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CCSB @ PVAMU

CRI Center

Seungchan Kim, Ph.D.

Chief Scientist and Executive Professor

Electrical and Computer Engineering

Director, CCSB

Who I am

- Ph.D. trained at TAMU EE, 2001
- Post-doctoral trainee at NIH, 2001 - 2003
- Faculty at TGen, 2003 – 2016
- Faculty at ASU, 2004 - 2011
- Chief Scientist and Executive Professor, ECE Director, CCSB@PVAMU, 2017 - current

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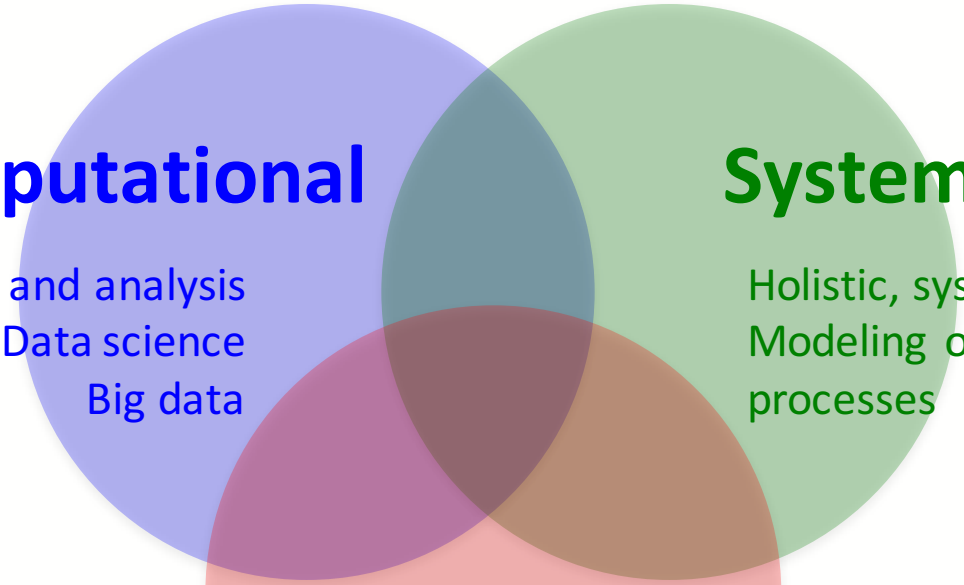
Computational Systems Biology



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So, exactly what does CSB do?

Cell PRESS

Cancer Cell
Article

Identification of Distinct Basal and Luminal Subtypes of Muscle-Invasive Bladder Cancer with Different Sensitivities to Frontline Chemotherapy

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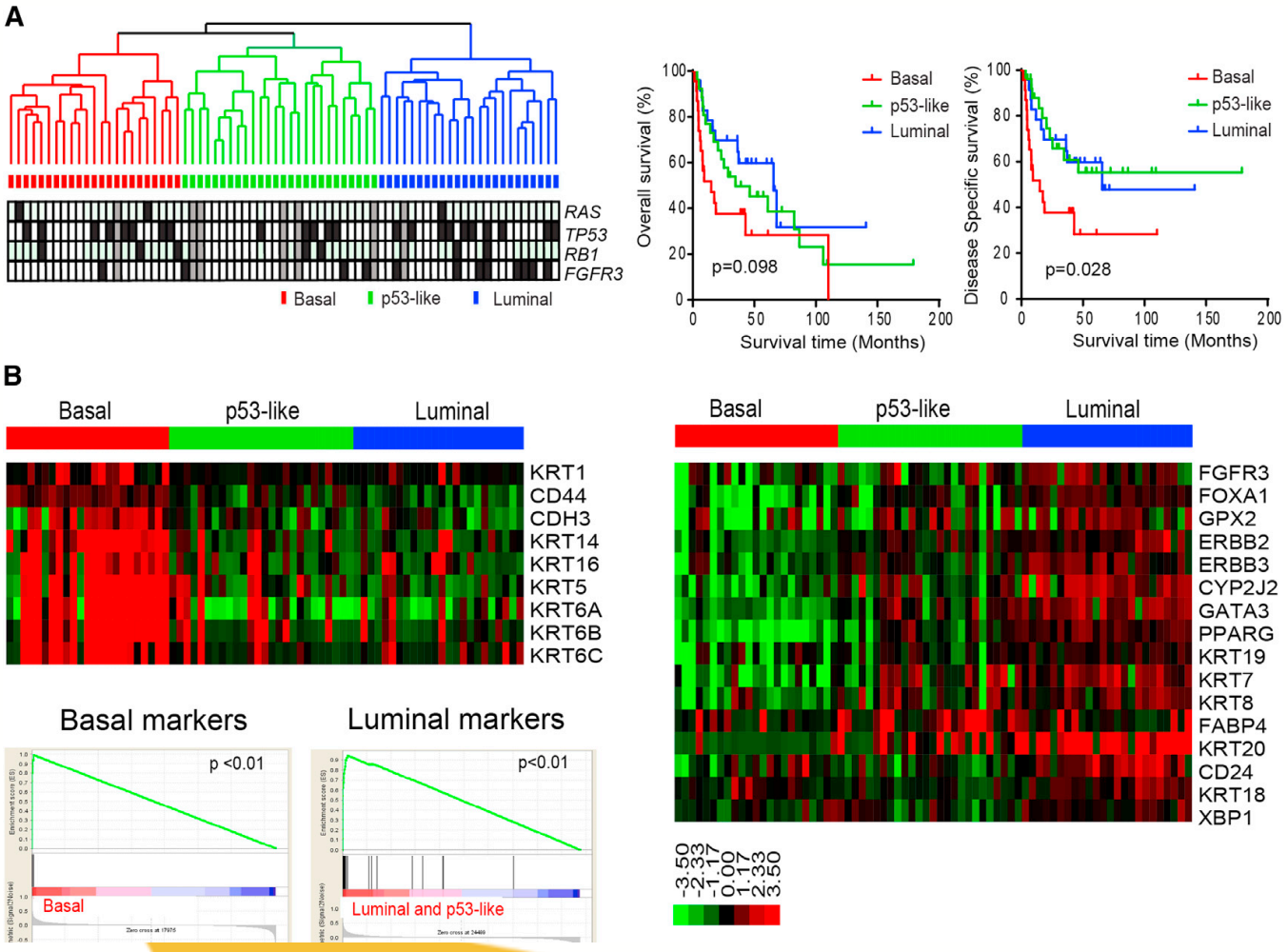
http://dx.doi.org/10.1016/j.ccr.2014.01.009

SUMMARY

Muscle-invasive bladder cancers (MIBCs) are biologically heterogeneous and have widely variable clinical outcomes and responses to conventional chemotherapy. We discovered three molecular subtypes of MIBC that resembled established molecular subtypes of breast cancer. Basal MIBCs shared biomarkers with basal breast cancers and were characterized by p63 activation, squamous differentiation, and more aggressive disease at presentation. Luminal MIBCs contained features of active PPARγ and estrogen recep-

Gene expression signatures for Bladder cancer subtypes



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Published online 5 February 2014 Nucleic Acids Research, 2014, Vol. 42, No. 7 e60
doi:10.1093/nar/gku099

EDDY: a novel statistical gene set test method to detect differential genetic dependencies

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Received June 11, 2013; Revised and Accepted January 10, 2014

ABSTRACT

Identifying differential features between conditions is a popular approach to understanding molecular features and their mechanisms underlying a biological process of particular interest. Although many tests for identifying differential expression of gene or gene sets have been proposed, there was limited success in developing methods for differential interactions of genes between conditions because of its computational complexity. We present a method for Evaluation of Dependency DifferentialitY (EDDY), which is a statistical test for differential dependencies of a set of genes between two conditions. Unlike previous methods focused on differential expression of individual genes or correlation changes of individual gene–gene interactions,

INTRODUCTION

Since the emergence of high-throughput genomic profiling techniques, numerous statistical methods gained high popularity in biomedical studies to assess diverse features in biological samples. One of such statistical approaches is identifying variables with differential patterns between different conditions, where genomic entities (such as genes or proteins) are often modeled as target variables. Such methods can vary based on the definition of differentiality or what a target feature of comparison is, but the general idea is comparing probability distributions of a target feature across given conditions.

The simplest case of identifying differentiality is differential expression of a single gene, where each gene is independently tested for differential expression. There have been many studies with this approach of independent tests for individual genes. For comprehensive reviews of

DIFFERENTIAL PATHWAY DEPENDENCY DISCOVERY ASSOCIATED WITH DRUG RESPONSE ACROSS CANCER CELL LINES *

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The effort to personalize treatment plans for cancer patients involves the identification of drug treatments that can effectively target the disease while minimizing the likelihood of adverse reactions. In this study, the gene-expression profile of 810 cancer cell lines and their response data to 368 small molecules from the Cancer Therapeutics Research Portal (CTRP) are analyzed to identify pathways with significant rewiring between genes, or differential gene dependency, between sensitive and non-sensitive cell lines. Identified pathways and their corresponding differential

KNOWLEDGE-ASSISTED APPROACH TO IDENTIFY PATHWAYS WITH DIFFERENTIAL DEPENDENCIES*

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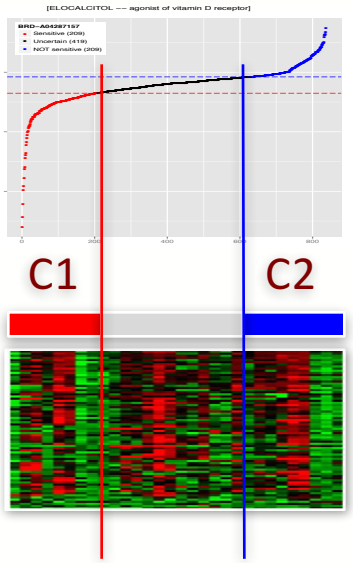
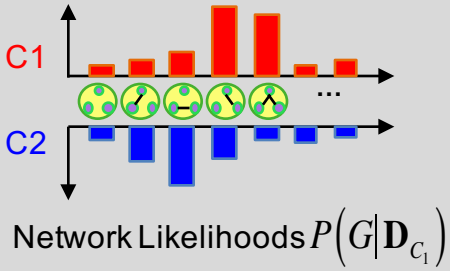
We have previously developed a statistical method to identify gene sets enriched with condition-specific genetic dependencies. The method constructs gene dependency networks from bootstrapped samples in one condition and computes the divergence

EDDY-CTRP Analysis Pipeline

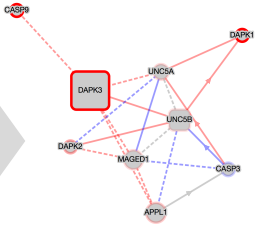
Gene Set DB

Known gene-gene Interactions

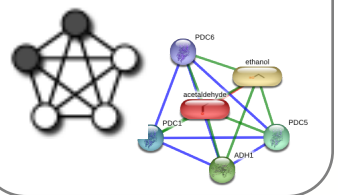




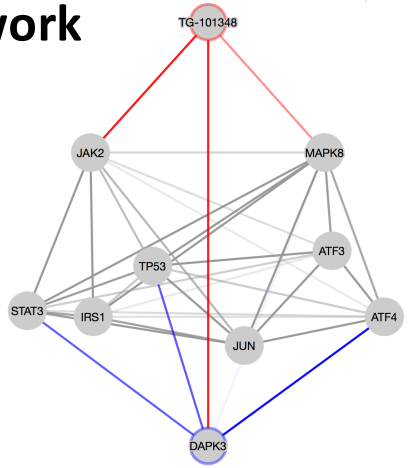
Pathway	DB	# genes	p-val	Rewiring
FIBRINOLYSIS	B	12	0.0062	0.56
IL4	B	11	0.0074	0.67
DCC MEDIATED ATTRACTIVE SIGNALING	R	13	0.0086	0.66
GRANULOCYTES	B	14	0.0093	0.53
P130CAS LINKAGE TO MAPK SIGNALING FOR INTEGRINS	R	15	0.0101	0.61
DSCAM INTERACTIONS	R	11	0.0105	0.6
TRAF3 DEPENDENT IRF ACTIVATION	R	14	0.0169	0.73
CARM1	B	13	0.0173	0.68
SPRY REGULATION OF FGF SIGNALING	R	14	0.0183	0.56
THE NLRP3 INFLAMMASOME	R	12	0.0185	0.72



STRING/STITCH



Evidence Network



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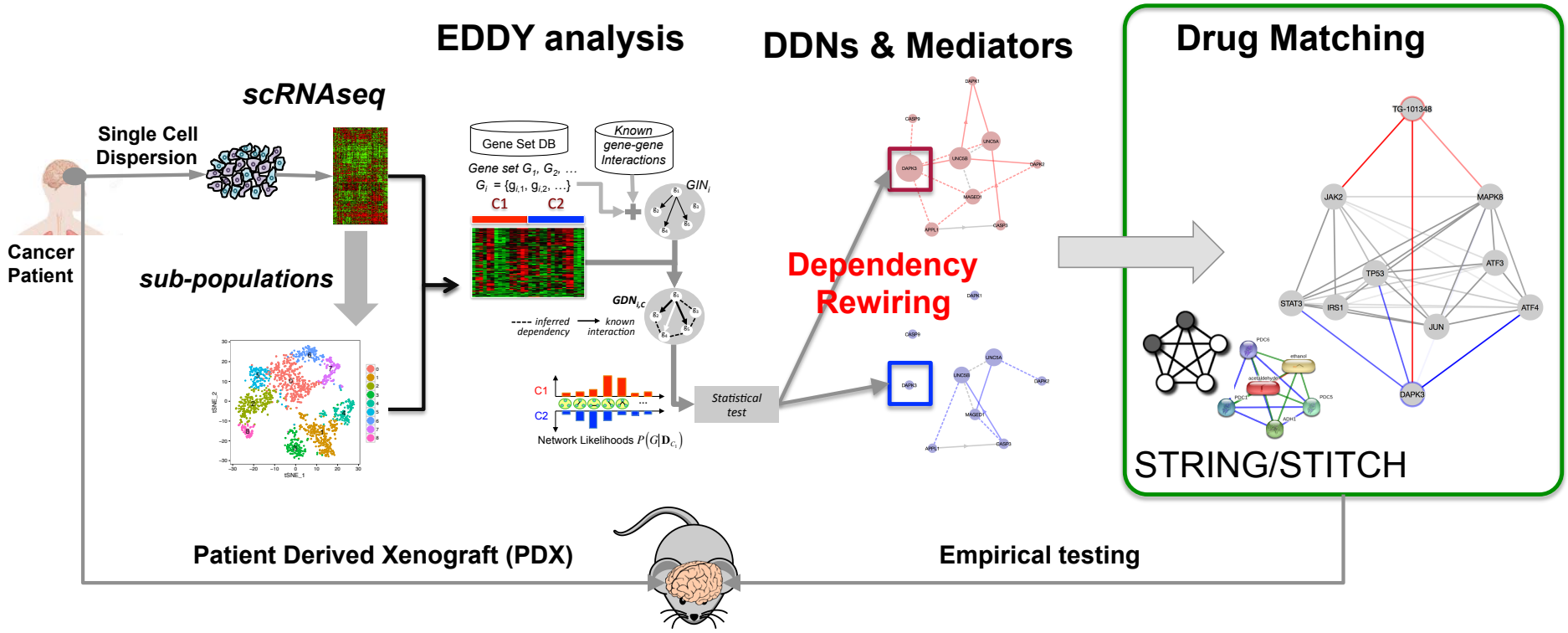
Fighting Cancer, Cell by Cell



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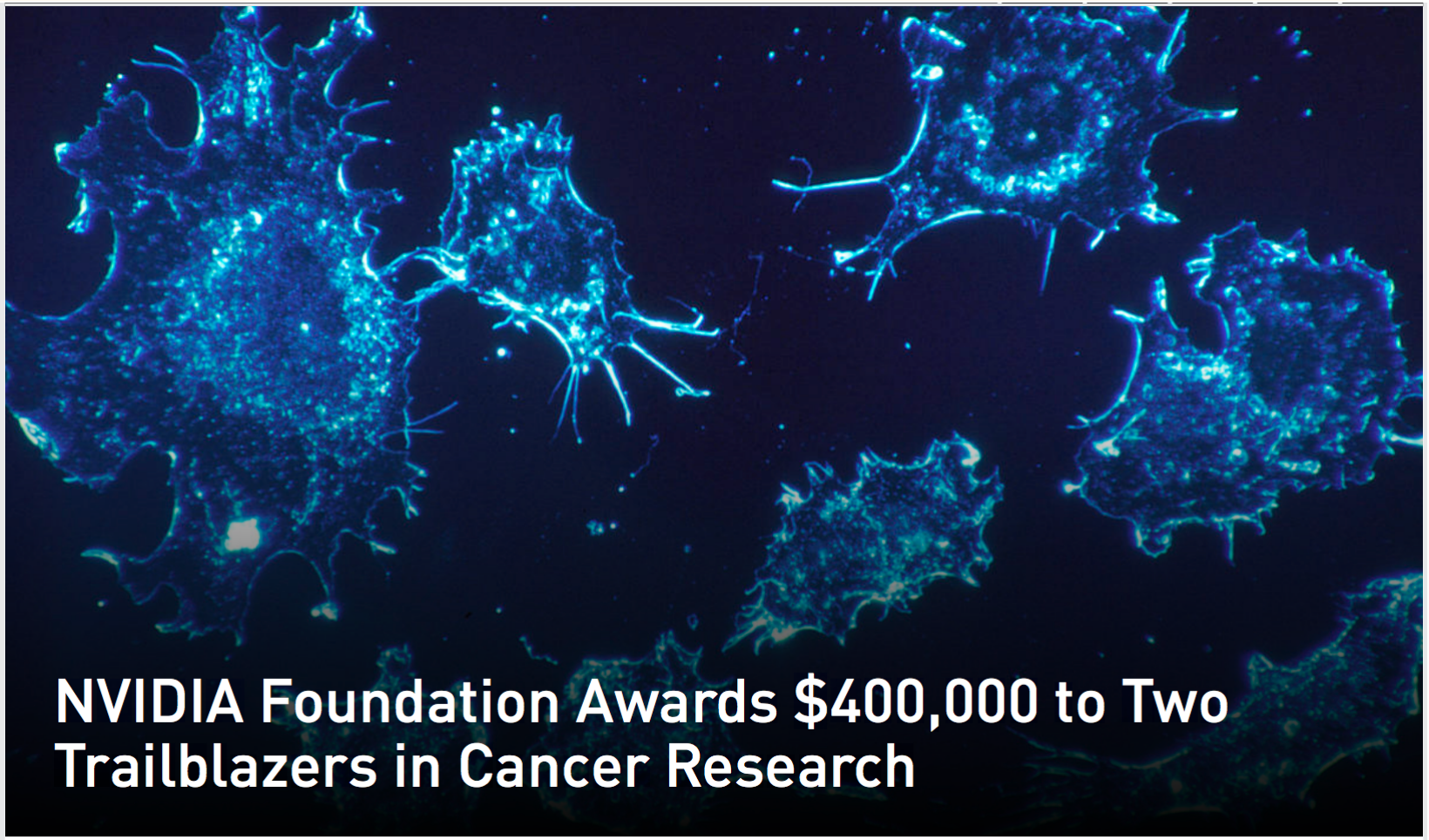
Fighting Cancer, Cell by Cell



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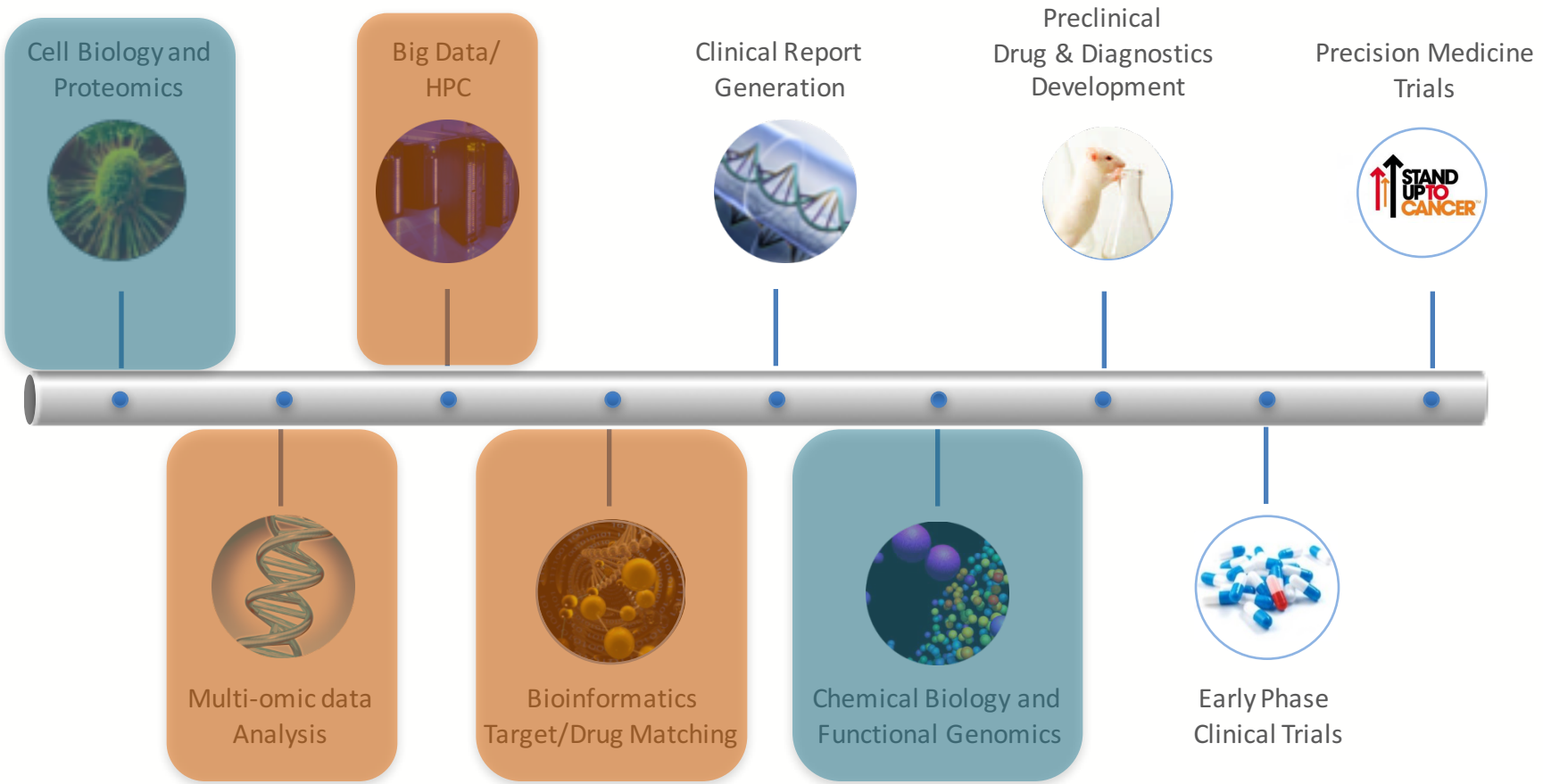
Precision Medicine Pipeline



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- Why PVAMU
  - Chancellor's Research Initiative provides resource
    - PI: Dr. Lijun Qian (ECE) for the proposal
    - Director: Dr. Seungchan Kim (ECE)
  - College of Engineering leads the initiative
  - Its proximity to Texas Medical Center provides numerous potential collaborators

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CCSB @ PVAMU

- Dry lab + Wet lab within the center
  - Wet lab is critical for validation of novel hypothesis generated by computational analysis

- Leading edge research
  - Recruit top-notch scientists and engineers
  - Train graduate students
  - Develop collaboration

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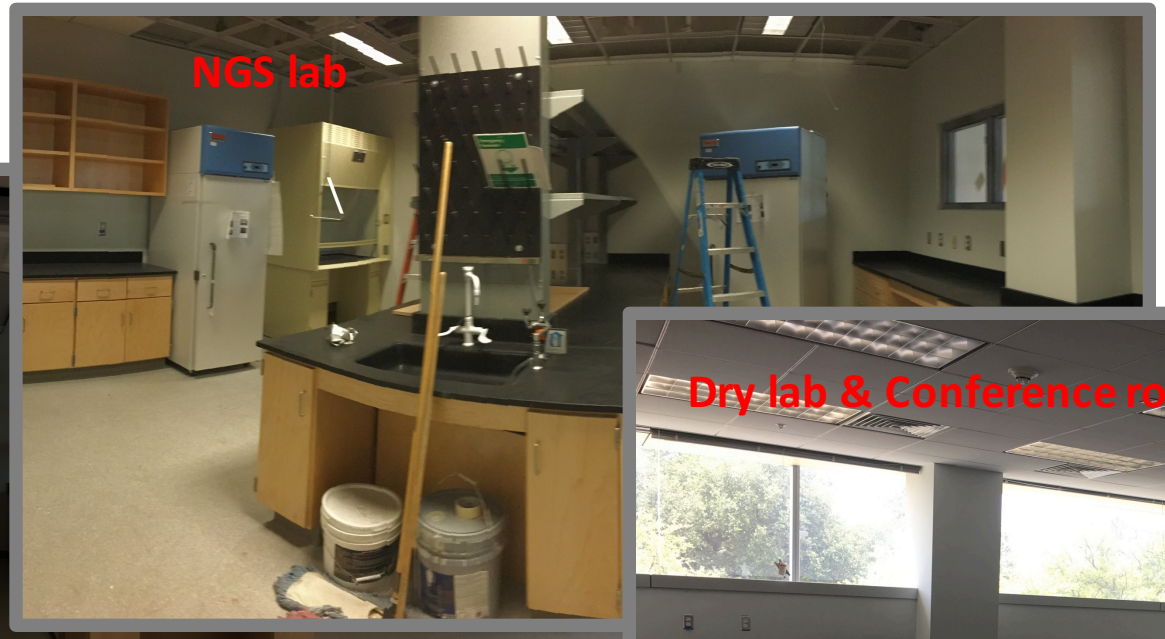
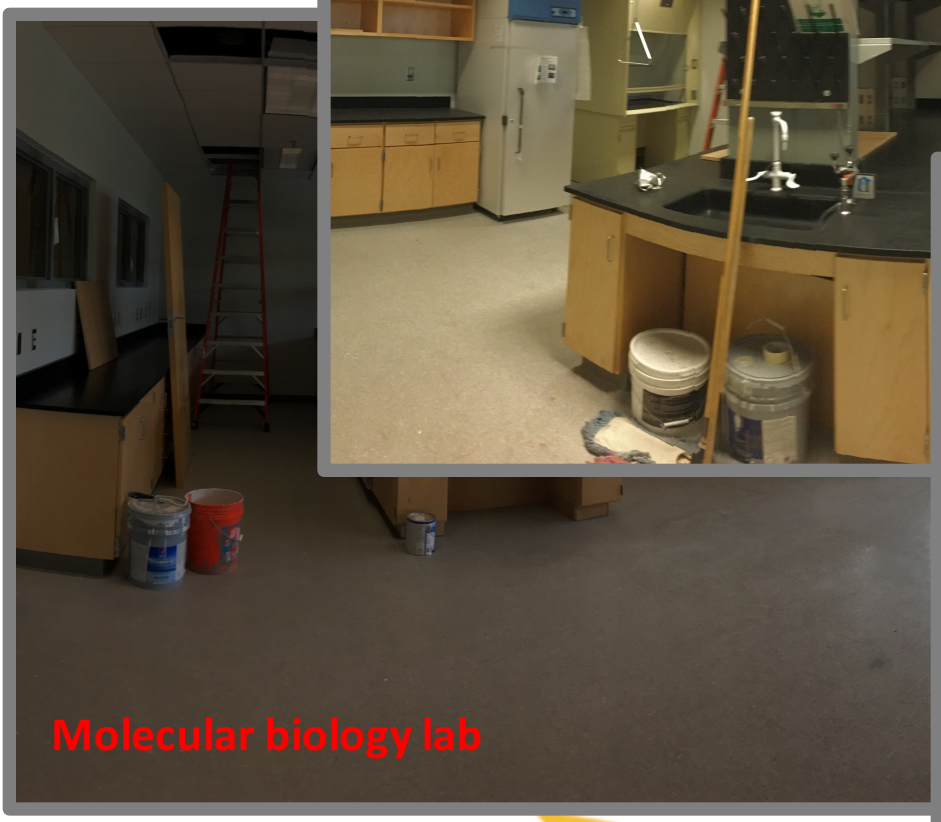
CCSB @ PVAMU under Construction





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Training Future Computational Biologists

- Bioinformatics concentration for undergraduate and graduate students

- Research Experience for Undergraduate (REU)
- Bioinformatics / Computational Biology training for graduate students

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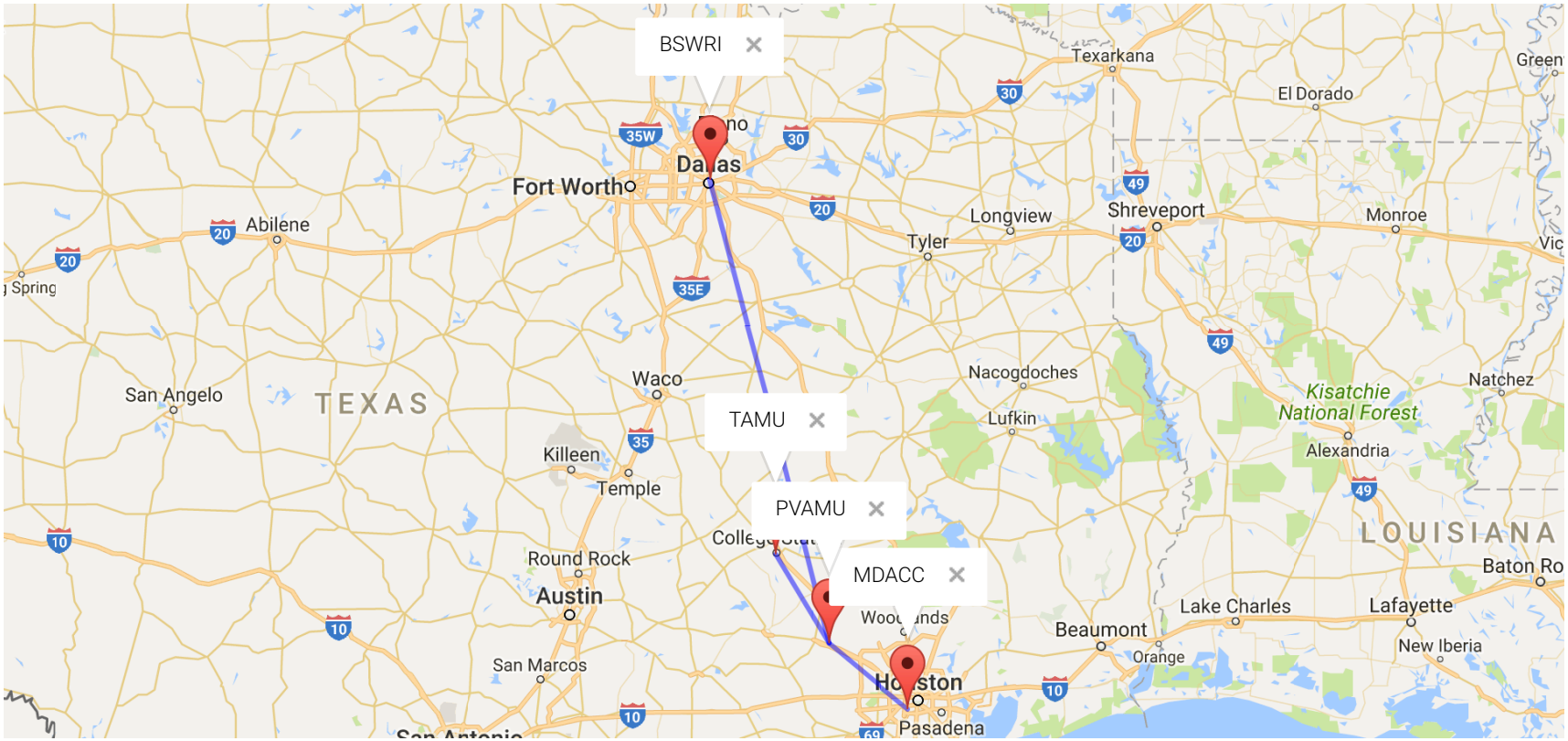
Developing Collaboration

- Local
  - Texas Medical Center (Baylor, M.D. Anderson Cancer Center)
  - Texas A&M University
- State-Wide
  - Baylor, Scott & White Research Institute (Dallas)
- Nation-wide
  - TGen
  - USC
  - NIH/NCI
  - U. Pittsburgh

CCSB @ PVAMU Collaboration (State-wide)



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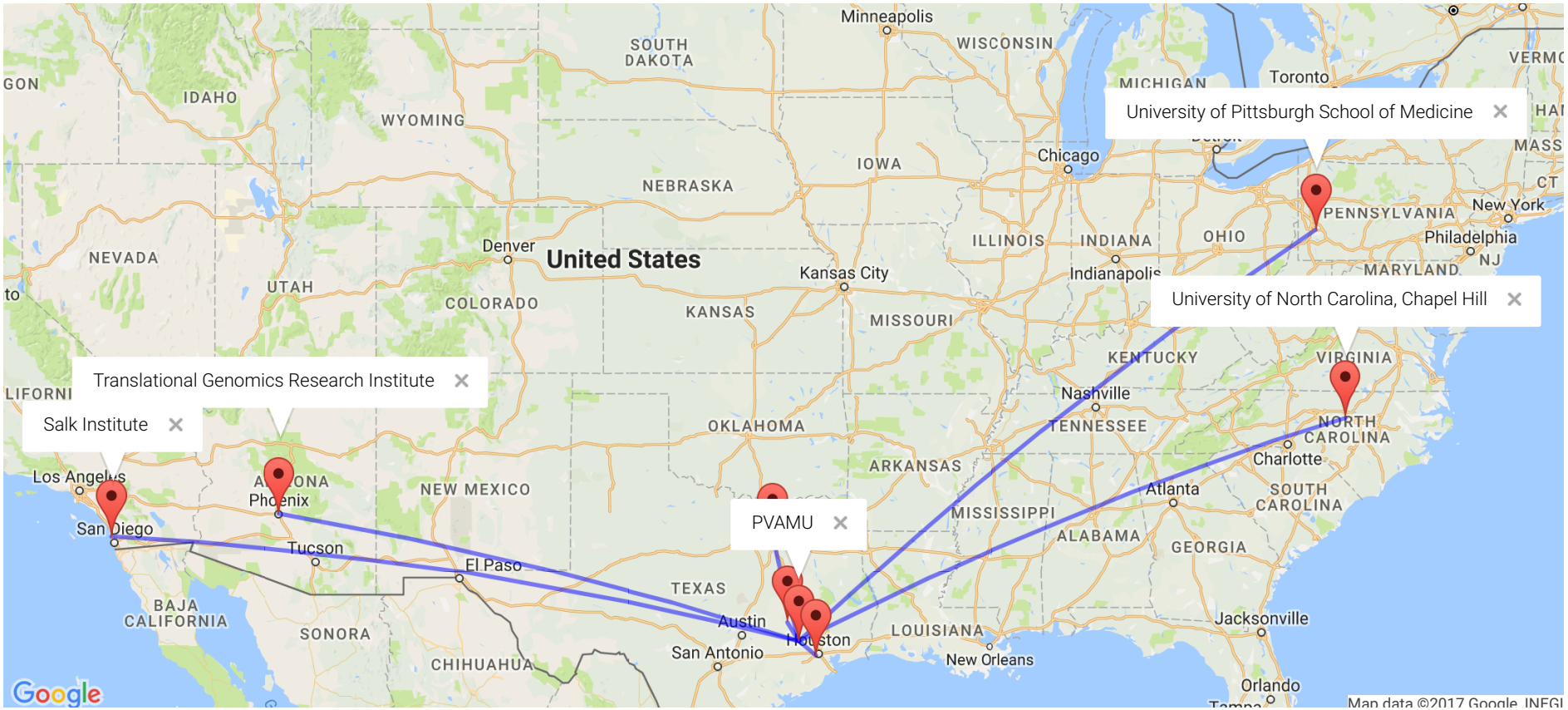
CCSB @ PVAMU Collaboration (Nation-wide)



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- Questions?