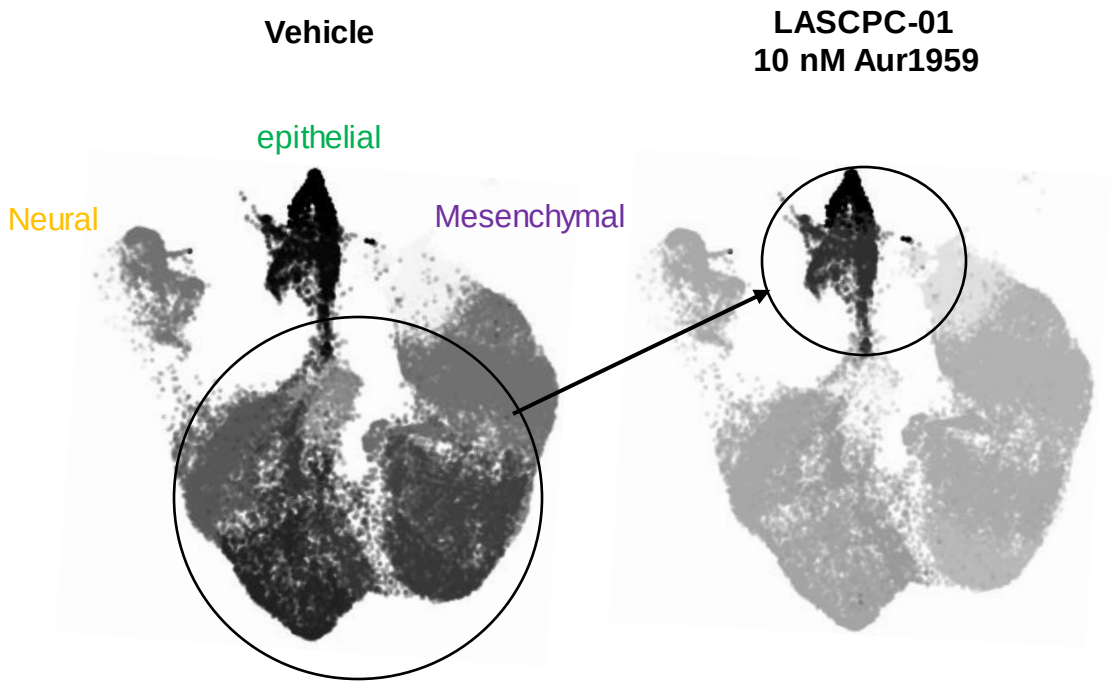


Validated in >70% of the SCLC patient population (>20,000 patients per year)

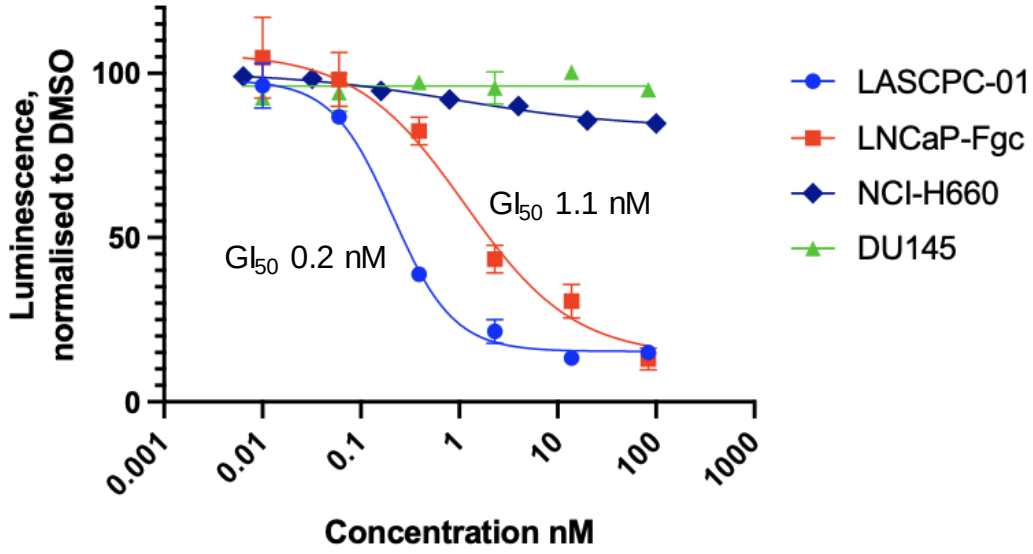
*Additional data available

In NEPC, degrading Target 1 shifts cell state, leading to growth arrest

AUR1959 induces cell state switch from neural progenitor (NPC) to adult epithelial*



AUR1959 induces potent growth inhibition in multiple NEPC cell lines

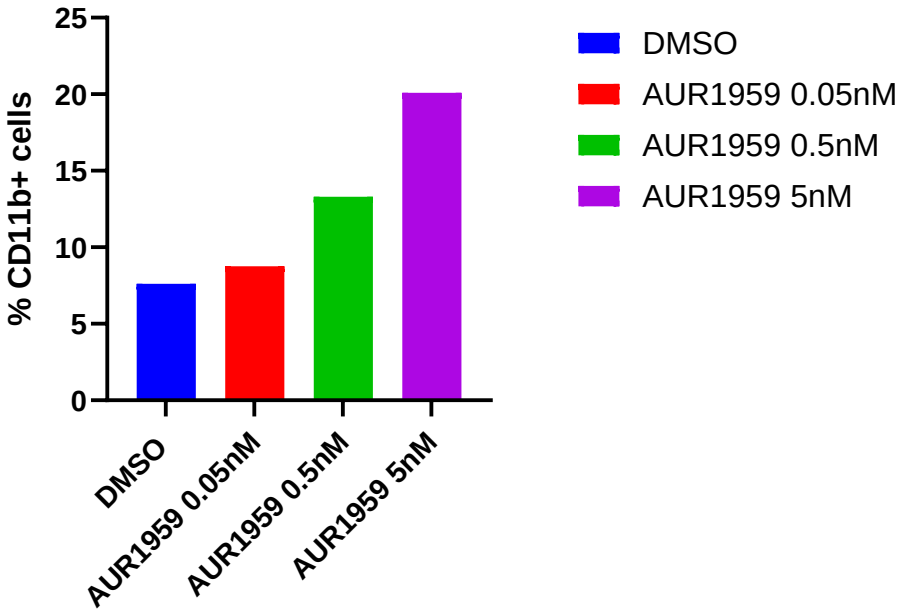


Initial validation in NEPC (large proportion of >50,000 patients per year expected to respond based on cell state)

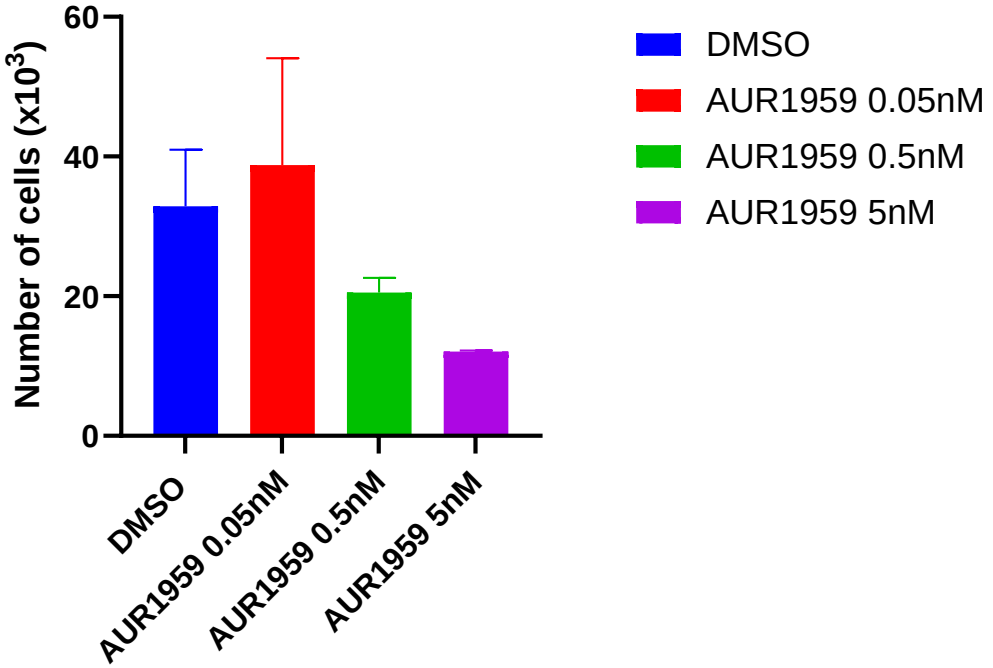
*Additional data pending

In AML, degrading Target 1 shifts cell state, leading to growth arrest

AUR1959 induces differentiation in AML primary patient sample



AUR1959 induces potent growth inhibition in AML primary patient sample

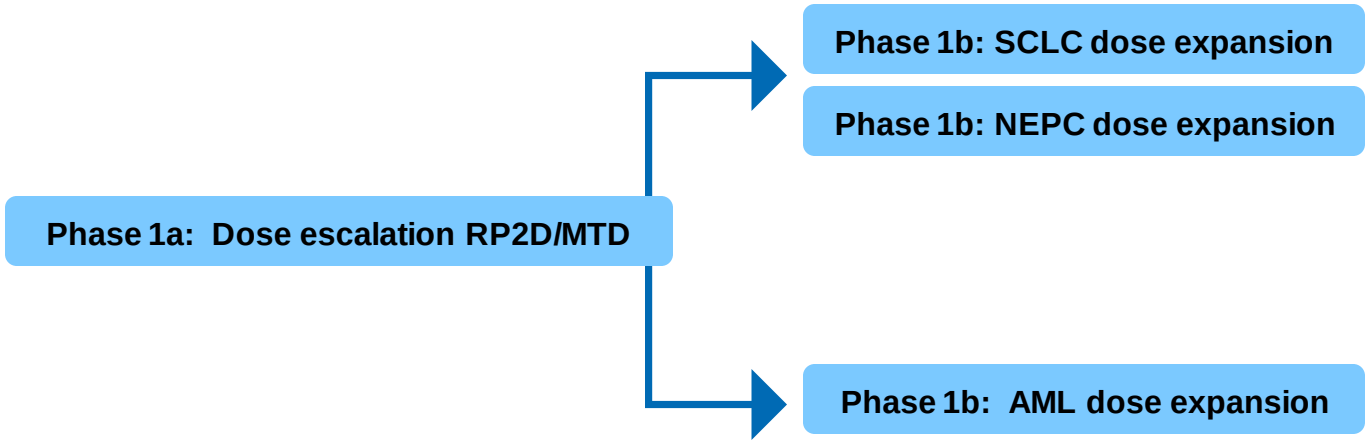


Validated in >25% of AML patient population (>5,000 patients per year)

*Additional data available

We will develop AUR1959 in solid tumors and heme malignancies with high unmet medical need

Phase 1a/b in relapsed/refractory patient population



Early registration opportunities

Solid tumor P1 study endpoints:

- ***SCLC: PFS >5 months vs 2-3 mons (historical controls), expand for registration in multiply pretreated metastatic population***
- ***NEPC: PFS >X months***

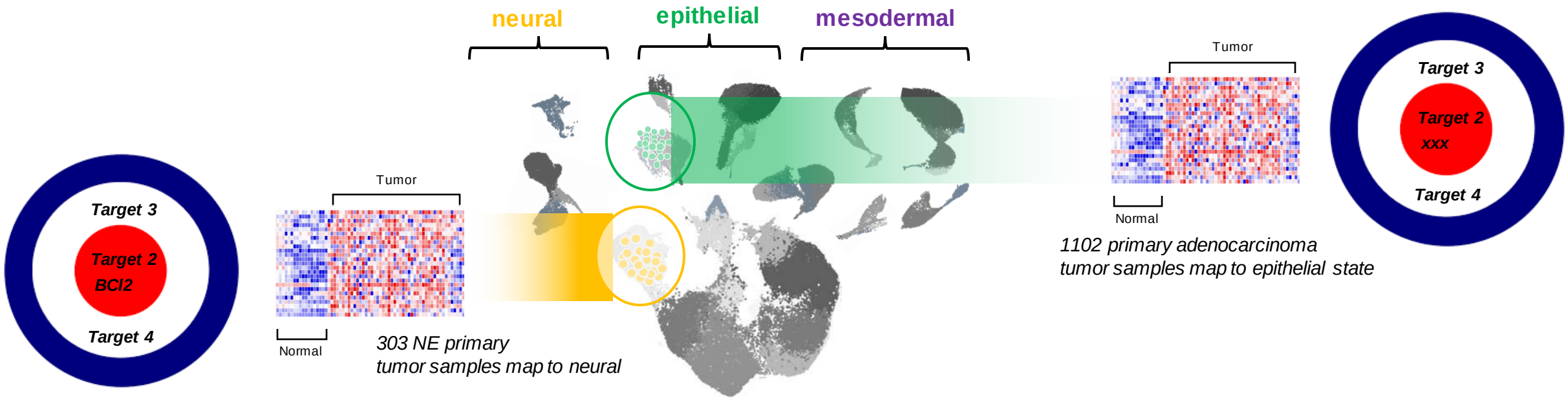
AML P1 study endpoints:

- **CR/CRh ≥ 20%, expand for registration in R/R population**

Capital efficient opportunity for early registration in late line indications with clear path to frontline combinations

Our 2nd program was derived from our platform and is validated in 2 indications

Target 2 is non-overlapping with Target 1 in SCLC and was identified alongside other known clinical targets, validating platform



Validated in SCLC, initial validation in colorectal with additional opportunities in tumors with neural and epithelial cell states

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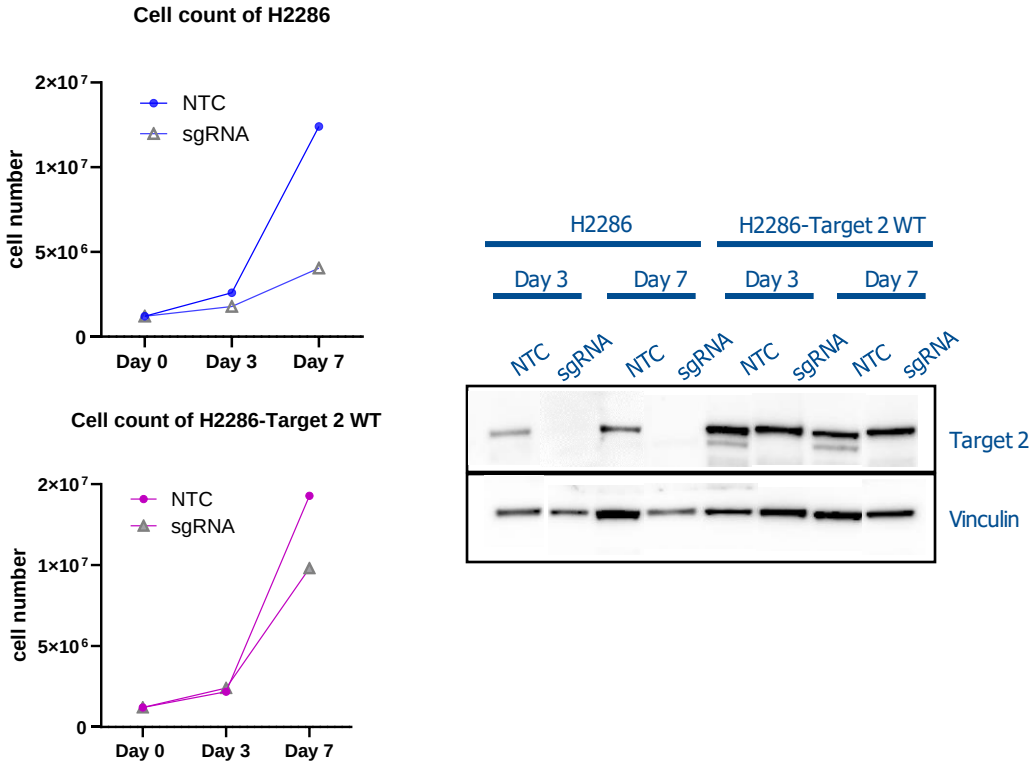
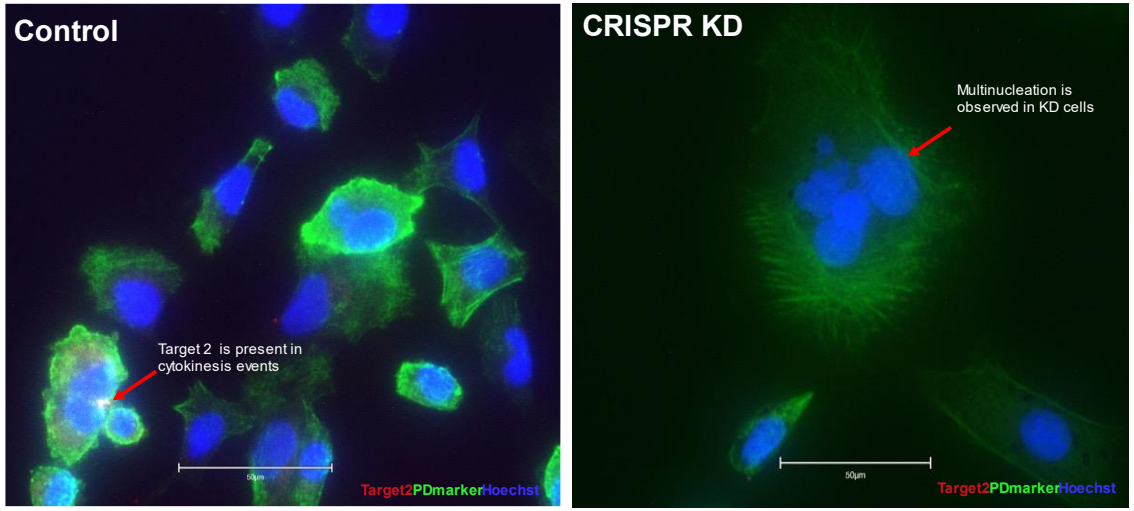
In SCLC, knock down of Target 2 leads to growth arrest and multi-nucleation

CRISPR knock down of Target 2 induces growth arrest which is rescued by WT add back



CRISPR knock down induces multi-nucleation phenotype which is indicative of on target mechanism

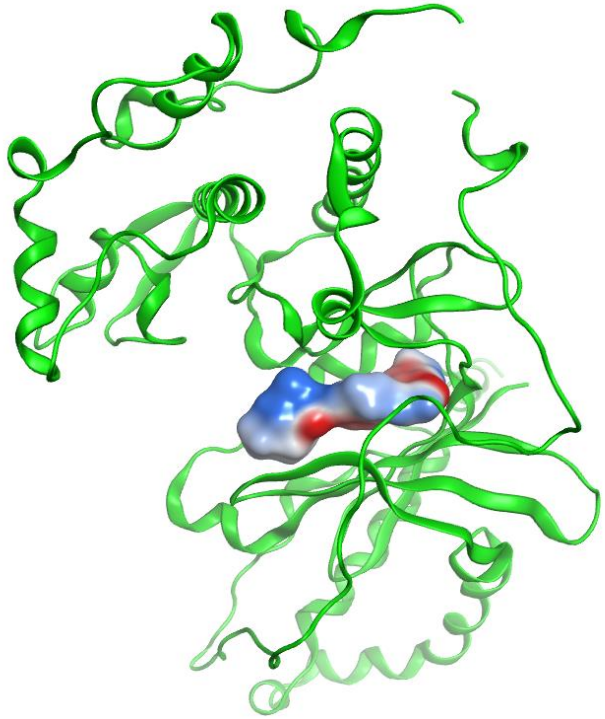


Strong genetic validation in SCLC

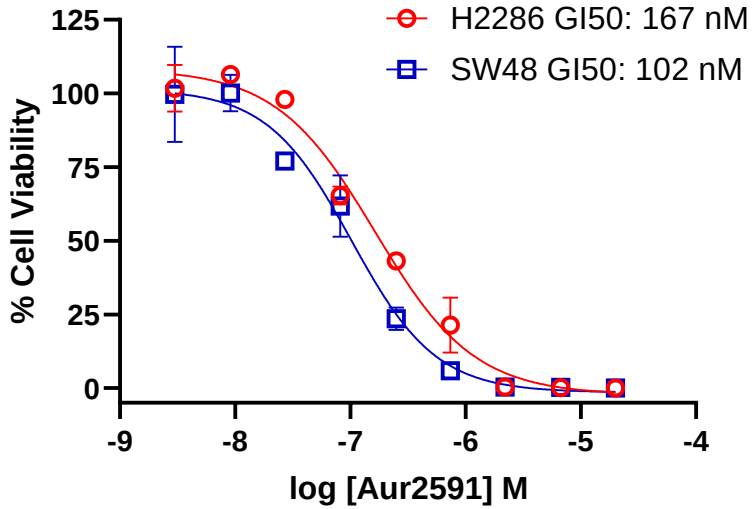
*Additional data available

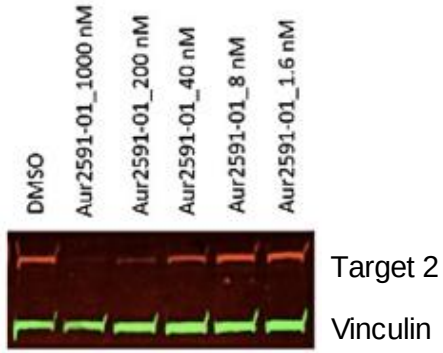
We designed potent inhibitors and degraders of Target 2

Structural modeling guiding design of potent inhibitors and degraders of Target 2



Potent degrader of Target 2 induces growth Inhibition in SCLC and colon cell lines

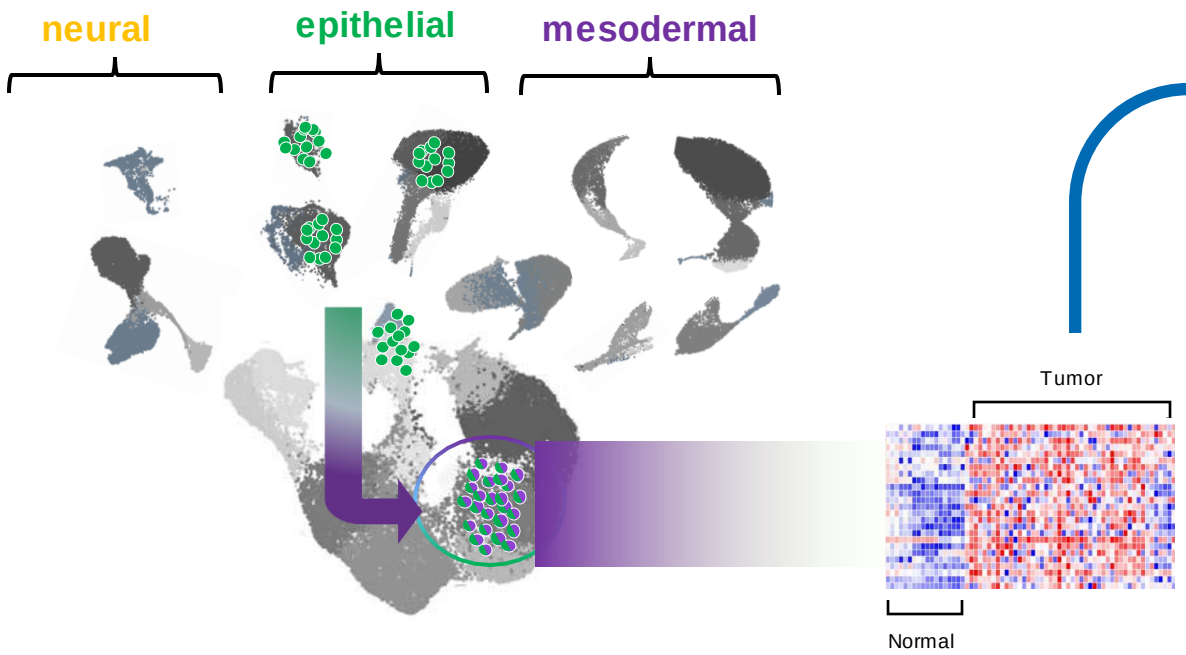




Opportunity to accelerate lead optimization

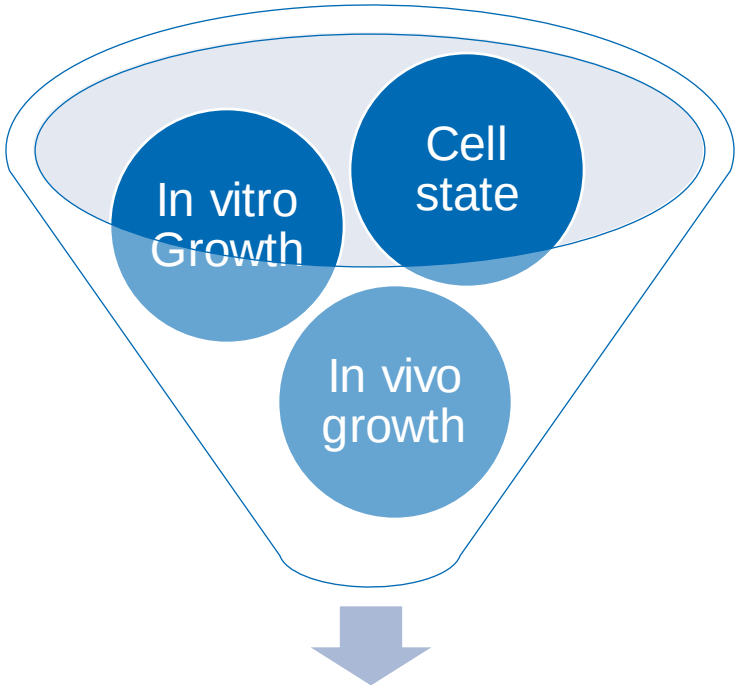
*Additional data available

Our 3rd program has identified targets for highly aggressive, drug-resistant epithelial-mesenchymal transition (EMT) Tumors



2,991 primary adenocarcinoma tumor samples mapped across epithelial to mesenchymal cell states

High through-put Perturb-seq screen on 500+ targets



- ***Rapid validation of multiple targets***
- ***Optimization of AURigin ML***
- ***In-licensing opportunities***

Targeting cell state is a well suited to address EMT tumors

AURON THERAPEUTICS

Team

Auron is led and financed by an experienced, successful and diverse team

Leadership Team

- **Kate Yen, PhD**
  - Chief Executive Officer
- **Dave Millan, PhD**
  - Chief Scientific Officer
- **Andrea Armstrong**
  - Chief People Officer
- **Laura Antipov, PhD**
  - VP, Portfolio
- **Chris Guiffre, JD, MBA**
  - President & COO
- **Tom Graeber, PhD**
  - Chief Data Officer
- **Colleen DeSimone**
  - SVP, Finance
- **Mark Bittinger, PhD**
  - VP, Biology

Board and Investors

- **Briggs Morrison, MD**
  - Independent chair
- **Alexandra Cantley, PhD**
  - Director
- **Anna French, PhD**
  - Director
- **Alon Lazarus, PhD**
  - Director
- **Vickie Richon, PhD**
  - Independent director
- **Eric Shiozaki, PhD**
  - Director
- **Kate Yen, PhD**
  - CEO & Director

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DC|Bio

CASDIN CAPITAL

Lilly

MUBADALA

APOLLO HEALTH VENTURES

American Cancer Society /BrightEdge

Auron was founded by experts and is advised by thought leaders

Our founders are experts in the plastic cell states of cancer

- **Kate Yen, PhD**
  - Auron
- **Matt Vander Heiden, MD, PhD**
  - MIT
- **Ross Levine, MD**
  - Memorial Sloan Kettering Cancer Center
- **Eytan Stein, MD**
  - Memorial Sloan Kettering Cancer Center

Our scientific advisory board members are thought leaders in multi-omic platforms, translational biology, drug discovery and clinical development

- **Stephane de Botton, MD, PhD**
  - IGR
- **Richard Chesworth, PhD**
  - Former CSO, Kymera
- **Ross Levine, MD**
  - Memorial Sloan Kettering Cancer Center
- **Misha Roshal, MD, PhD**
  - Memorial Sloan Kettering Cancer Center
- **Charles Rudin, MD, PhD**
  - Memorial Sloan Kettering Cancer Center
- **Kim Stegmaier, MD**
  - Dana Farber
- **Eytan Stein, MD**
  - Memorial Sloan Kettering Cancer Center
- **Michael Su, PhD**
  - CSO, Volastra Therapeutics
- **George Thomas, MD**
  - OHSU
- **Matt Vander Heiden, MD, PhD**
  - MIT
- **Paresh Vyas, MD**
  - Oxford University

Series B

AURON THERAPEUTICS

Design firm to work on making this feel more like a pitch deck slide and les like a board deck slide

Auron has a strong track record of capital-efficient progress

Seed ◆ Series A ◆

	2021				2022				2023			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Internal	KAT2A POC in primary AML samples	HAT Screen KAT2A	Degrader landscape assessed for KAT2A	AURigin fully internalized	KAT2A indication expansion Solid tumors (SCLC)	KAT2A degrader campaign kickoff	Selective degradation of KAT2A/B	KAT2A Degrader LO Kat2A in Vivo POC SCLC		Oral Kat2A Degraders	Kat2A Pre-DC Kat2A expansion to NEPC	Non-GLP Tox
External			Tibsovo approved in cholangiocarcinoma		Hanahan: Disrupted differentiation & cellular plasticity key hallmarks of cancer			FDA Breakthrough Therapy granted for Revumenib in AML		Vorasidenib transformational P3 data in low grade glioma presented at ASCO	*Nature:* Mutant Kras disrupts differentiation to promote tumorigenesis WT p53 suppresses lung cancer by promoting differentiation	

We are raising a Series B to take the lead program through Clinical PoC

Value creation in Series A

- Platform validation in first two platform-derived programs
- Platform productivity demonstrated via successful target ID in multiple tumor types
- Lead program DC nomination Q1 '24
- Second program in hit ID
- Third program target ID complete
- External validation from Hanahan, *Cancer Discovery,* 2022; Kaiser, et.al., *Nature,* 2023; Juul, et.al, *Nature,* 2023
- External validation from Servier's vorasidenib solid tumor (low grade glioma) data presented at ASCO '23
- Built management team
- Added two independent Board members

Value-creating milestones in Series B

- Lead program
  - IND Q4 '24
  - Clinical site readiness Q1 '25
  - FPI Q1 '25
  - Clinical PoC in solid and heme tumors in '26
- 2nd program
  - Chemical leads identified to support lead opt in '24
  - DC in '25
- 3rd program
  - Expansion into EMT tumors in '24
  - DC in '26
- Platform
  - Expand database
- Company-building
  - Hire CMO at Series B close
  - Expand platform to support BD
  - Expand syndicate to support dual track exit scenarios

Series B closing after AUR1959 development candidate nomination

Citation

AURON THERAPEUTICS

References

There is growing enthusiasm for targeting cell state within the scientific community

- [Citations]
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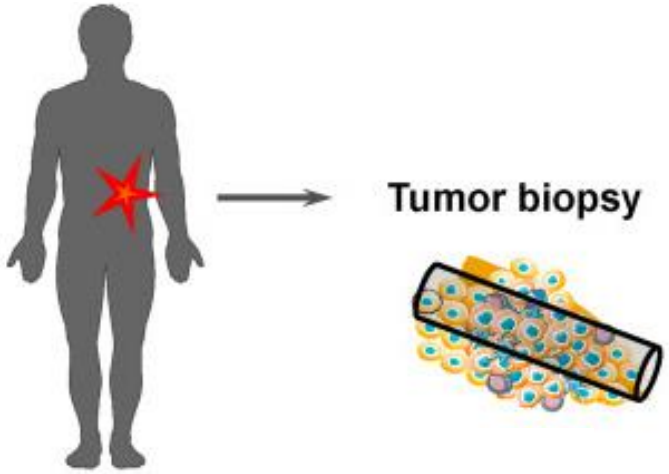
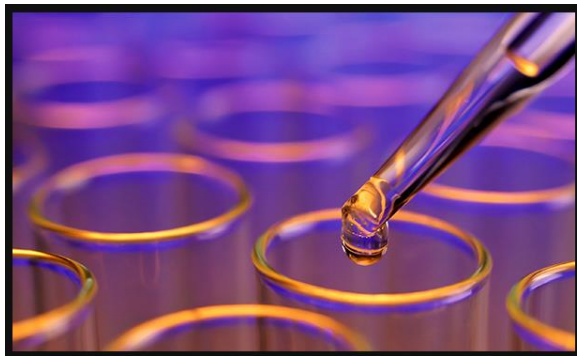
Holding bin for potential reuse

Finally, we pair drug targets with cell state response and efficacy biomarkers

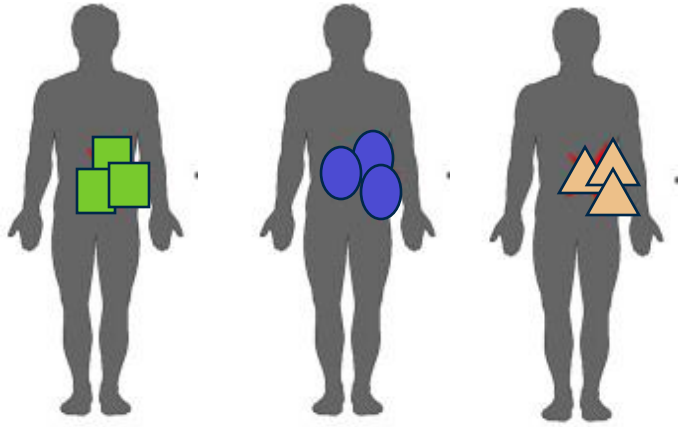
AURigin identifies unique cell state biomarkers that are used to select patients and assess efficacy



AURigin defined cell state biomarkers



Patient stratification and efficacy assessment based on tumor cell state



We know which patients we want to treat based on cell state

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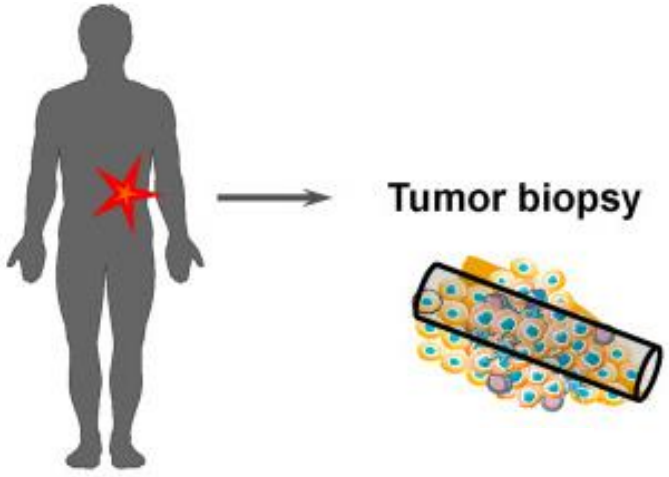
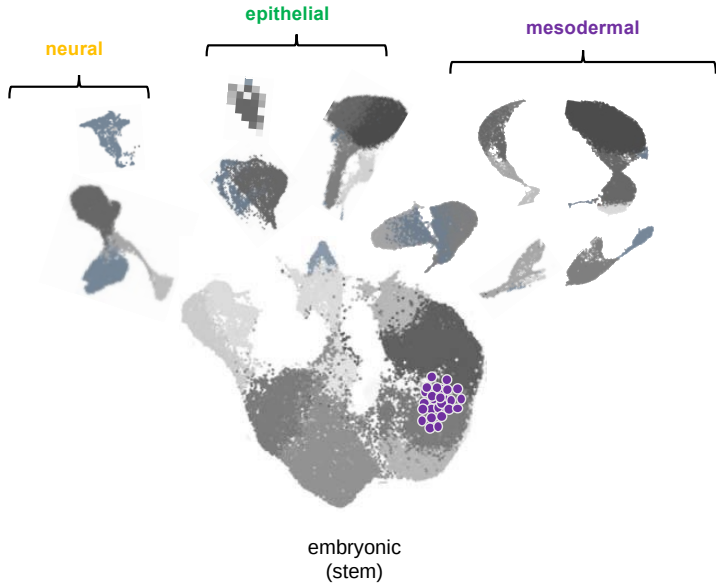
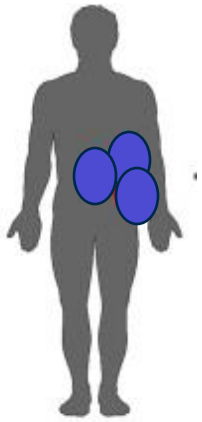


AURigin defined cell state biomarkers

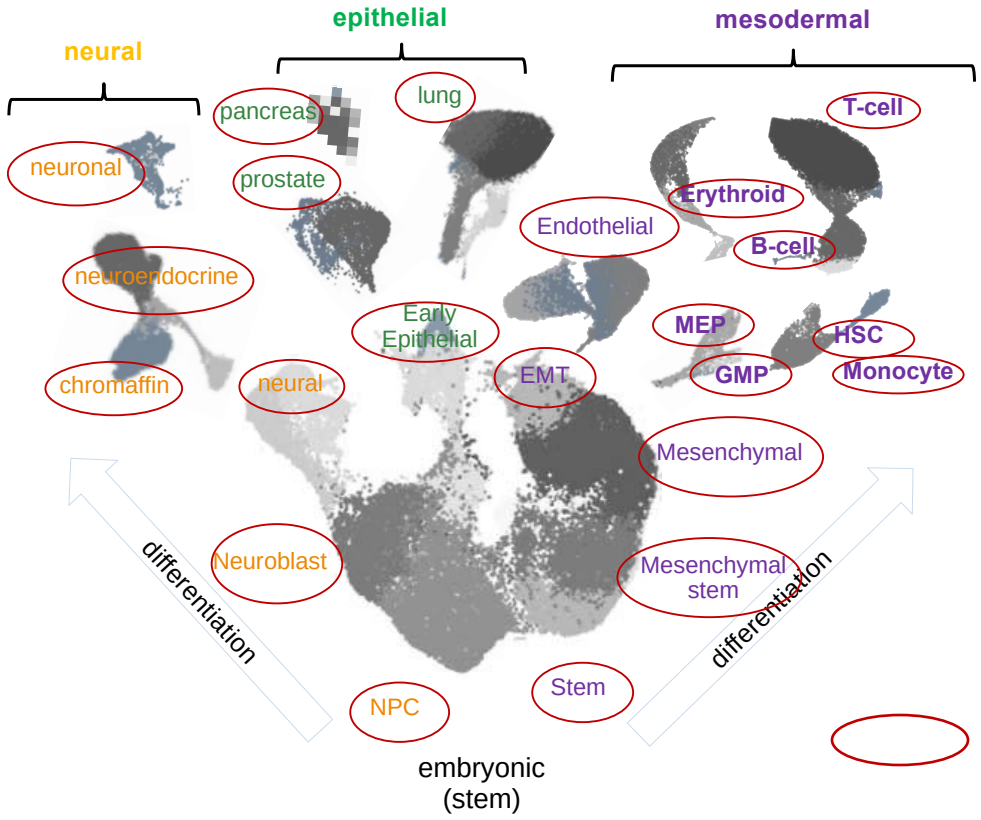


Patient stratification and efficacy assessment based on tumor cell state



We know which patients we want to treat based on cell state

First, we build an atlas of human cell development to define normal cell states



Proprietary AI algorithms used to create a map of normal cell states

- Define the normal states of human development using single cell -omics data
- Train ML classifiers to define developmental cell states of a tumor sample

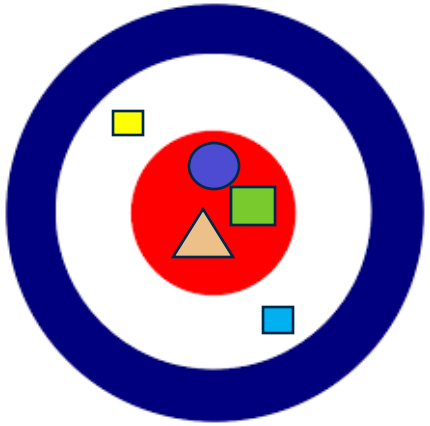
- Proprietary ***Normal Cell State Classifiers***
- Currently >200 normal states mapped
- Comprising > 1000 donors

The most comprehensive proprietary atlas of normal human development

Citation

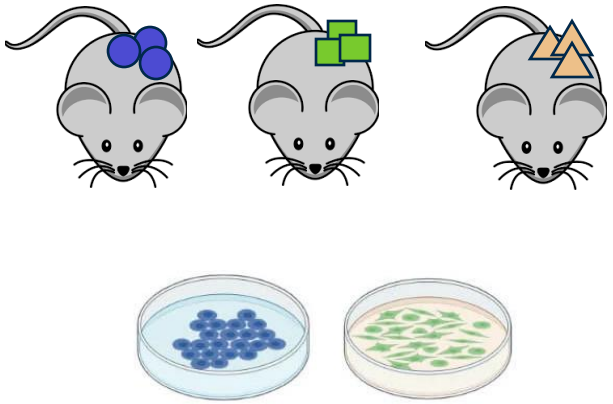
AURigin accelerates drug discovery and increases PoS in the clinic

Cell state specific ML derived high-quality targets

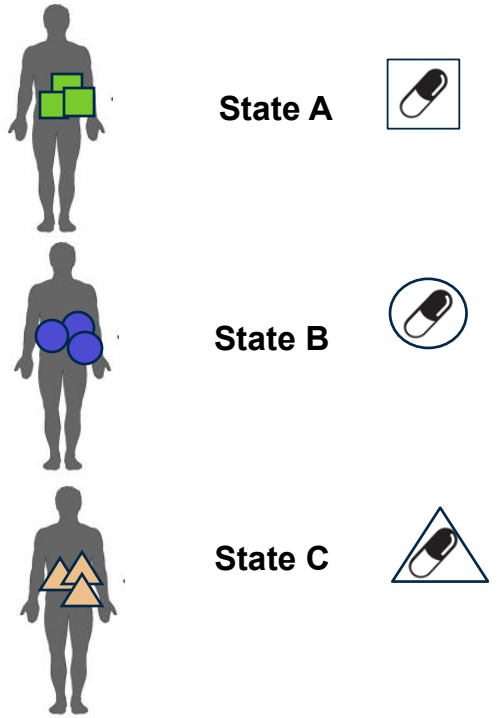


Cell state targets:

Cell state specific models for target validation



Cell state specific biomarkers for patient selection and efficacy assessment

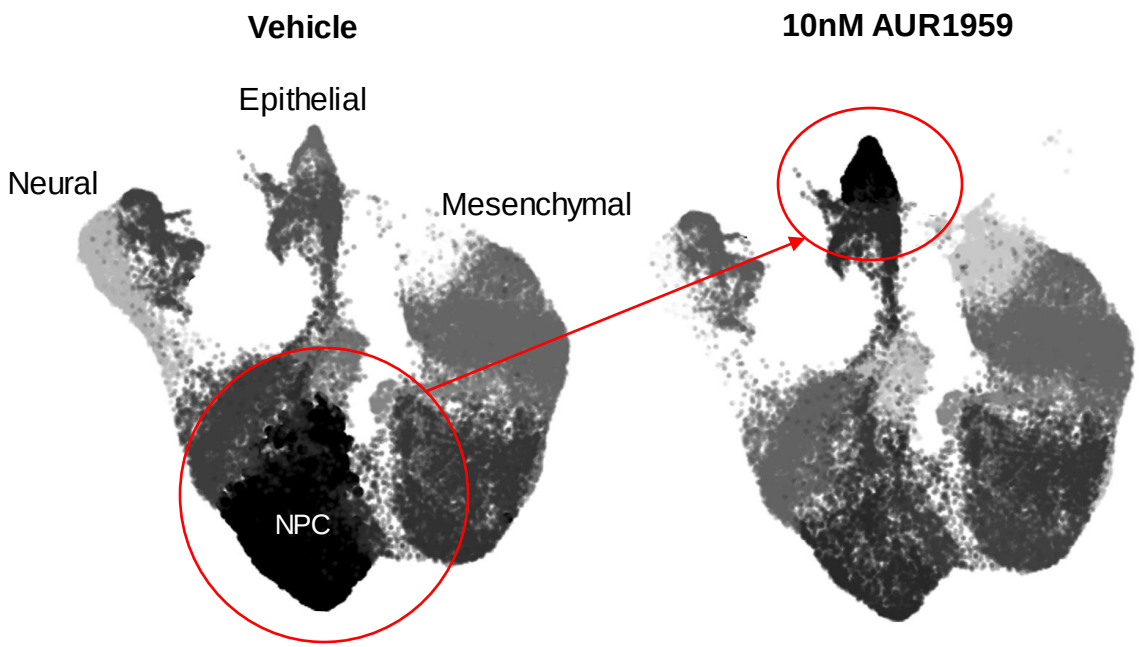


Focus on cell state to identify the right targets and right therapies for the right patients

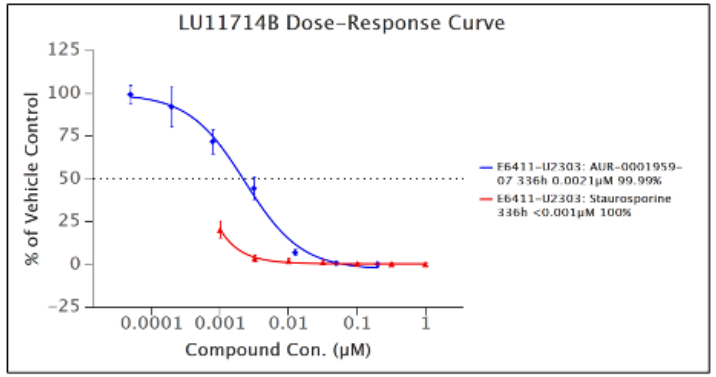
AURON THERAPEUTICS

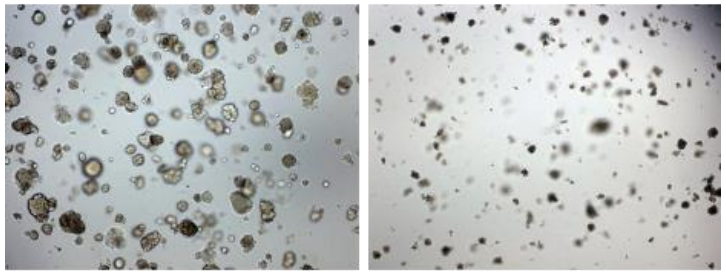
In SCLC, degrading Target 1 shifts cell state, leading to growth arrest

AUR1959 induces cell state switch from neural progenitor (NPC) to adult epithelial*



AUR1959 induces potent growth effects in patient derived organoid models of SCLC





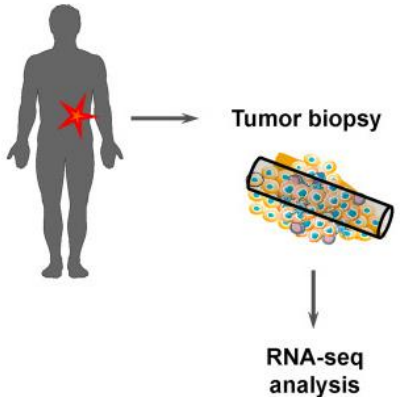
Vehicle 200nM Aur1959

Validated in >70% of the SCLC patient population (>20,000 patients per year)

*Additional data not shown: In vivo data showing cell state shift and growth arrest in 2 CDX models

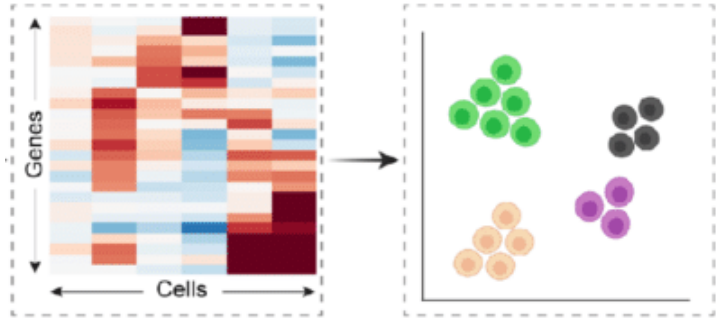
AURON THERAPEUTICS

Finally, pair drug targets with cell state response and efficacy biomarkers



- We have unique cell state biomarkers that can be used to select patients and assess efficacy

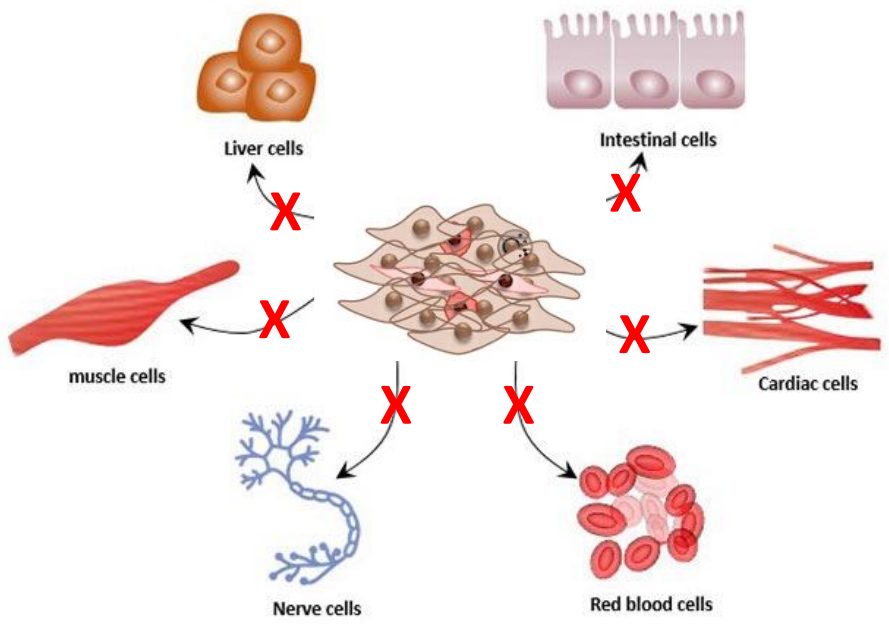
Cell state biomarkers (response & efficacy)



We know which patients we want to treat based on cell state

Platform-based, product-driven company that uses artificial intelligence (AI) to target the plastic cell states of cancer

Perturbation of normal cell differentiation induces cell state plasticity and proliferation of cancer cells



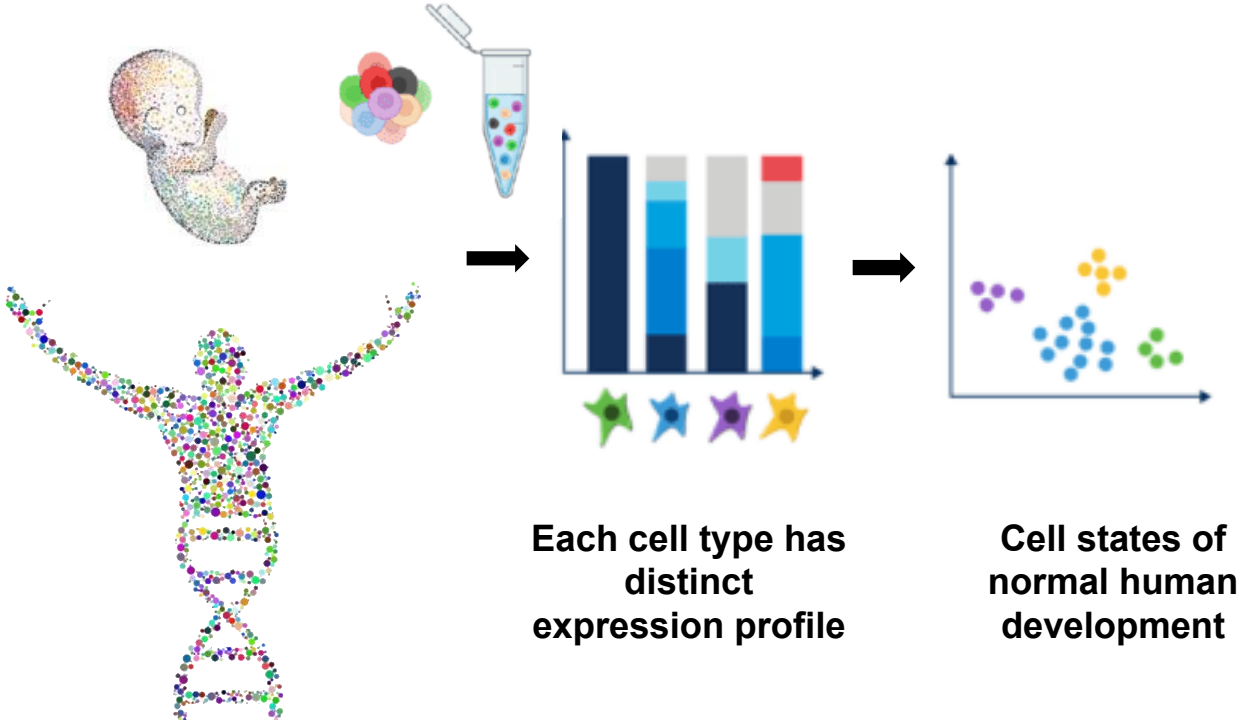
Drivers of cell state plasticity offer new therapeutic targets for oncology

- AI algorithms identify targets with higher probability of biological validation and higher probability of success (PoS) in the clinic
- Platform already has delivered two validated programs with a third in validation

Better, faster, cheaper drug development with higher PoS

Citation

We use AURigin, our AI platform, to identify the drivers of plastic cell states in tumors



- Recent explosion of single cell -omics datasets allow us to define normal cell states of human development at high resolution
- Guided by developmental biology, AURigin engineers the ML paradigm to identify drivers of cancer cell state

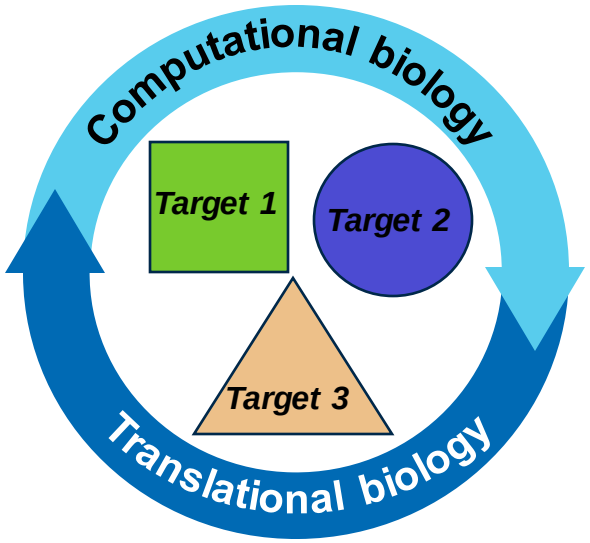
Significant first mover advantage in newest frontier for oncology drug development

Wilbrey-Clark et al, BiochemicalJournal, 2020

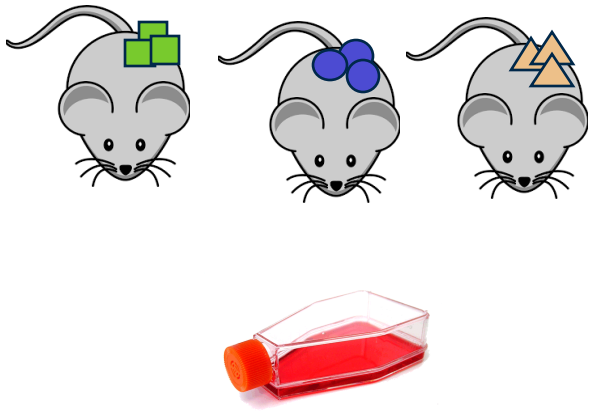
AURON THERAPEUTICS

AURigin accelerates drug discovery and increases PoS in the clinic

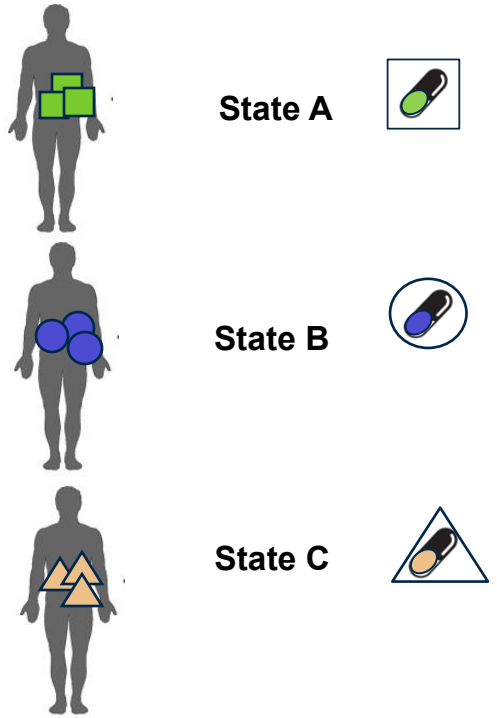
Cell state specific ML derived high-quality targets



Cell state specific models for target validation



Cell state specific biomarkers for patient selection



Focus on cell state to identify the right targets and right therapies for the right patients

AURON THERAPEUTICS

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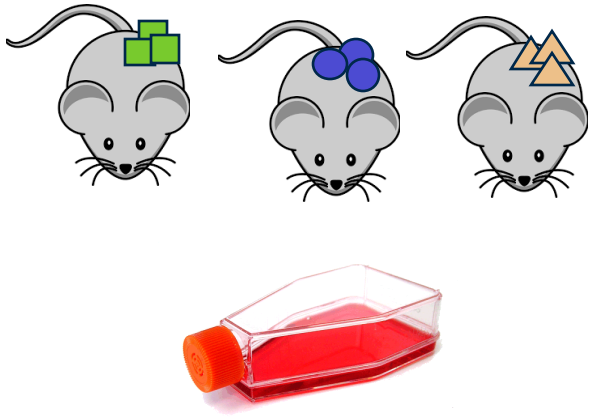

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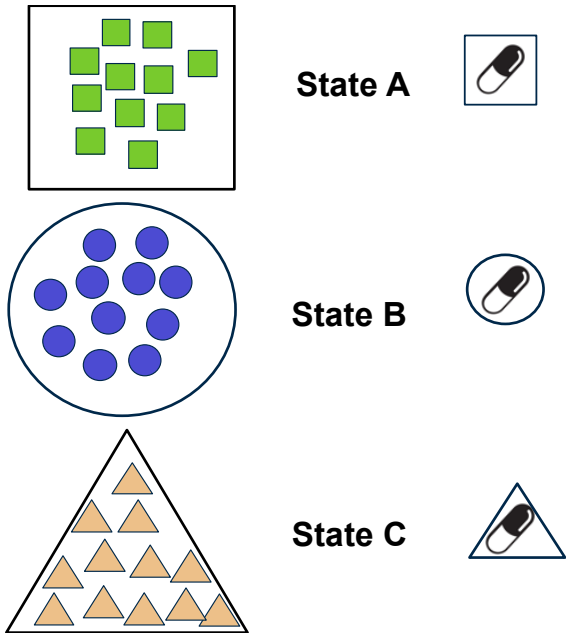
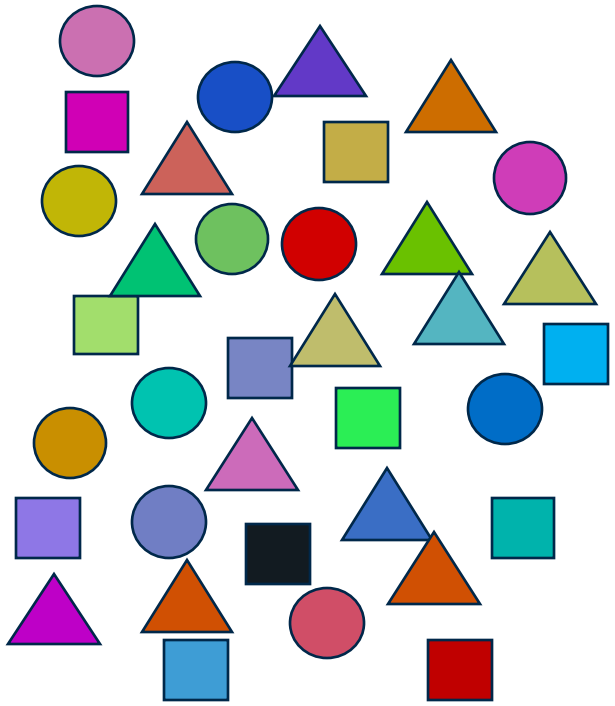


Focus on cell state to identify the right targets and right therapies for the right patients

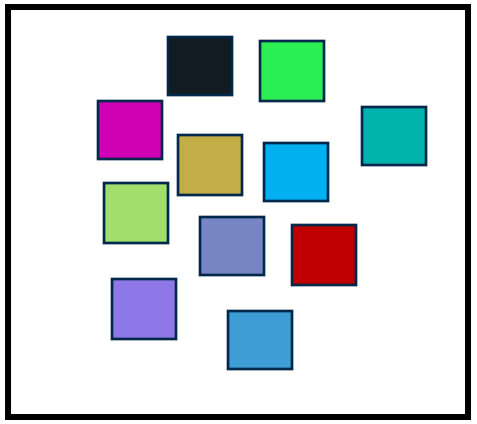
AURON THERAPEUTICS

Added in case it's useful

Genetic landscape lens of cancer is very heterogeneous

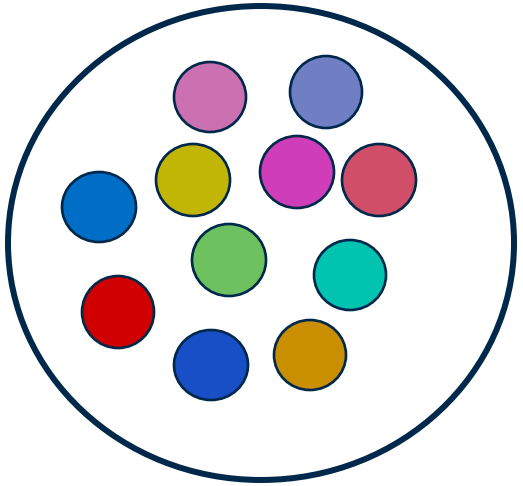


Cell State Lens allows us to see discrete states



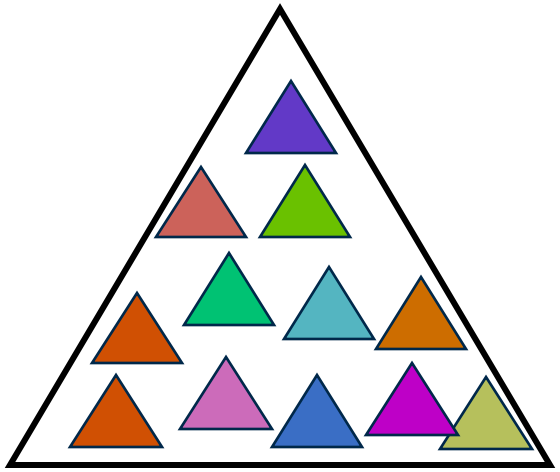
State A

Drug A



State B

Drug B

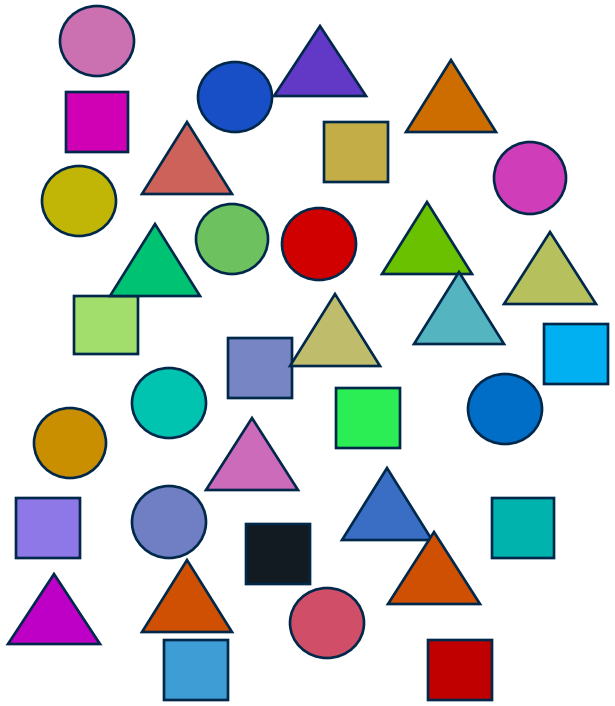


State C

Drug C

Added in case it's useful

Genetic landscape lens of cancer is very heterogeneous



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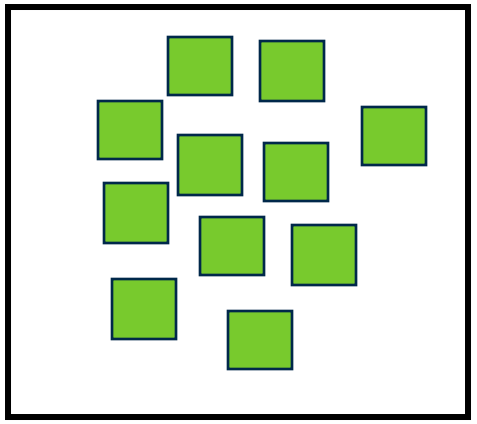

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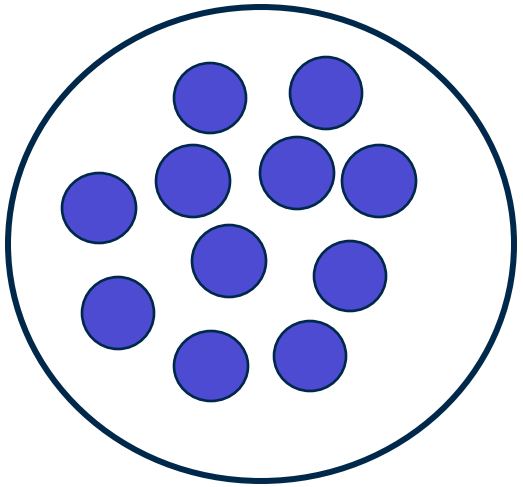
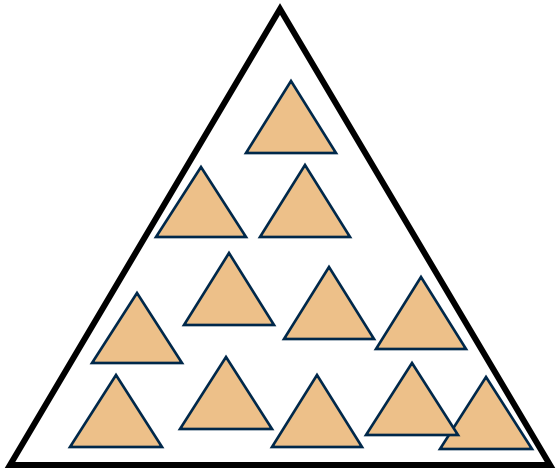


State B

Drug B

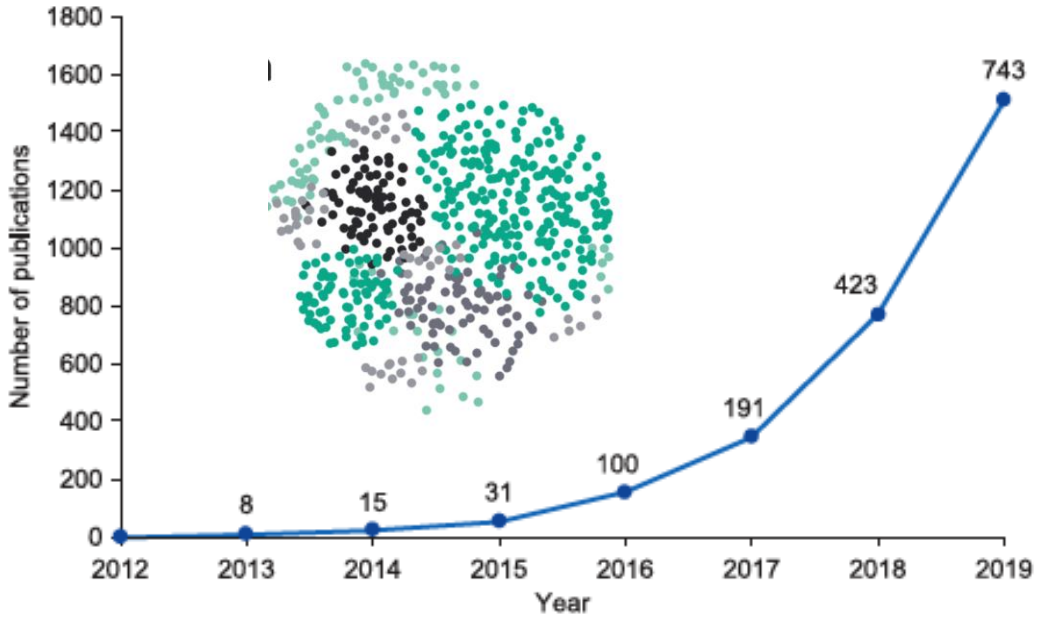


State C

Drug C

We use AURigin to identify the drivers of plastic cell states in tumors

Tom: new figure that goes out to 2023



- Recent explosion of single cell -omics datasets allow us to define normal cell states of human development at high resolution
- Guided by developmental biology, AURigin engineers the AI/ML paradigm to identify drivers of cancer cell state

Significant first mover advantage in newest frontier for oncology drug development

Wilbrey-Clark et al, BiochemicalJournal, 2020

AURON THERAPEUTICS

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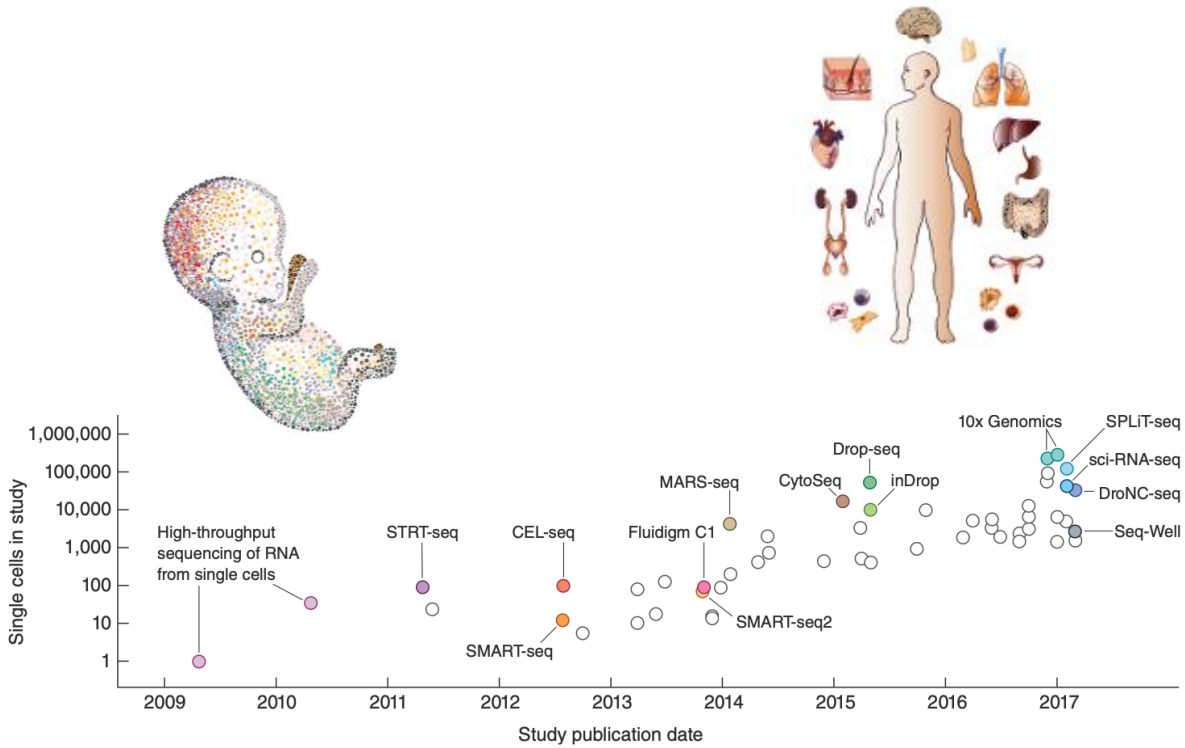

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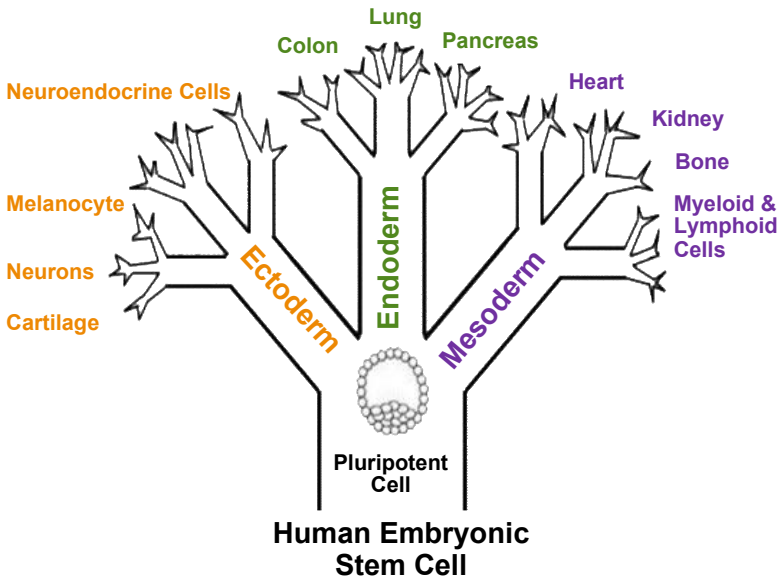
Significant first mover advantage in newest frontier for oncology drug development

Svensson et al, Nature Protocols, 2018

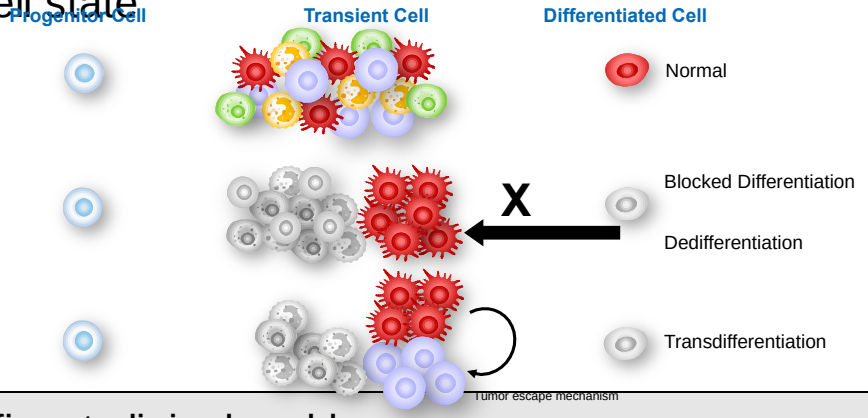
Cancer cells hijack developmental biology pathways to induce proliferative, plastic cell states

Differentiation

Plasticity



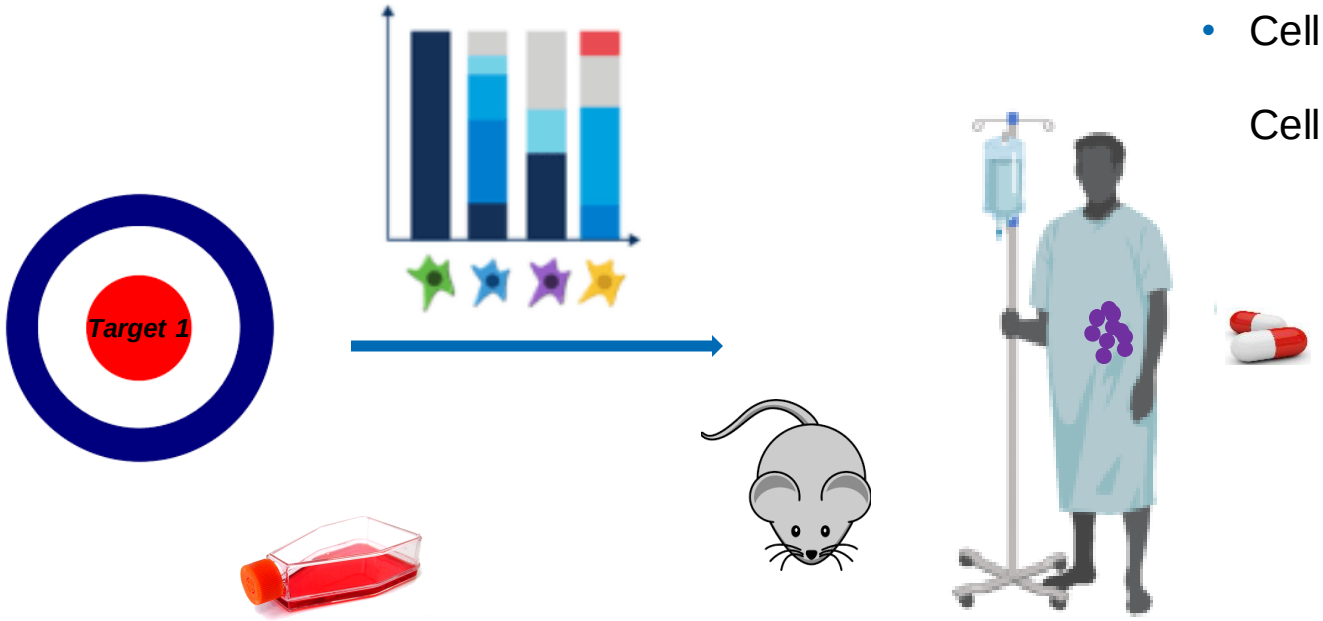
- During normal development, cells go through a plastic, proliferative state on their way to becoming mature, terminally differentiated stable cell
- Reprogramming of cancer cells prevents maturation and shifts the cells to a more plastic and proliferative cell state



Cancer cell plasticity causes significant clinical problems

Citation

AURigin accelerates drug discovery and increases PoS in the clinic



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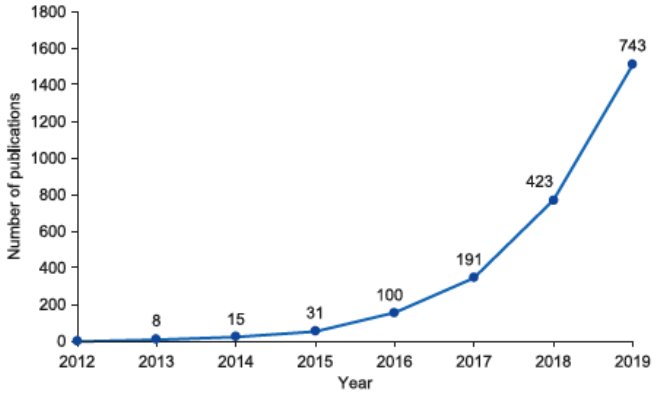

Increase in single-cell RNA sequencing publications

- Recent explosion of single cell -omics datasets allow us to define normal cell states of human development at high resolution
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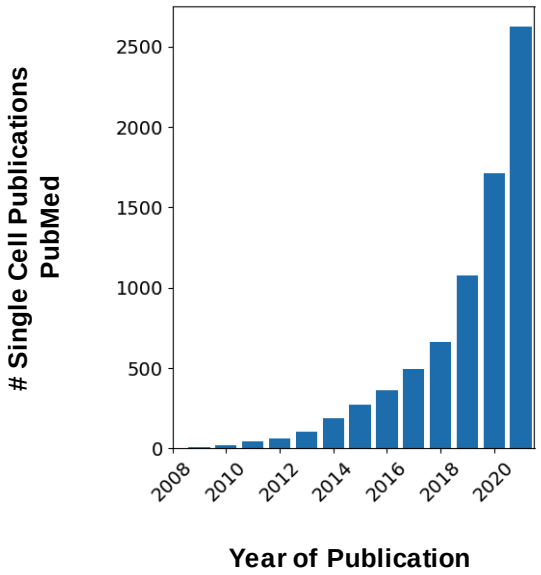
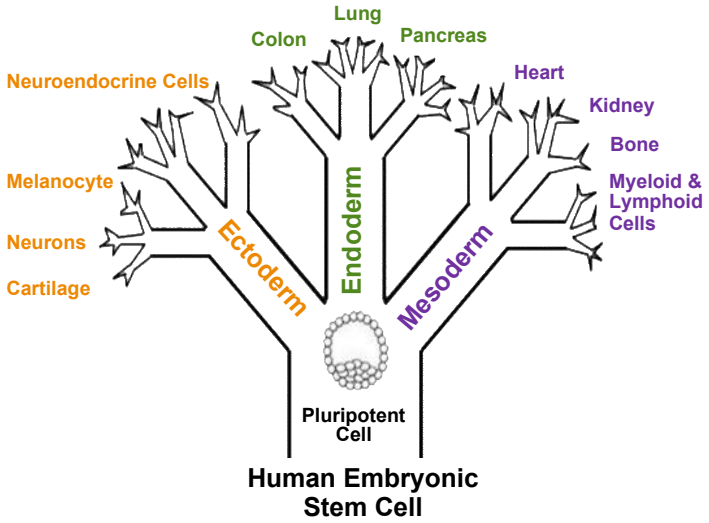


Guided by single cell datasets, we have built an integrated atlas of normal human development



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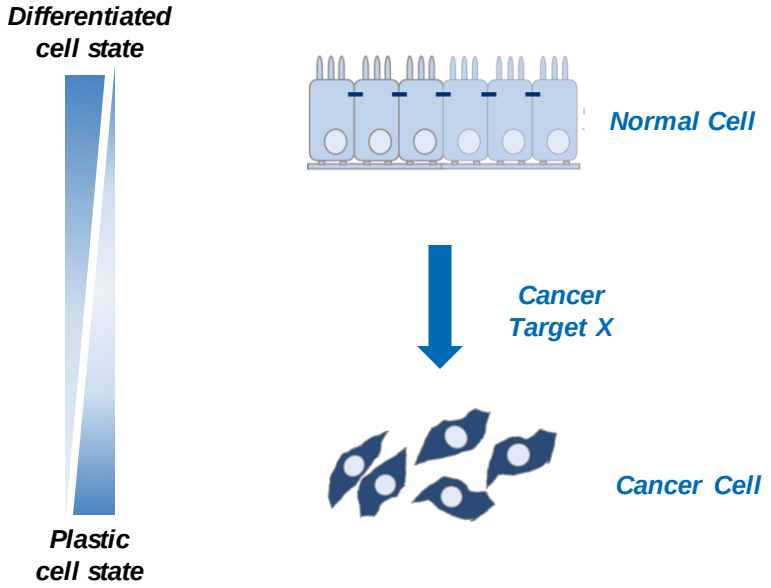

Significant first mover advantage in newest frontier for oncology drug development

Put in tree reference if we do not redraw with graphic artist