



A Physical Sciences Approach to Biospecimen Research via High Content Screening

Nicole Moore, Helen Moore, David Litwack, Sherilyn Sawyer, Emily Greenspan, Carolyn Compton, and Larry A. Nagahara, Jerry S.H. Lee

Center for Strategic Scientific Initiatives (CSSI)
National Cancer Institute (NCI), National Institutes of Health (NIH)

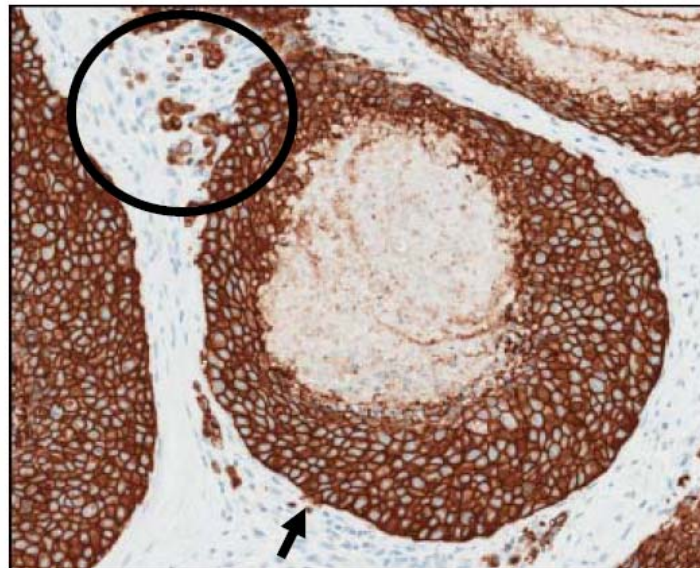
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Merging “Perspectives”

OPSO and OBBR

Physical Scientist

- How much energy is needed to do this?
- How much force does it take to cross this barrier?
- Are reactions rates altered during this process?
- How much time does it take?
- What is the spatial effect? Diffusion coefficient?
- How many variables are needed to describe the system?
- What is the critical length scale?



Cancer Biologist/Oncologist

- What cell, molecule, tissue is it?
- What changed?
- What's up/down regulated?
- Do I see the same thing in several tumors?
- Do I see specific biomarkers?
- What are the important signal transduction pathways?

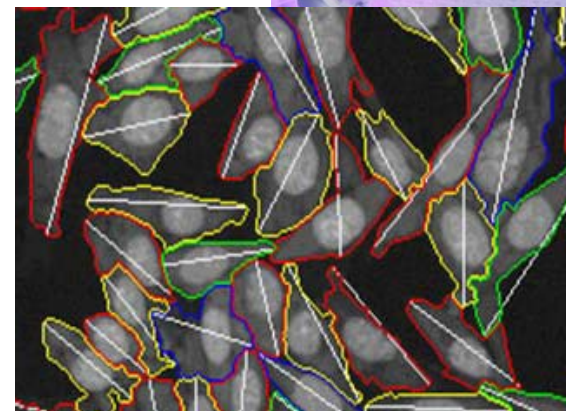
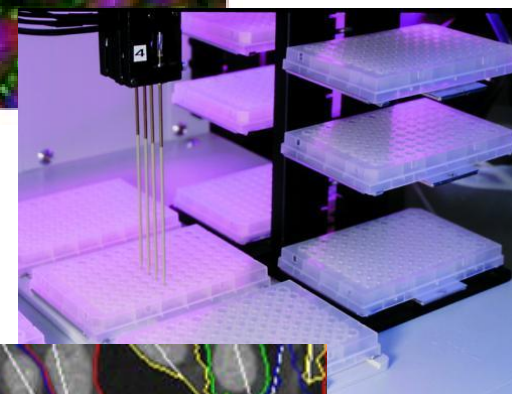
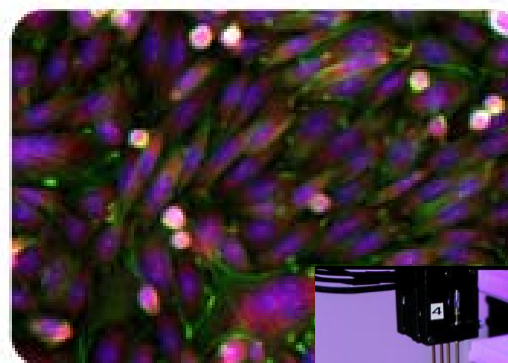
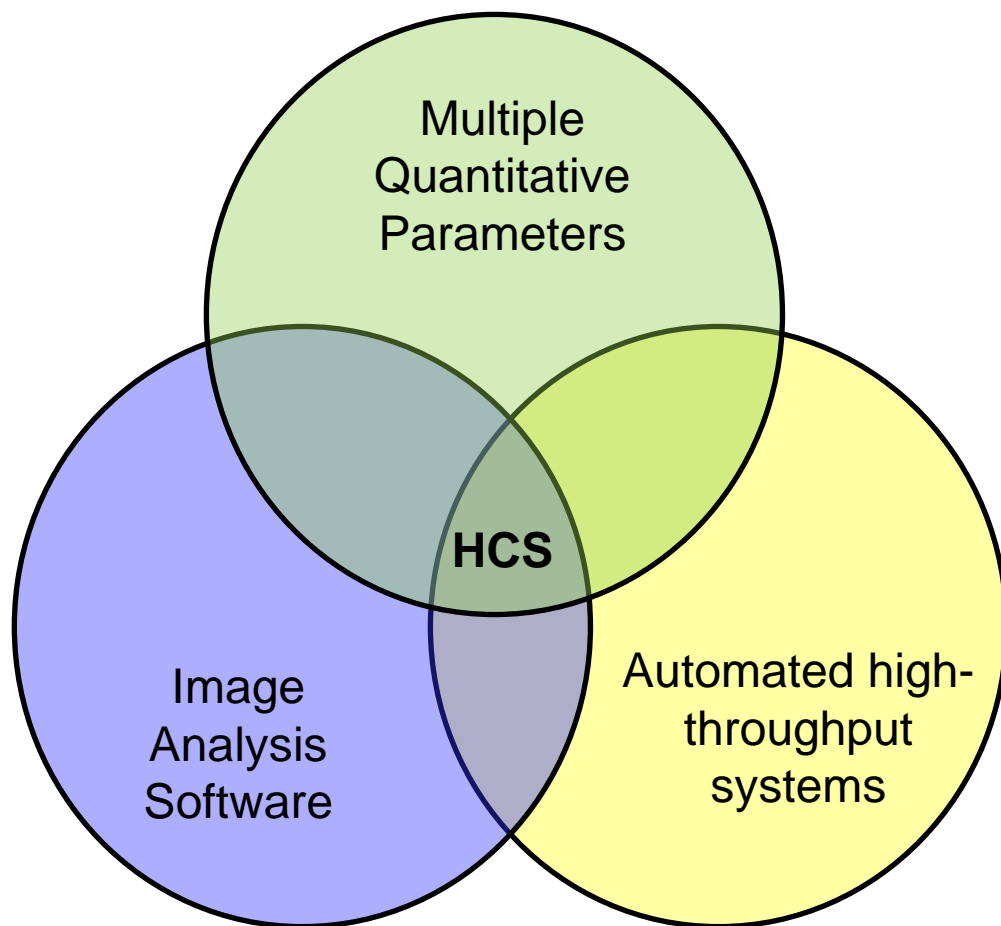
Different ‘views’ of the same picture

Having both perspectives yields a more comprehensive (clearer) picture of what cancer is and how it functions at all levels – especially at the sub-molecular/atomic scales

Physical Sciences Perspective (PSP) High Content Screening (HCS)

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A combination of high throughput technology & multiple parameter analysis



Physical Sciences Perspective (PSP) High Content Screening (HCS)

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Advantages of HCS

- ❑ Bridge the gap between depth and throughput of biological experiments
- ❑ Standardize processing and analysis
- ❑ Capture large quantities of key data not typically detected with single assays
- ❑ Speed



Perkin Elmer Opera High Content
Screening System



GE In Cell Analyzer Workstation

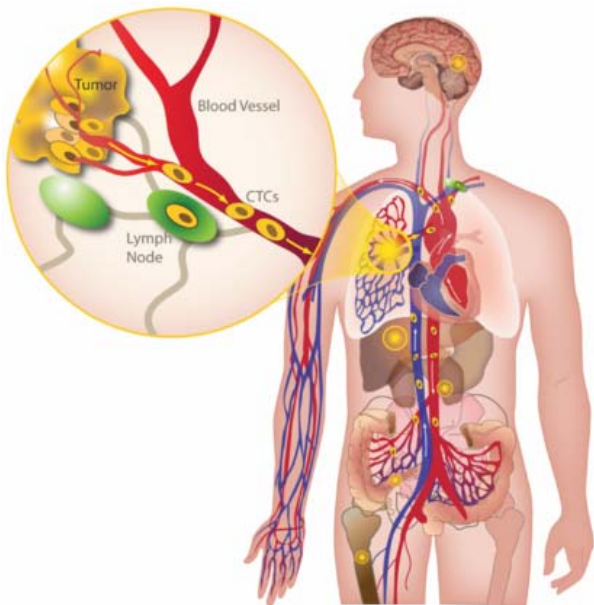


BD Pathway Bioimager

Systems optimized for single cells analysis for drug screening & discovery applications

Can we use this technology with a PSP for biospecimen research?

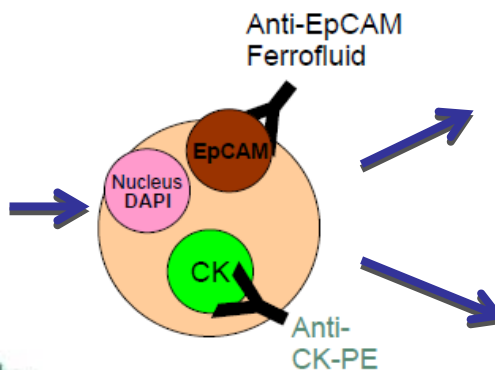
Example #1: Fluid biopsy collection, handling, and processing (CHP)



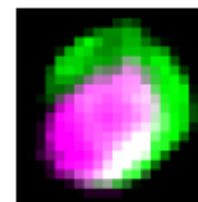
CellSave Tube



CellSearch
Circulating Tumor Cell Test



Circulating Tumor Cell



Cytokeratin +
CD45 -
Number
per 7.5 mL
Blood

CHP Variables

- Blood draw location
- Laying down vs. Sitting up
- Tube type/ Anti-coagulant
- Time to processing sample
- Shipping temperature
- Order of blood draw
- Length of time for tourniquet
- Many others.....

Difficult to measure the impact of CHP variables
due to limited information

What about?

- Cell viability and integrity
- EpCAM negative cells
- Cell and nuclear morphology
- Cell clusters
- Pathological diagnosis
- Apoptotic cells
- Other molecular biomarkers

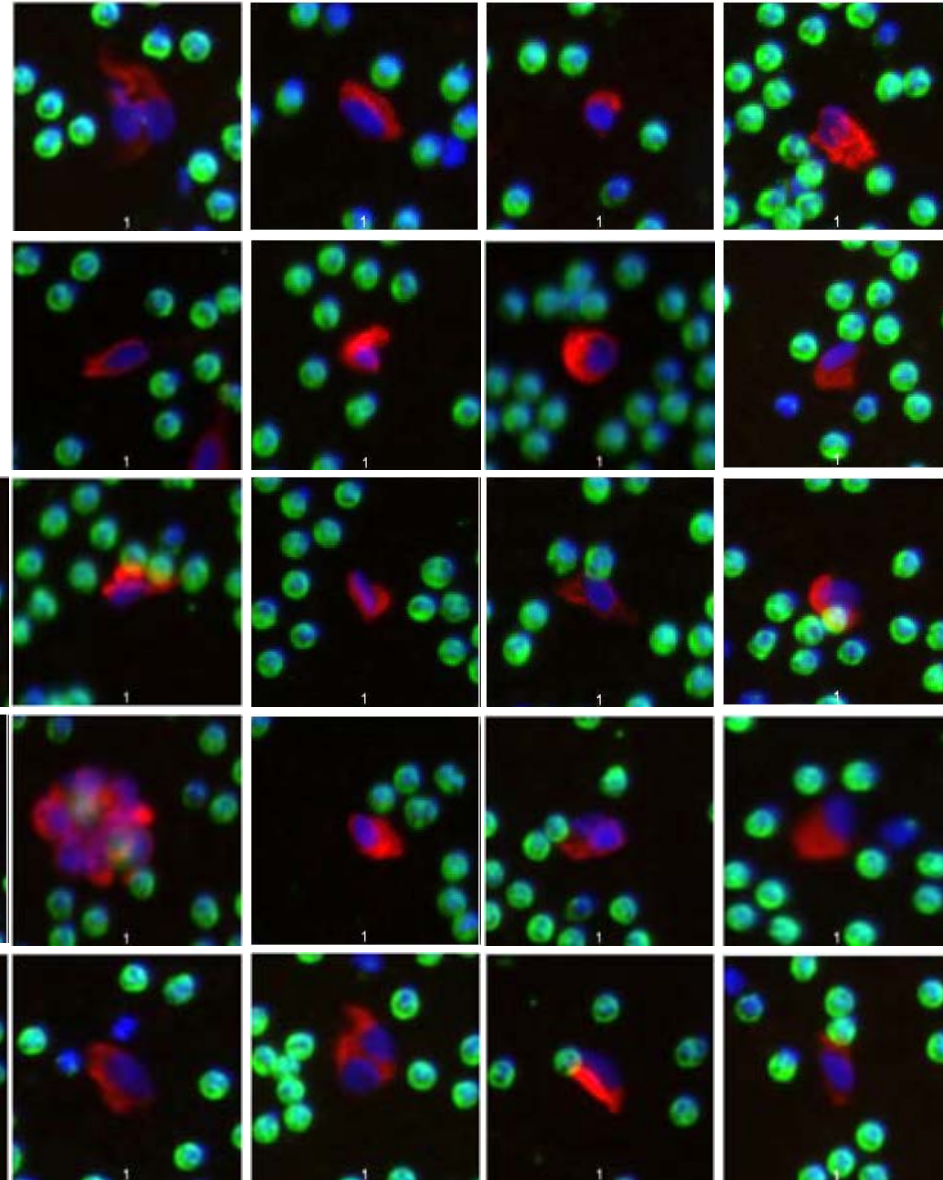
A Physical Sciences Perspective

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Peter Kuhn, Ph.D.
The Scripps
Research Institute

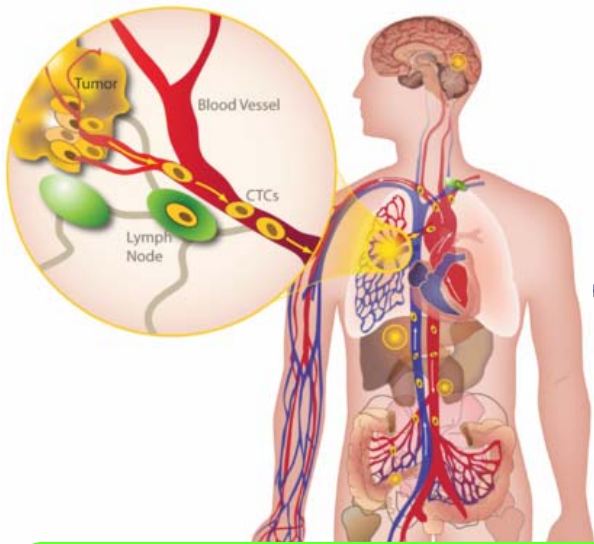
- What information are we missing by using “single content” techniques?
- What can't we just look at everything?



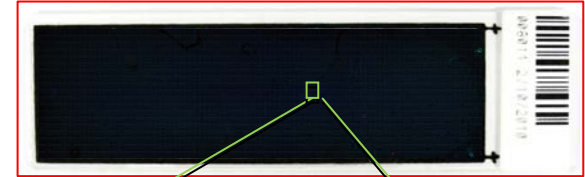
Scripps PS-OC PSP Platform

PI: Peter Kuhn

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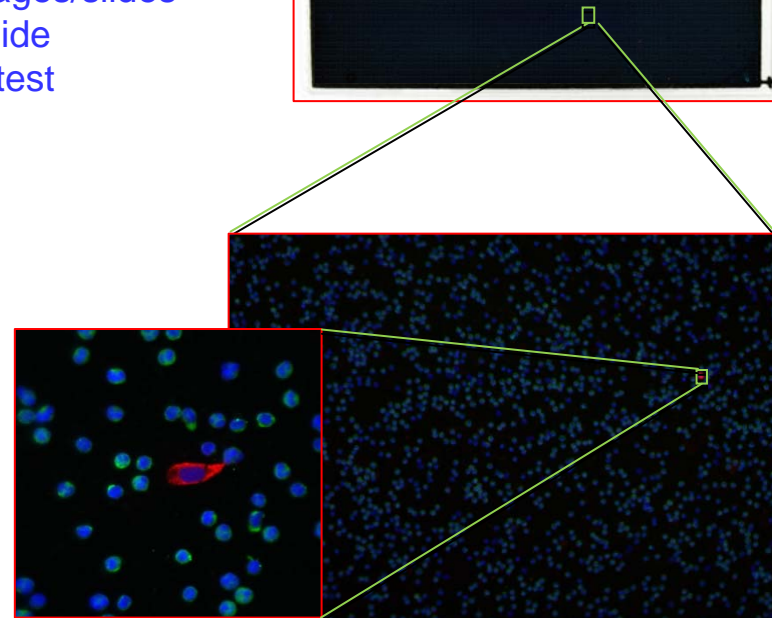


- ~3 million cells
- 9216 images/slides
- 25 GB/slide
- 4 slides/test



Rare blood cells?

- Has an intact nucleus (DAPI+)
- and has cytokeratin (tissue origin marker)
- and LACKS CD45 (leukocyte origin marker)
- and is morphologic distinct from surrounding leucocytes
- and is displayed in diagnostic pathology quality



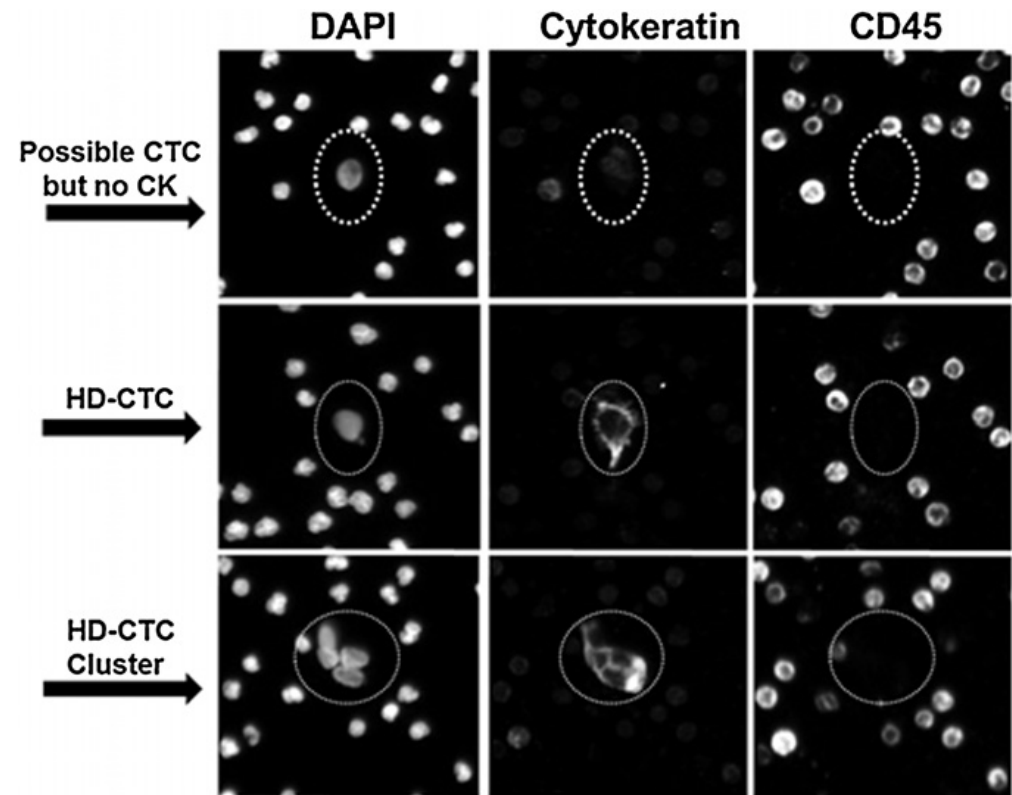
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High content with PSP platform

More Cells

Cancer type	HD-CTCs mL ⁻¹	CellSearch/mL
Breast #1	49.3	0.1
Breast #2	87	0
Breast #3	33.4	0.1
Breast #4	199.3	0.1
Breast #5	5	3.1
Prostate #1	2.3	0
Prostate #2	8.4	0.4
Prostate #3	107.3	2.8
Prostate #4	1.3	0
Prostate #5	150.5	0.1
Prostate #6	0	0
Prostate #7	1.4	0.5
Prostate #8	1.5	0.1
Prostate #9	145.3	0.8
Prostate #10	57.6	0



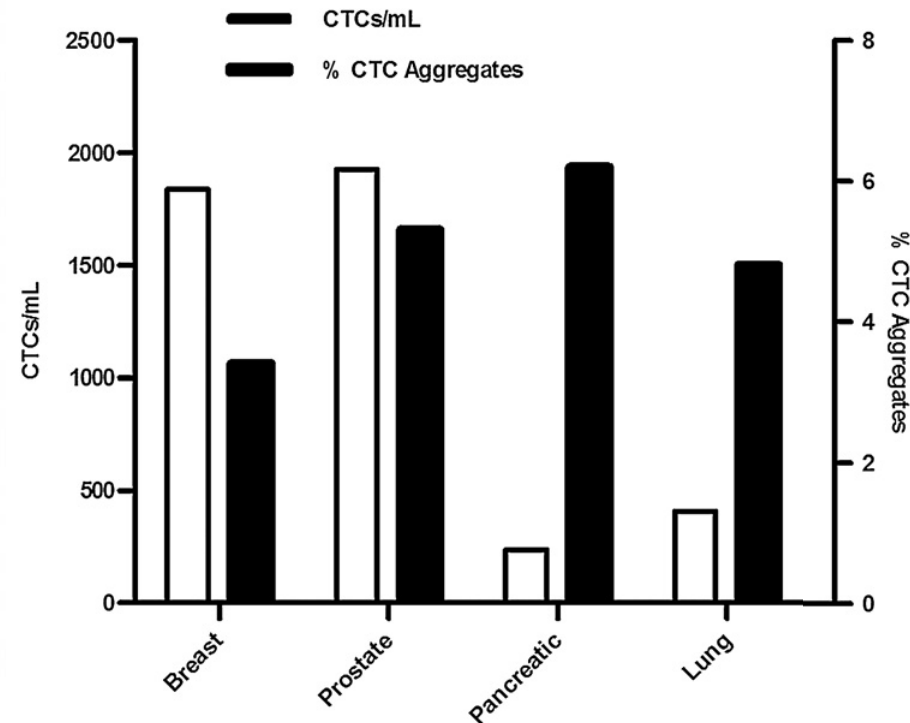
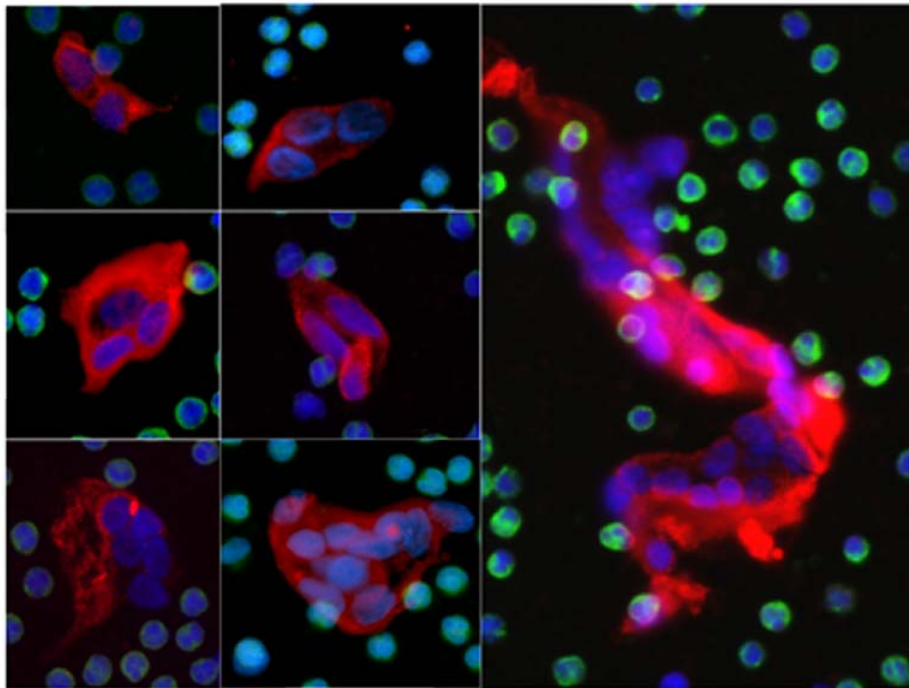
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High content with PSP platform

Cell Clusters



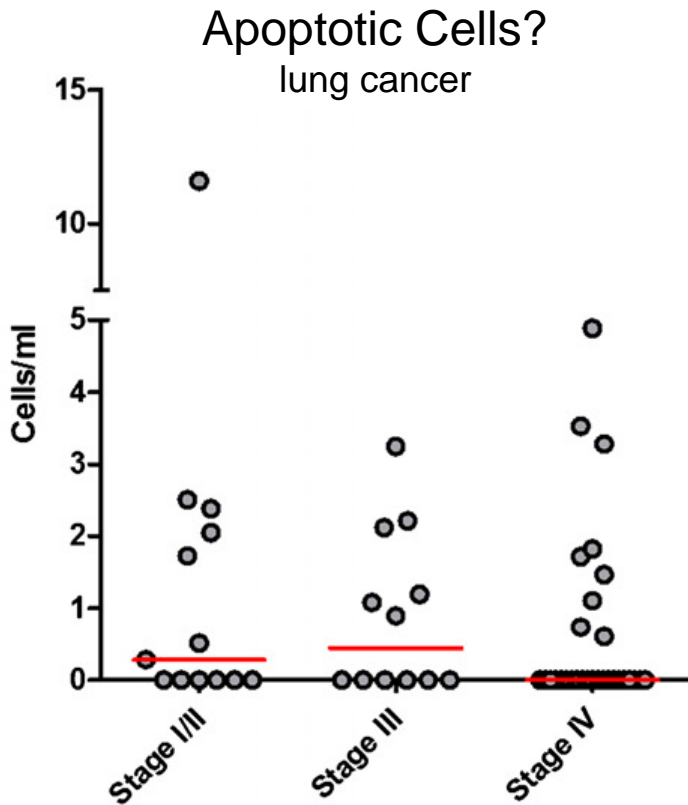
Marrinucci D et al. Physical Biology 2012
Wendel M et al. Physical Biology 2012
Cho E et al. Physical Biology 2012

Scripps PS-OC PSP Platform

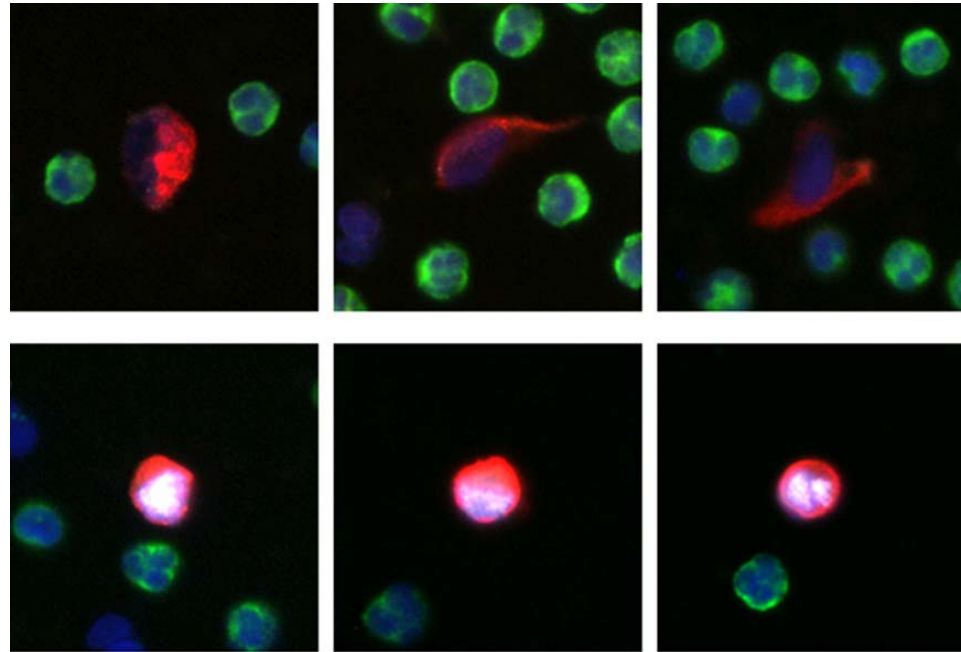
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High content with PSP platform

Specific disease biomarkers or response to treatment

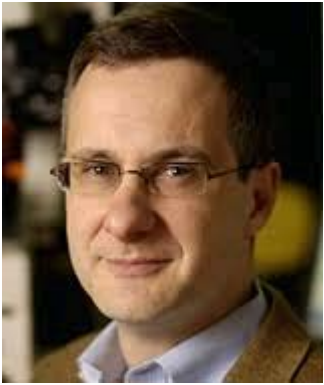


Androgen Receptor Positive?
prostate cancer



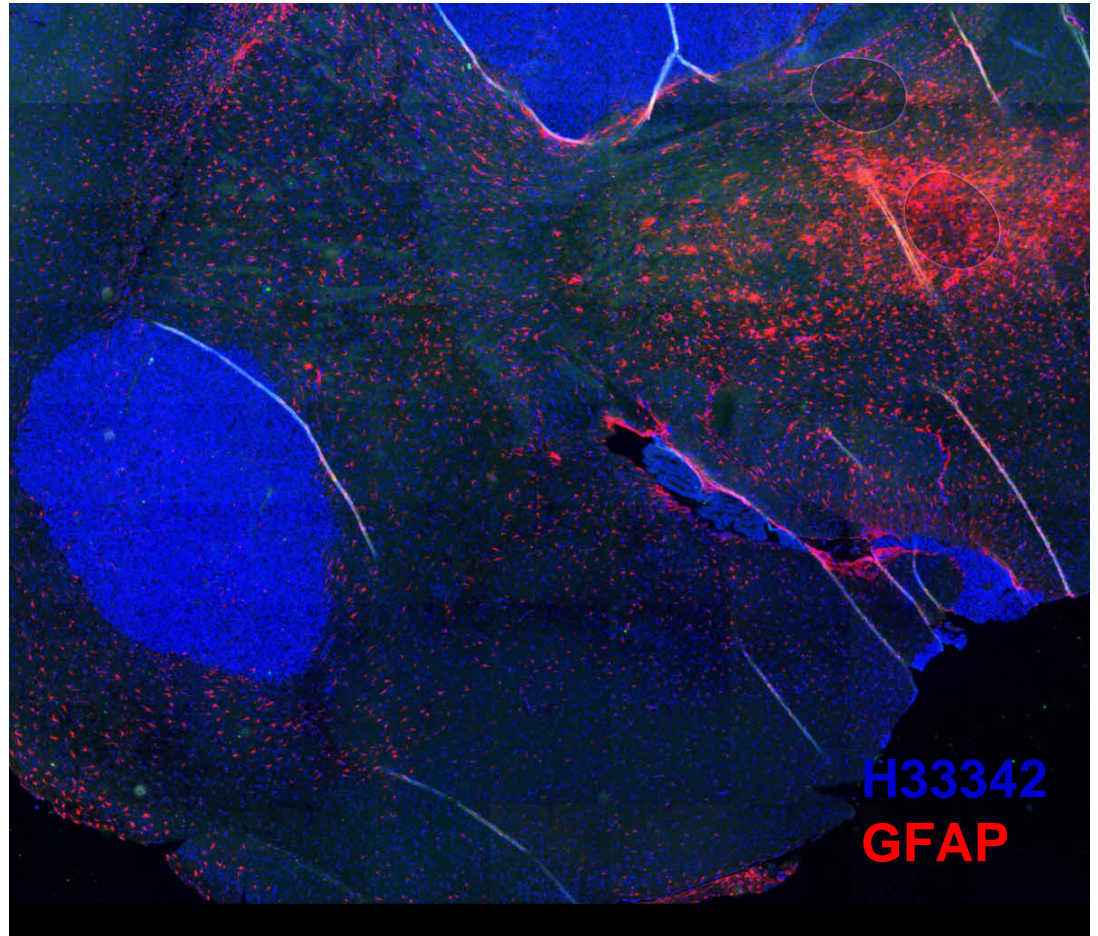
Example #2:

Quantitative Pathology with PSP



Denis Wirtz, Ph.D.
Johns Hopkins University

- ❑ What are the “physical” biomarkers in cancer?
- ❑ How do we quickly measure these markers?

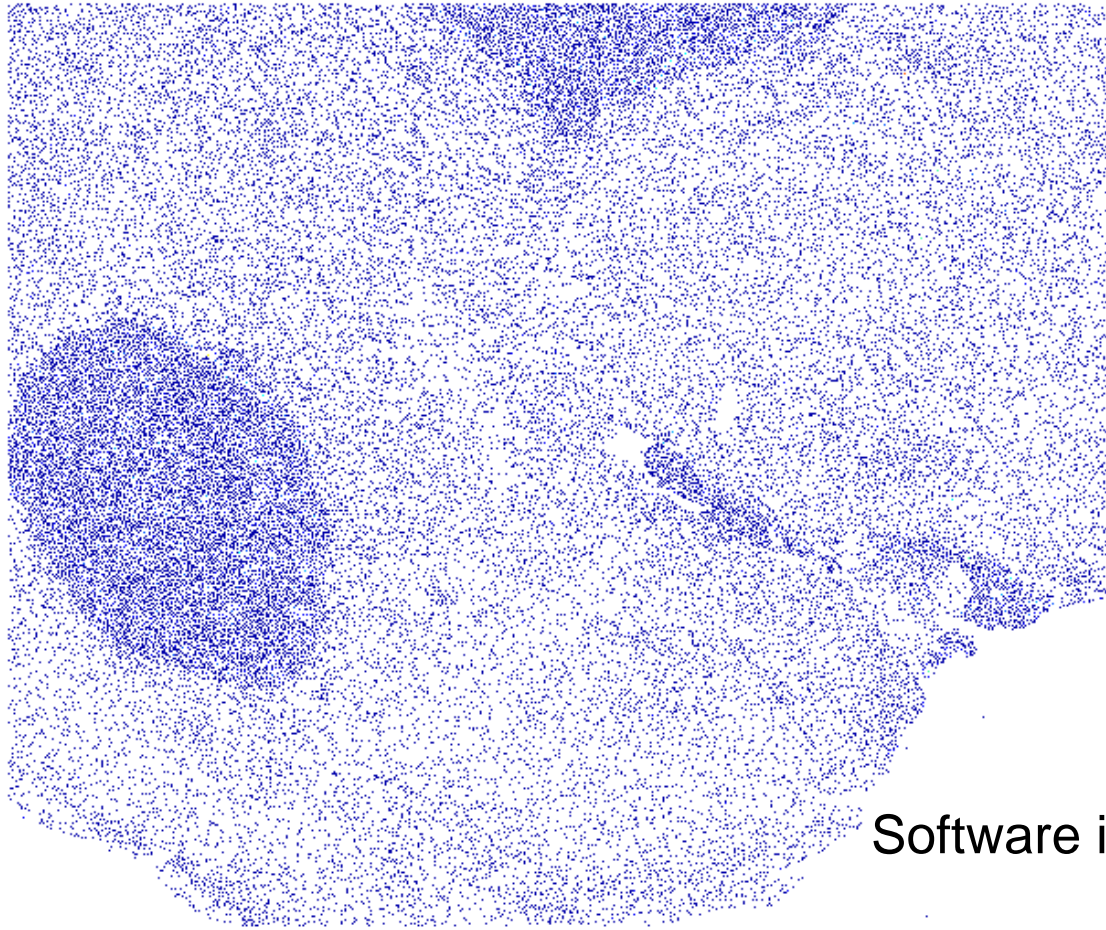


GBM, male,
35 years old

JHU PS-OC PSP Platform

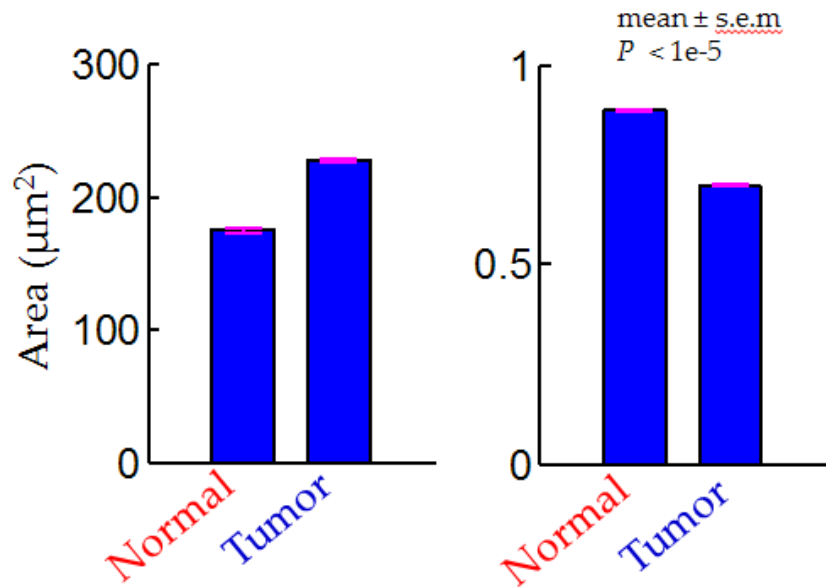
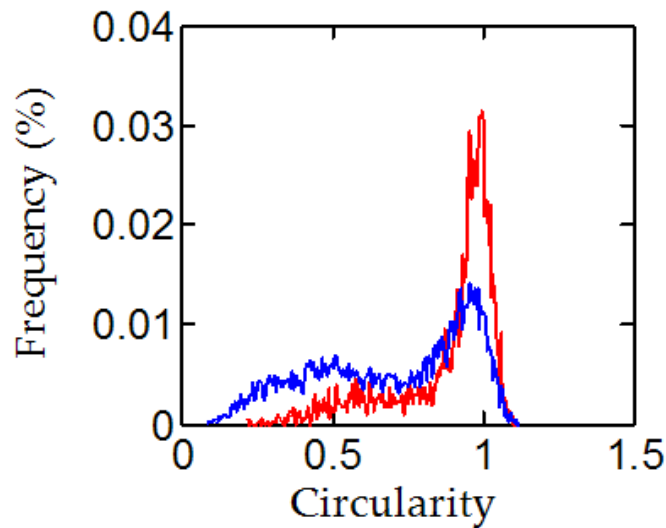
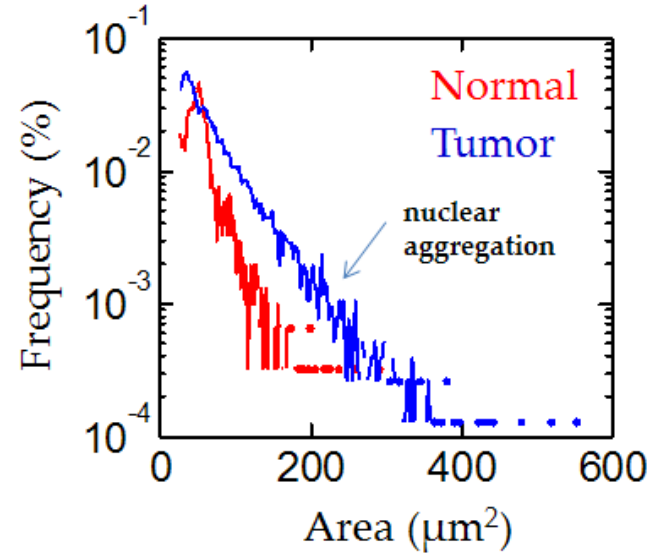
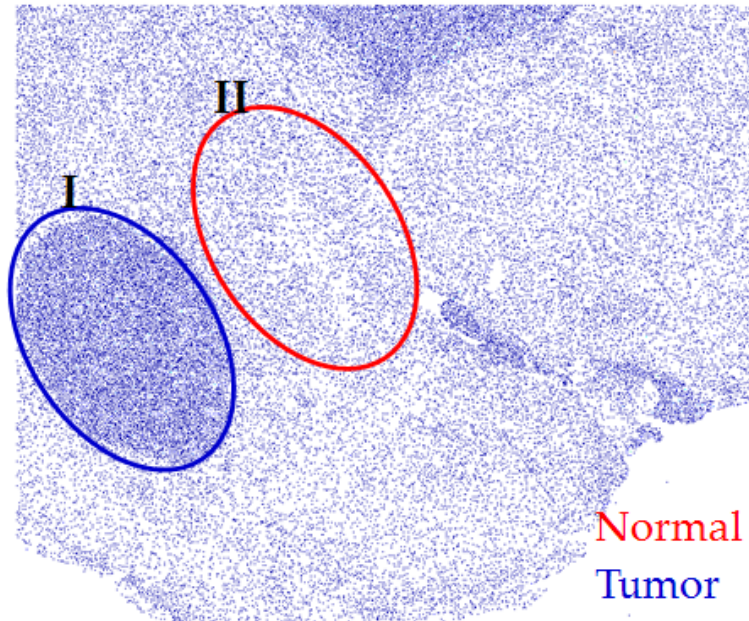
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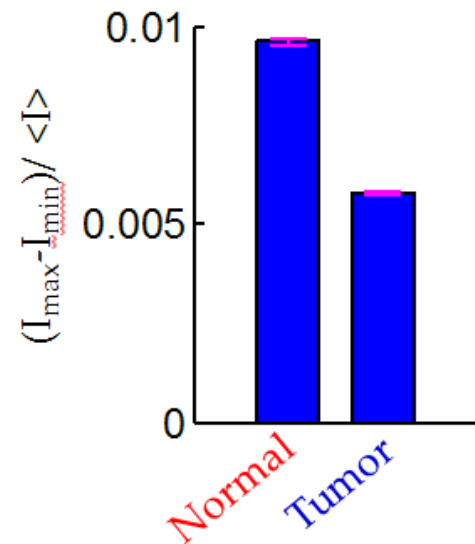
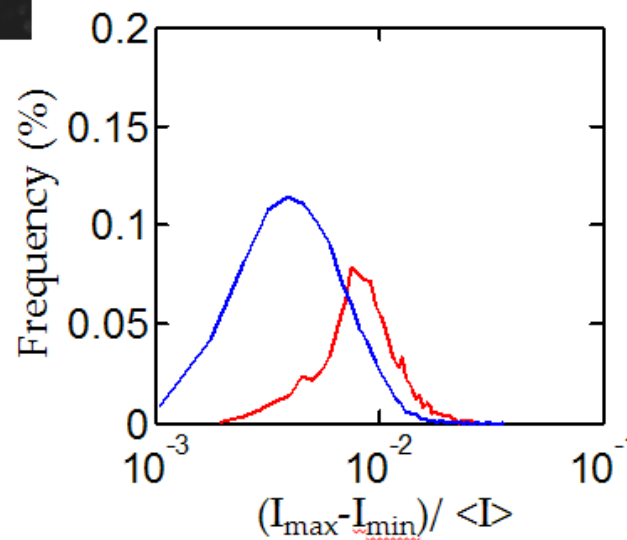
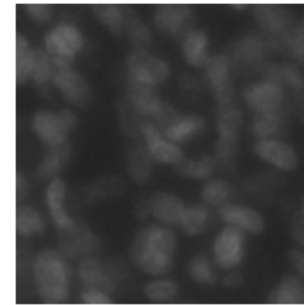
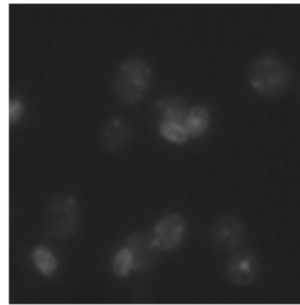
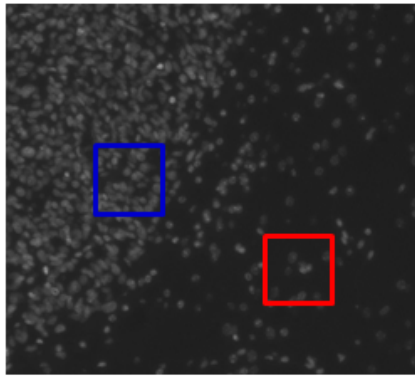
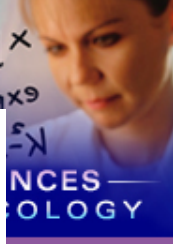


Software identified 41,622 nuclei

Courtesy of Denis Wirtz



Intensity texture as tumor marker

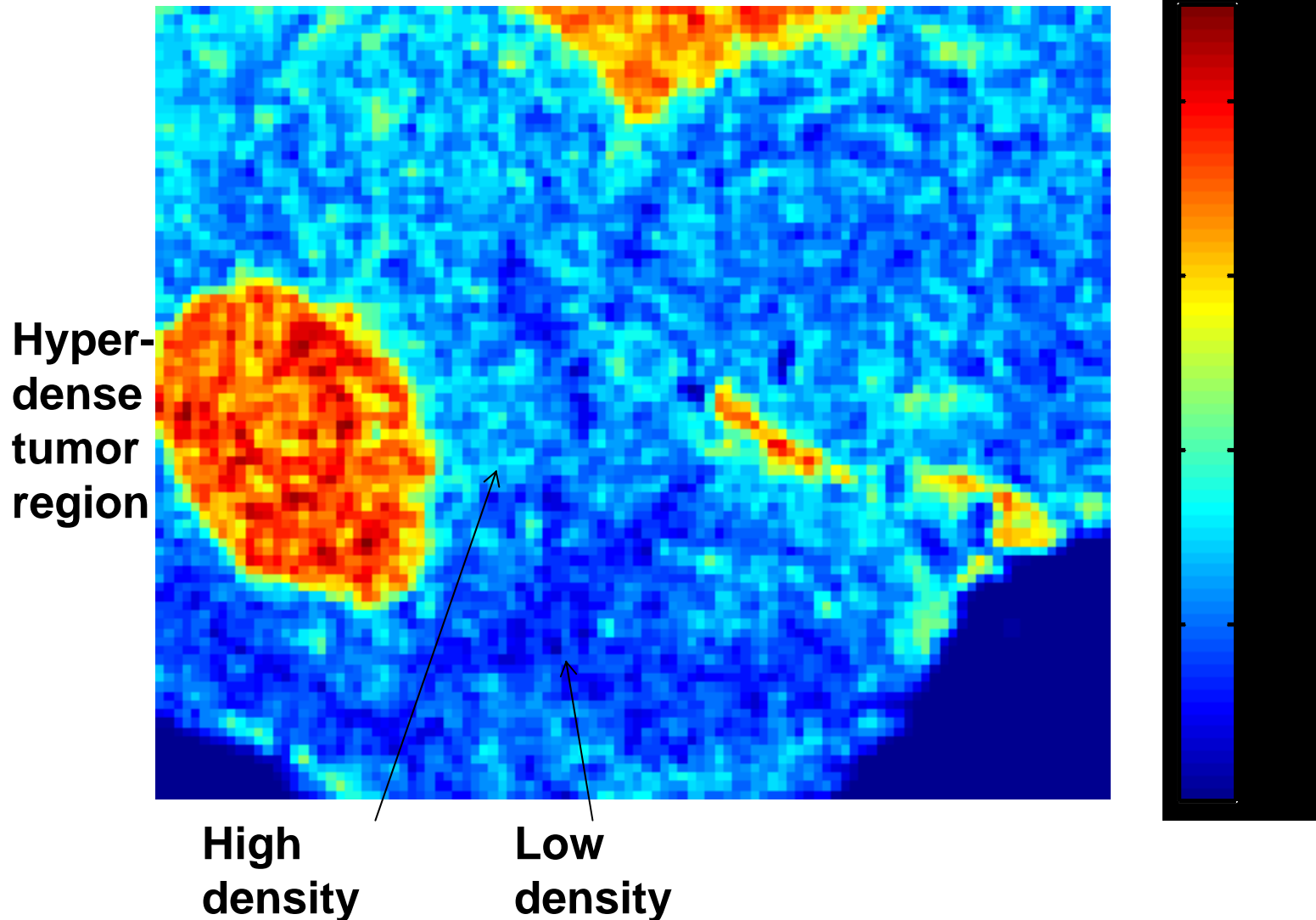


- Intensity of H33342 staining is more homogeneous in tumor.
- Can be quantitative marker for evaluation of invasion.

JHU PS-OC PSP Platform

PI: Denis Wirtz

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Courtesy of Denis Wirtz

Conclusions

- ❑ Incorporating a physical sciences perspective in cancer research forces us to ask new questions and can potentially expand our knowledge
- ❑ Combining a PSP with high content assays provides new information to probe the effects of collection, handling, and processing variables quickly with multiple parameters

Physical Sciences in Oncology (physics.cancer.gov)

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NCI is building multidisciplinary teams
with physical scientists to

Tackle Barriers in Cancer Research Using Novel Approaches

Meeting the Challenge

The National Cancer Institute (NCI) is exploring new and innovative approaches to better understand and control cancer through initiatives that enable the convergence of the physical sciences with cancer biology. Building on stunning progress in the molecular sciences and advanced technologies, we envision the development of new fields of study based on the application of physical sciences approaches to address major questions and barriers in cancer research. [Learn More](#)

News

Toolbox

NIH Challenge Grants in Health and Science Research (RFA-OD-09-003) The National Institutes of Health (NIH) has received new funds for Fiscal Years 2009 and 2010 as part of the American Recovery & Reinvestment Act of 2009 (Recovery Act). [[Read more](#)]

Oncology and the Physical Sciences Converge In this guest update to the *NCI Cancer Bulletin*, Dr. Anna Barker reveals how oncology and the physical sciences come together to identify the promising new research questions and strategies in cancer research. [[Read more](#)]

ThinkTank



NCI brought together leaders from the physical sciences during a series of three Think Tanks to help basic and clinical cancer researchers brainstorm approaches that could help solve intractable problems that stand in the way of our better understanding and controlling cancer. [[Learn more](#)]



More Information

Jerry S.H. Lee, Ph.D.

Email: leejerry@mail.nih.gov

Larry A. Nagahara, Ph.D.

Email: larry.nagahara@nih.gov

Nicole M. Moore, Sc.D.

Email: nicole.moore@nih.gov

Nastaran Z. Kuhn, Ph.D.

Email: Nastaran.kuhn@nih.gov

Sean E. Hanlon, Ph.D.

Email: hanlonse@mail.nih.gov