EPISTEME
PROGNOSTICS

Personalized Epigenetics™

We asses the risk of recurrence in malignant diseases at the time of diagnosis, and help tailoring the therapy

How bad is my tumor, and what should I do if it is bad?

April 2020
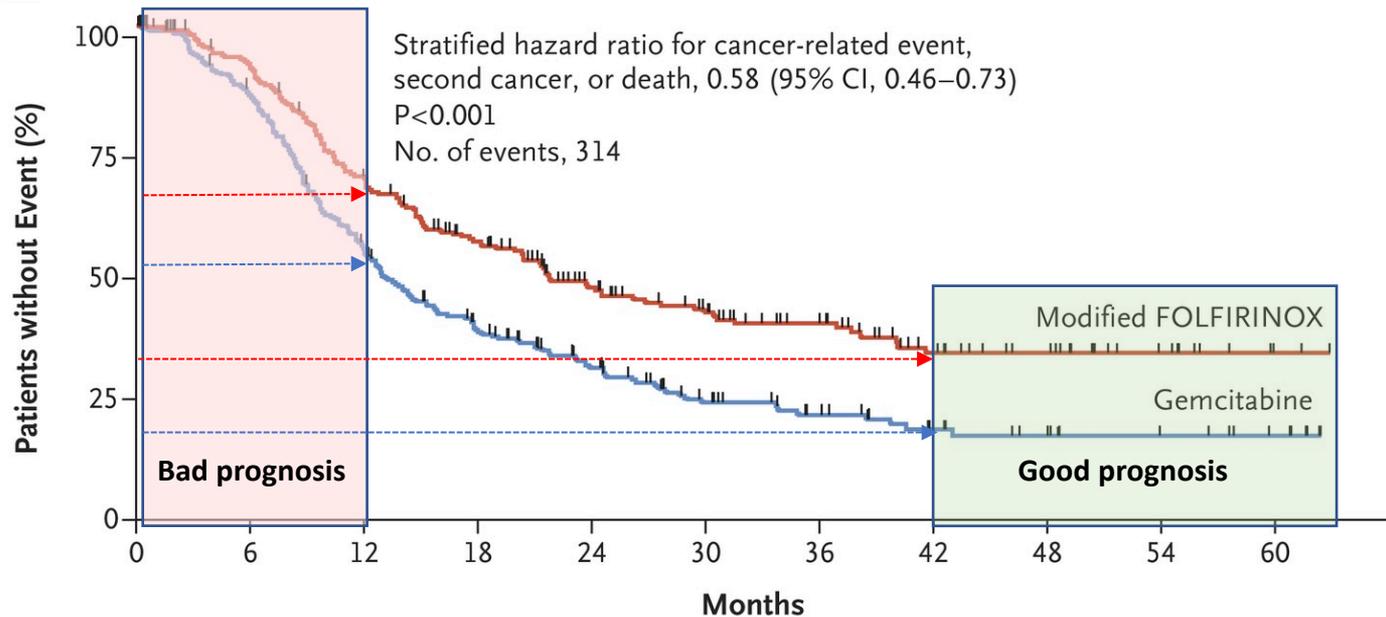
Memorial Sloan Kettering Cancer Center

DARTMOUTH

Surajit Dhara Ph. D.
Senior Research Scientist, NCCC
Co-founder, President and CSO
Episteme Prognostics LLC

First-line of chemotherapy fails in about half of the cancer patients

Pancreatic Cancer Patients on the First-Line of chemotherapy

Post resection
adjuvant chemotherapy

A Disease-free Survival

Stratified hazard ratio for cancer-related event,
second cancer, or death, 0.58 (95% CI, 0.46–0.73)
P<0.001
No. of events, 314

No. at Risk										
Modified FOLFIRINOX	247	210	156	118	80	60	46	29	21	11	2
Gemcitabine	246	205	127	85	59	34	24	15	10	7	3

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First-line of chemotherapy fails in about half of the cancer patients
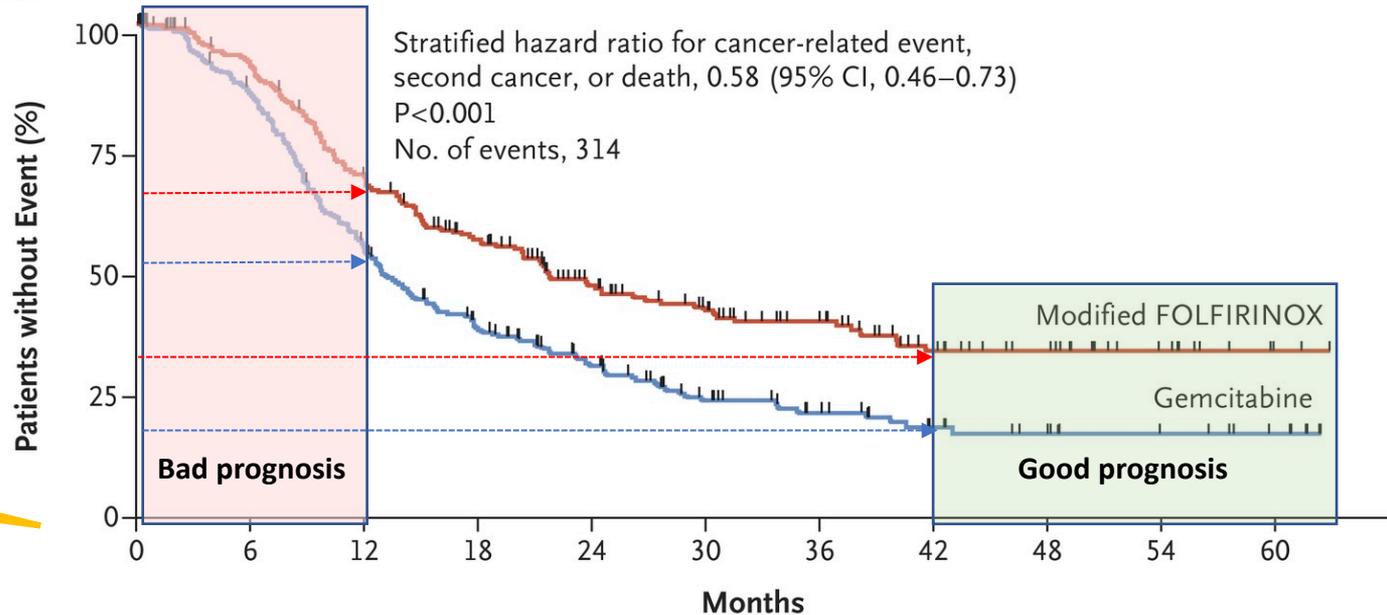
Pancreatic Cancer Patients on the First-Line of chemotherapy

A Disease-free Survival

Post resection
adjuvant chemotherapy

At diagnosis:
1. How *bad* is my tumor?
2. What should I do if it is *bad*?

Stratified hazard ratio for cancer-related event, second cancer, or death, 0.58 (95% CI, 0.46–0.73)
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No. of events, 314

Patients without Event (%)

Bad prognosis

Good prognosis

Modified FOLFIRINOX

Gemcitabine

Months

No. at Risk										
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EPISTEME PROGNOSTICS

We invented ATAC-array – the only microarray that reads chromatin accessibility and detects "epigenetic imbalance" in "bad" tumors
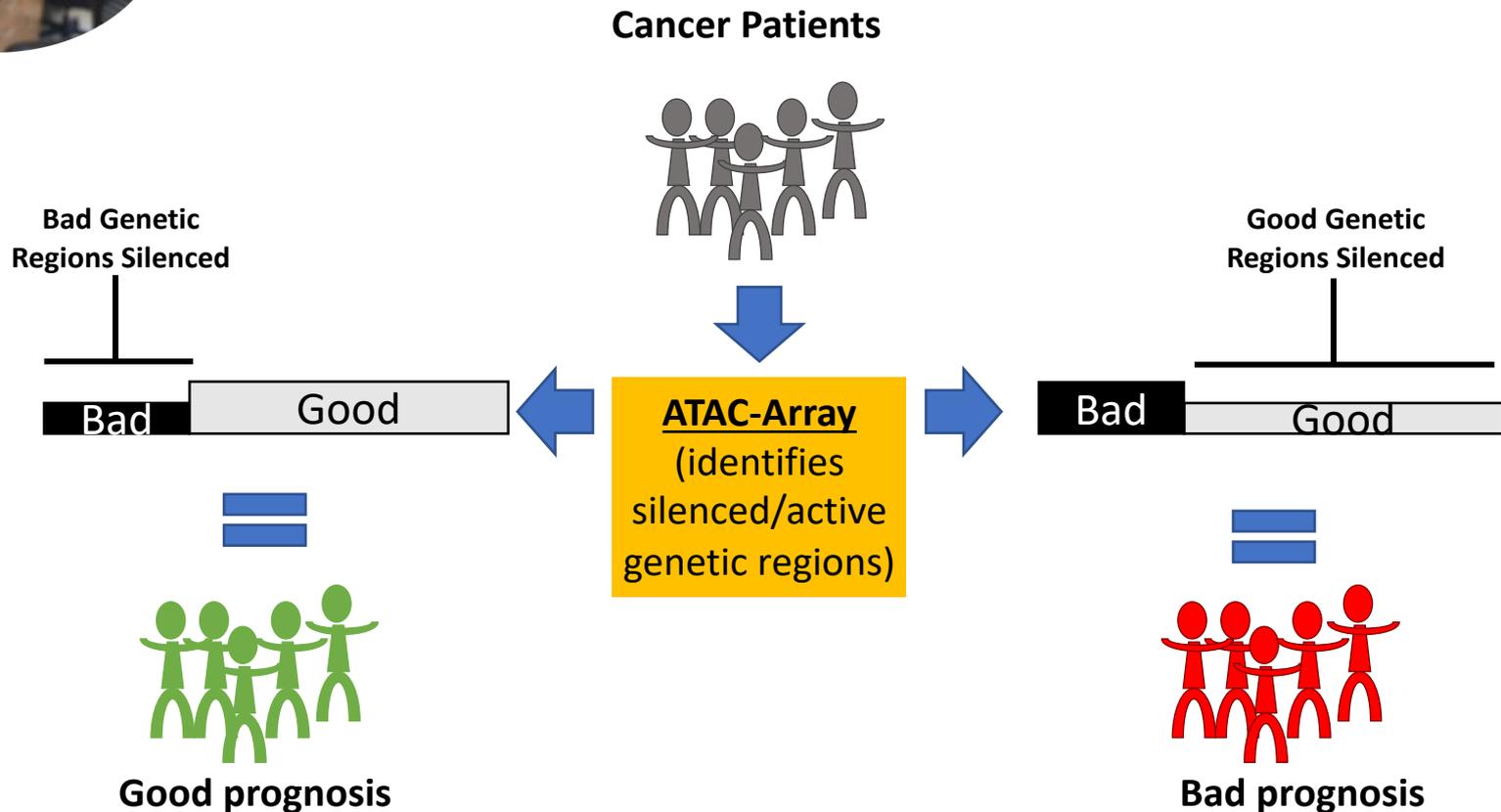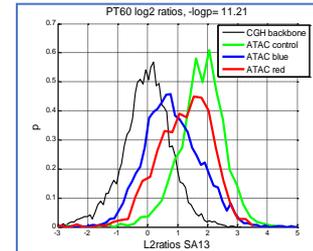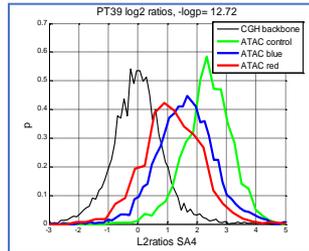
Cancer Patients

ATAC-Array
(identifies silenced/active genetic regions)

We invented ATAC-array – the only microarray that reads chromatin accessibility and detects "epigenetic imbalance" in "bad" tumors

Cancer Patients

Bad Genetic Regions Silenced

Bad | Good

=

Good prognosis

ATAC-Array (identifies silenced/active genetic regions)

Good Genetic Regions Silenced

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EPISTEME
PROGNOSTICS

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Cancer Patients
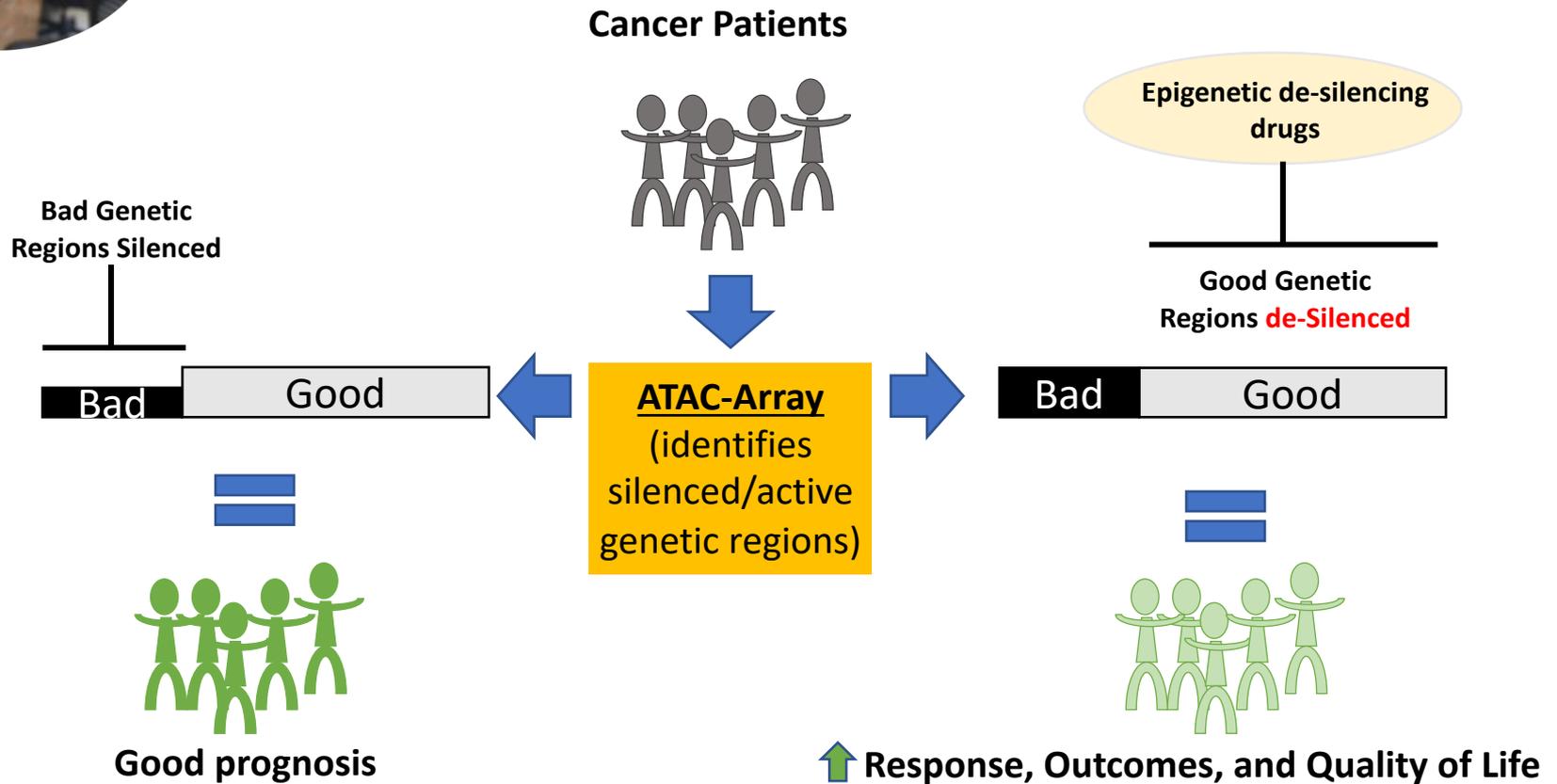
Bad Genetic Regions Silenced

Good Genetic Regions Silenced

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ATAC-Array
(identifies silenced/active genetic regions)

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Bad prognosis

EPISTEME
PROGNOSTICS

Potential therapeutic opportunity – predicted non-responders can be treated with de-silencing epigenetic drugs

Cancer Patients

Epigenetic de-silencing drugs

Bad Genetic Regions Silenced

Good Genetic Regions de-Silenced

Bad | Good

ATAC-Array (identifies silenced/active genetic regions)

Bad | Good

=

=

Good prognosis

⬆ **Response, Outcomes, and Quality of Life**

EPISTEME
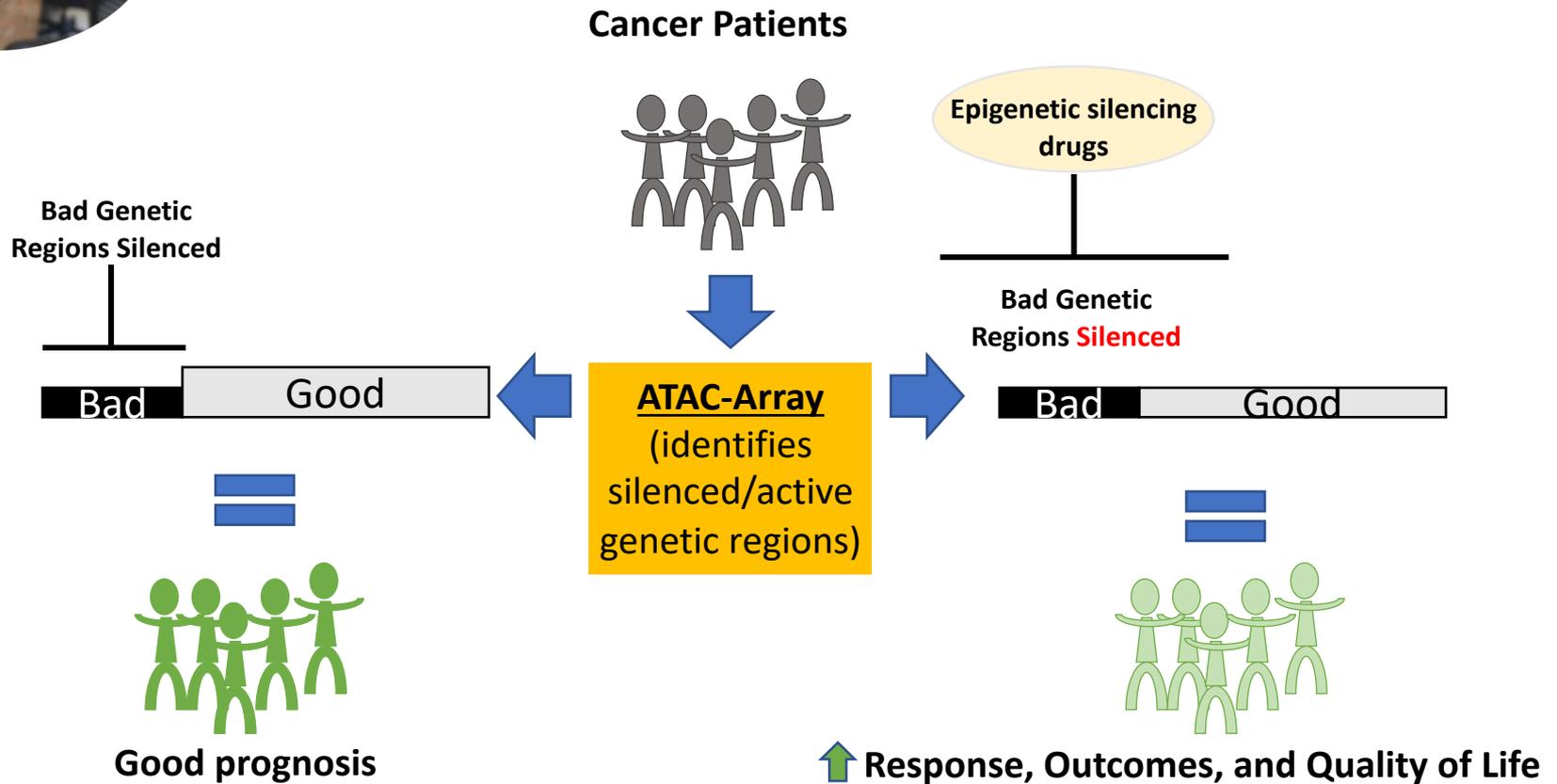PROGNOSTICS

Potential therapeutic opportunity – predicted non-responders can also be treated with silencing epigenetic drugs

Cancer Patients

Epigenetic silencing drugs

Bad Genetic Regions Silenced

Bad Genetic Regions Silenced

Bad | Good

ATAC-Array
(identifies silenced/active genetic regions)

Bad | Good

=

=

Good prognosis

↑ Response, Outcomes, and Quality of Life

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PROGNOSTICS

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Proof of concept studies have been conducted in pancreatic cancer

ATAC-array alone

Classified as non-responders (n=16)
Classified as responders (n=17)
Classified as ambiguous (n=5)
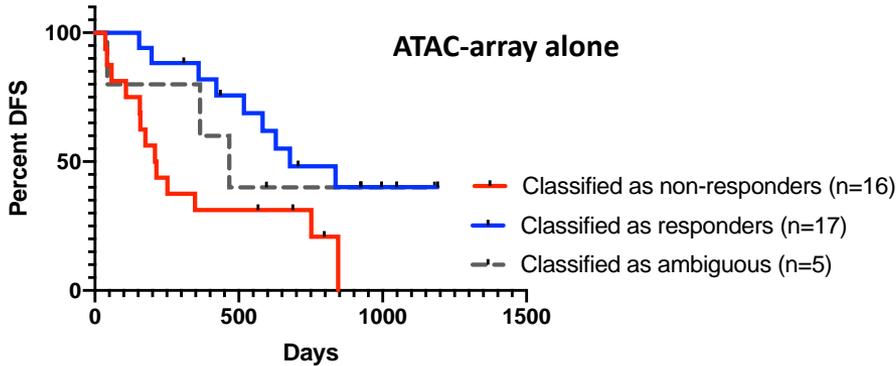
Gehan-Breslow-Wilcoxon test
P value   0.0076

Median survival (days)
Classified as non-responders	211
Classified as responders	678
Classified as ambiguous	467

Immunohistochemistry alone

HNF1b positive in nuclei (n=18)
HNF1b negative in nuclei (n=22)
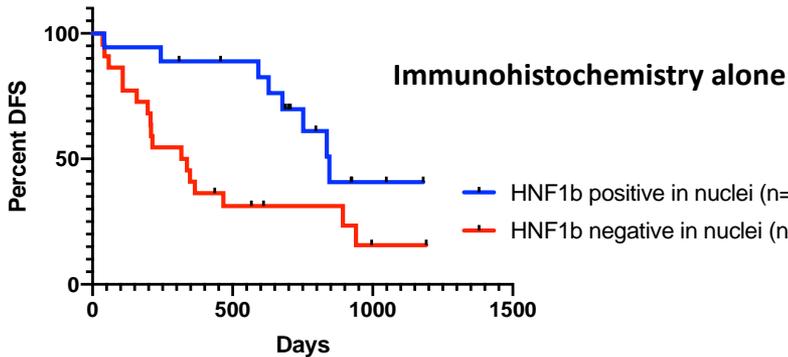
Gehan-Breslow-Wilcoxon test
P value   0.0043

Median survival (days)
HNF1b negative in the nuclei	327
HNF1b positive in the nuclei	845
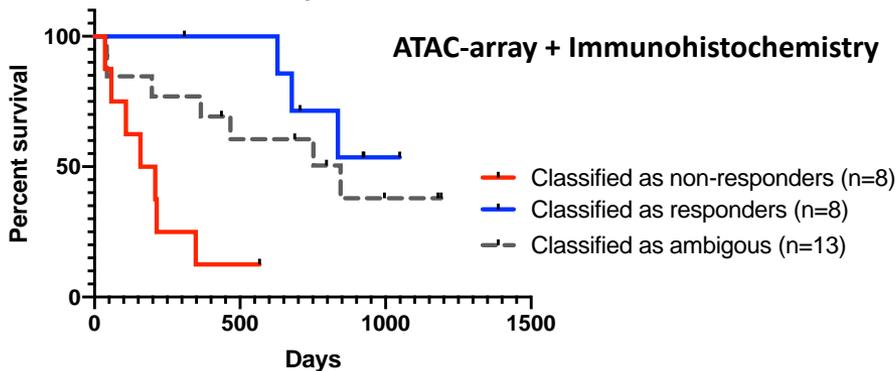
ATAC-array + Immunohistochemistry

Classified as non-responders (n=8)
Classified as responders (n=8)
Classified as ambigous (n=13)

Gehan-Breslow-Wilcoxon test
P value   0.0019

Median survival (days)
Classified as non-responders	183
Classified as responders	Undefined
Classified as ambiguous	845

Who are to treat and who are not to treat with Epigenetic drugs
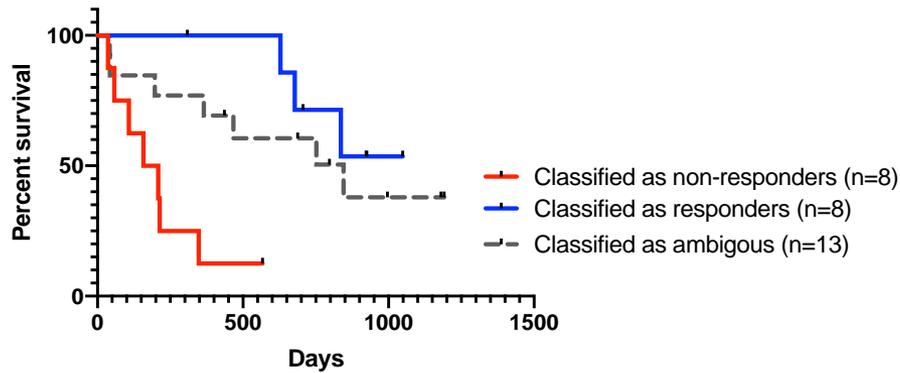
Percent survival vs **Days**

- Classified as non-responders (n=8)
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Median survival (days)

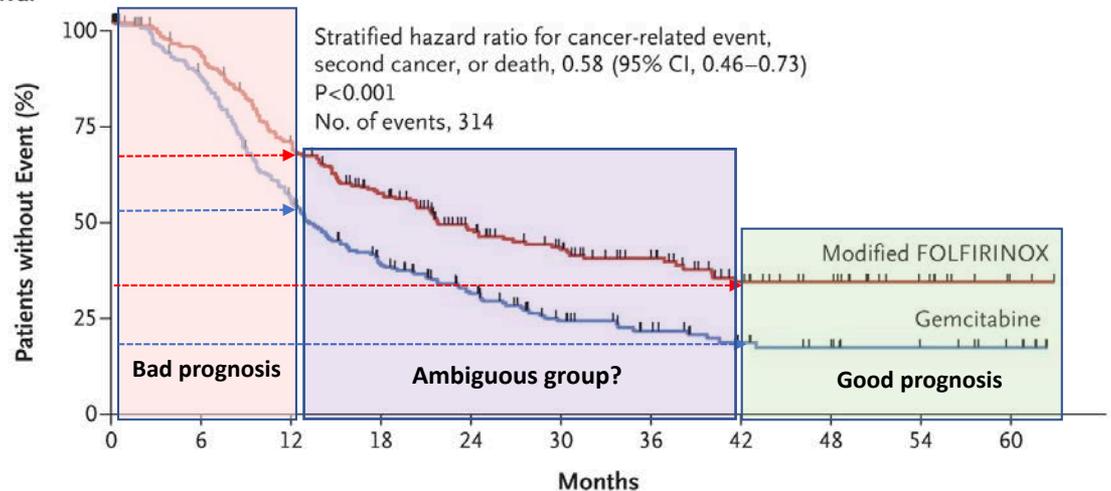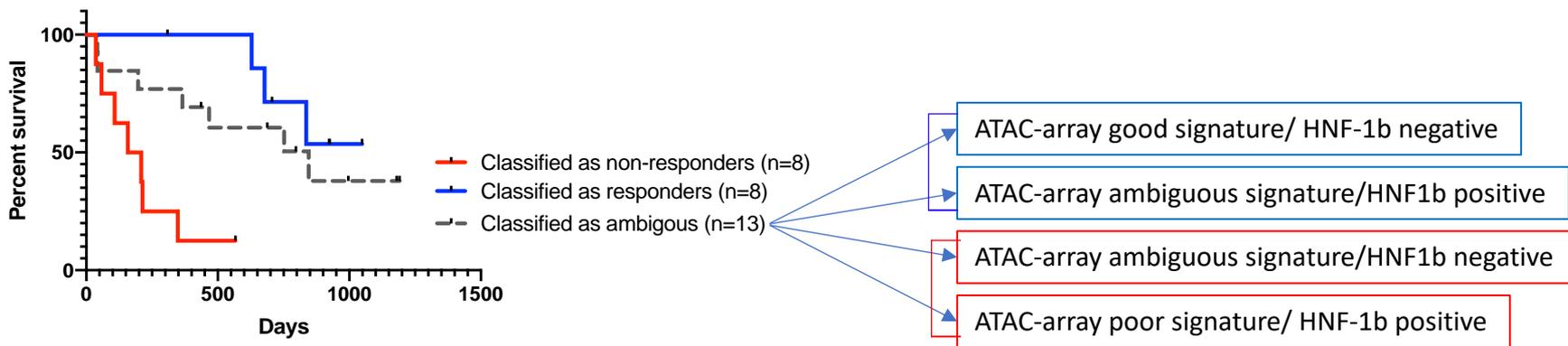|	
Classified as non-responders (27.5%)	183
Classified as responders (27.5%)	Undefined
Classified as ambiguous (44.8%)	845

A Disease-free Survival

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$P<0.001$
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Modified FOLFIRINOX
Gemcitabine

Bad prognosis | Ambiguous group? | Good prognosis

Patients without Event (%) vs **Months**

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Unpublished Data

EPISTEME
PROGNOSTICS

Who are to treat and who are not to treat with Epigenetic drugs

Percent survival vs Days plot:
- Classified as non-responders (n=8)
- Classified as responders (n=8)
- Classified as ambigous (n=13)

- ATAC-array good signature/ HNF-1b negative
- ATAC-array ambiguous signature/HNF1b positive
- ATAC-array ambiguous signature/HNF1b negative
- ATAC-array poor signature/ HNF-1b positive

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Who are to treat and who are not to treat with Epigenetic drugs

NOT to be treated with Epigenetic drugs.. only chemo is good

NOT to be treated with Epigenetic drugs.. only chemo is good

Classified as non-responders (n=8)
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ATAC-array good signature/ HNF-1b negative

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Target group for Epigenetic drugs + chemo as the first line of intervention

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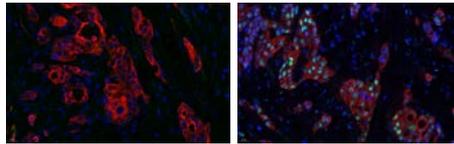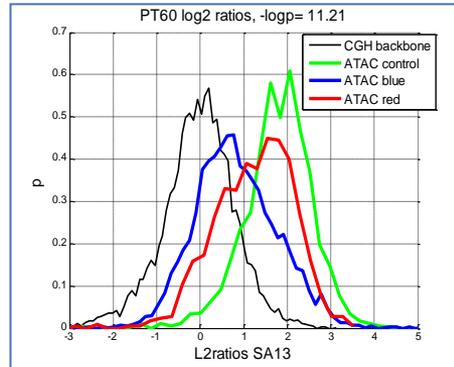| No. at Risk										
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Hypothetical stratification and quantitatively measuring the direction of the reprogramming with epigenetic drugs
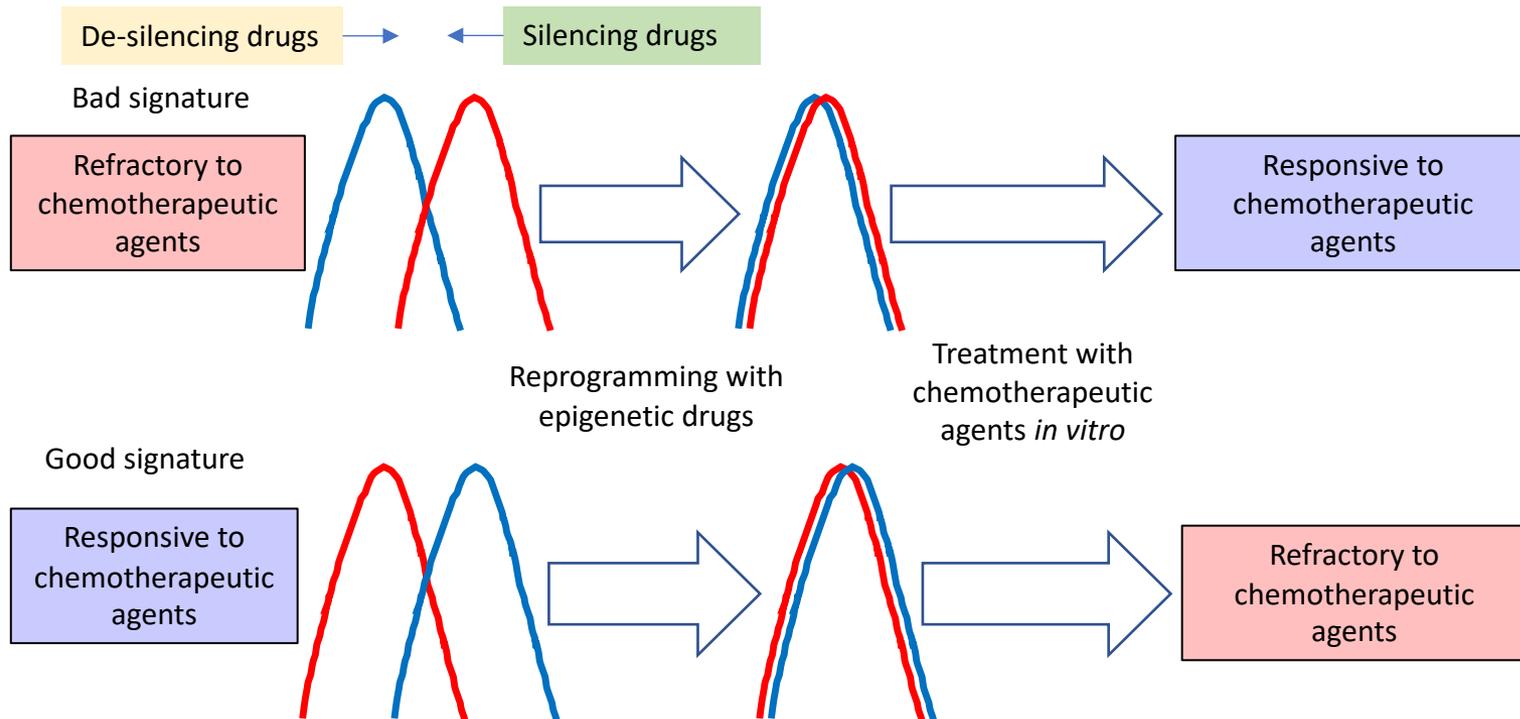
A classical example is MGMT promoter silencing by hyper-methylation in GBM, where you wouldn't want to de-silence it back

Episteme fits seamlessly into the current standard of care and will increase patients' chance of response to chemotherapy

PT60 log2 ratios, -logp= 11.21

Legend: CGH backbone, ATAC control, ATAC blue, ATAC red

L2ratios SA13

At diagnosis

Biopsy/surgically resected tumor specimen

PT39 log2 ratios, -logp= 12.72

Legend: CGH backbone, ATAC control, ATAC blue, ATAC red

L2ratios SA4

ATAC-array and optional immunohistochemistry

Results in 3 days

Higher risk of chemoresistance and recurrence
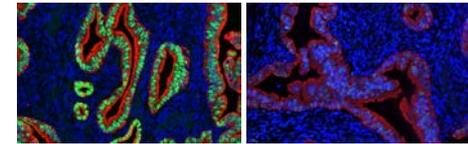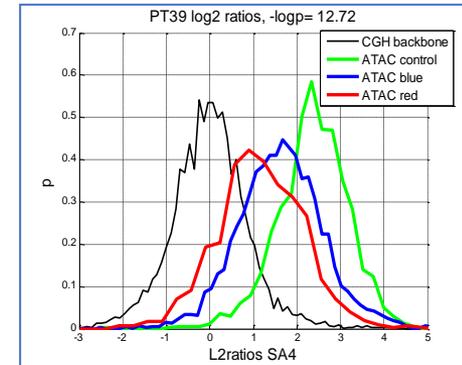
Lower risk of chemoresistance and recurrence

Combine the chemotherapy with the epigenetic drug

Personalizing the first line of chemotherapy

No epigenetic drugs Continue with standard therapy

EPISTEME PROGNOSTICS

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1. **It will increase the probability of success of clinical trials with epigenetic drugs in combination with chemotherapy**

   It is applicable to wide range of epigenetic drugs and therefore, can develop companion diagnostics for each

2. **It will enable clinicians to identify chemo non-responders and begin this stratification at the time of diagnosis**

   Our long-term goal is to be an integral part of the process for determining the best course of treatment for all cancer patients at the time of diagnosis, side-by-side with standard biopsy.

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Precision medicine is the future of oncology; many companies in this space are moving, but Episteme's technology is superior

Company	Technology	Why is our technology superior?					Annual Revenue
		Speed	Cost effective	Ease of use	Widely applicable epigenetic information	Broad clinical utility	
Episteme Prognostics	ATAC-array+	✔	✔	✔	✔	✔	$TBD
Exact Sciences	Oncotype Dx	✔	✔	✔	✘	✘	$142.5 M
MDx Health	Methylation specific PCR (MGMT in GBM)	✔	✔	✔	✘	✘	$27.7 M
Ribomed Biotechnologies	DNA Methylation array	✔	✔	✔	✘	✘	$16.1 M
The Diagenode	DNA methylation array	✔	✔	✔	✘	✘	$14.8 M

EPISTEME PROGNOSTICS

Go-to-market strategy and milestones

Timeline	DEVELOPMENT 20 Q1 & Q2		20 Q3 & Q4	21 Q1
Need	Current status	Raise $2.5M (SBIR-FT/VC)	Raise $5M (VC)	
M I L E S T O N E S	**Assay in hand, Proof-of-the concept study is done on 38 pancreatic cancer patients..**	**Laboratory set up**	Expanding the company **510K/CLIA**	Continue to engage big Pharmaceutical companies & Institutional clinical studies
	Corporate infrastructure building and marketing communications	Hiring technicians & other FTE	Hiring C-suite employees, more technicians, marketing & other FTE	
	Customer engagement is actively ongoing: Pharmaceutical companies/ medical doctors	**1st Entry to the market (size):** 138 clinical trials by 31 companies/ 55K new Pancreatic cancer patients per year in the USA alone	**2nd Entry to the bigger market – Aggressive penetration into the market**	**To all pancreatic cancer patients in the hospital set-up**
Value created	Reputation & contact build up in pharmaceutical companies & hospital set up		Expected revenue $2M	Expected revenue $10M

EPISTEME
P R O G N O S T I C S

Episteme team – people with strong scientific, clinical, business legal & pharma backgrounds

Surajit Dhara, Ph. D.
Co-founder, President & CSO,
Episteme Prognostics LLC
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Dartmouth-Hitchcock Norris
Cotton Cancer Center,
Lebanon, NH, USA

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Episteme Prognostics LLC
Director of the Dartmouth-
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Advisor,
Episteme Prognostics LLC,
President & CEO,
PhageNova Bio Inc.,
Scarsdale NY, USA

Juan Carlos Serna, M.B.A.
Advisor,
Episteme Prognostics LLC,
President & Co-founder
Right Submission, Newton
MA, USA

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Advisor,
Episteme Prognostics LLC,
Co-founder & CSO, MITRA
Biotech, Woburn MA, USA

Jake M. Reder, Ph. D.
Advisor,
Episteme Prognostics LLC,
Co-founder, President and
CEO of Celdara Medical,
Lebanon, NH, USA

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development, Tuck School of
Business, Hanover, NH, USA

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Division Chief, Surgical
Oncology
Surgical Director, Islet Cell
Transplant Program
Assistant Professor of Surgery,
Geisel School of Medicine,
Dartmouth

Jason E Faris, MD
Clinical collaborator
Director of Early Phase Trial Program,
Norris Cotton Cancer Center,
Dartmouth-Hitchcock Medical Center
Member, Gastrointestinal Cancer
Clinical Oncology Group, Norris
Cotton Cancer Center, Dartmouth-
Hitchcock Medical Center

THANK YOU!

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