

American Association for Cancer Research (AACR)

Scientist Survivor Program (2020)

Preparing for the Virtual Annual Meeting

Anna D. Barker, Ph.D.

June 19, 2020



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Cancer Declining for Some Cancers – But Numbers of U.S. Cases Projected to Increase Significantly

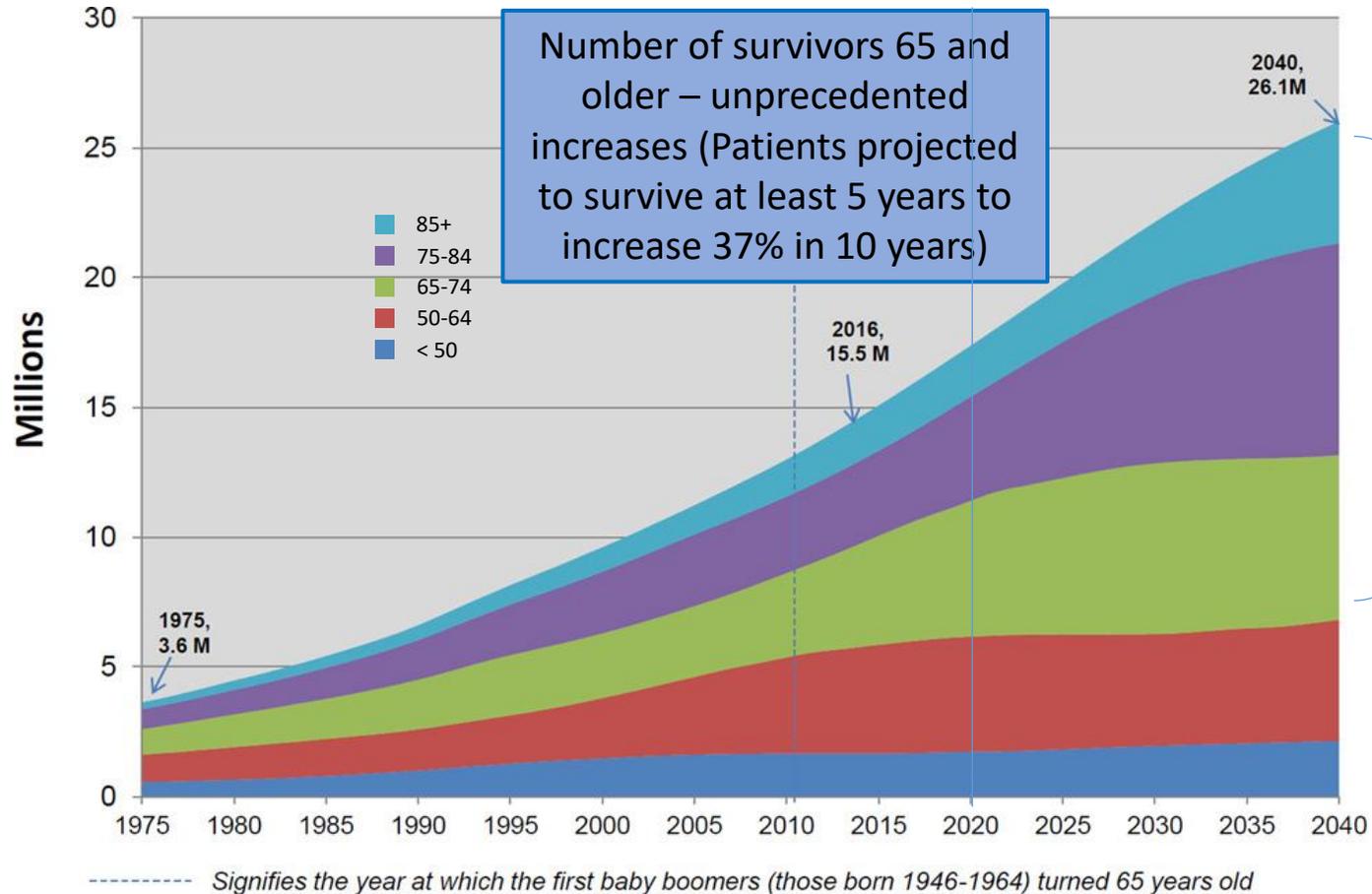
- In 2020, there will be an estimated 1,762,450 new cancer cases diagnosed and 606,880 cancer deaths in the United States
- Cancer risk increases significantly beyond age 50, and half of all cancers occur at age 66 and above (10,000 baby boomers turn 65 every day)
- Estimated cost of cancer care in the U.S. for 2017 was \$147.3 billion in direct medical costs
- Worldwide cancer predicted to increase by 70% by 2030. There were 14 million cases and 8,2 million deaths in 2012; 21.7 million cases and 13 million deaths/year projected by 2030

- *National Cancer Institute (NCI), American Cancer Society (ACS), Facts and Figures, 2019*
- <https://www.cancer.org/latest-news/facts-and-figures-2019.html>
- *World Health Organization (WHO)*



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The Not – So- Distant “Tsunami” of Older U.S. Cancer Survivors



% Survival (Post Diagnosis) – Current U.S. Population of Cancer Survivors

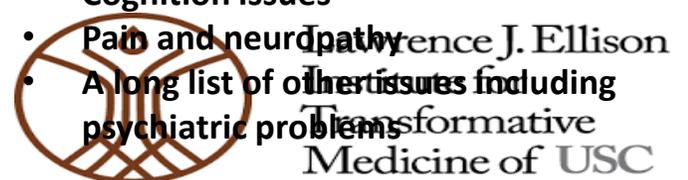
67% will live at least 5 years

44% will live at least 10 years

17% will live at least 20 years

(Additional healthcare costs):

- Other types of cancer in many patients
- Delayed toxicities (e.g. immunotherapies)
- Co-morbidities (heart disease, pain, lack of mobility, etc.)
- Cognition issues
- Pain and neuropathy
- A long list of other issues including psychiatric problems



....The Scientist<->Survivor Program, launched in 1998 was designed to enable progress against cancer by building bridges and unity among the leaders of the scientific, cancer survivor and patient advocacy communities – through information and knowledge exchange on the state of cancer research, survivorship, advocacy and public cancer policy....



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Goals for the 2020 Scientist Survivor Class

Our Goals for SSP”are to:

- Inform and educate survivors on the status of cancer research across the complex fields that comprise the cancer research enterprise
- Enable a better understanding of the challenges we all face in developing a fundamental understanding of a disease as complex disease as cancer
- Help cancer researchers develop a deeper understanding of the cancer patient’s journey, problems and challenges
- Provide survivors/advocates with information that they can take back to their communities to create/inform cancer education through a better understanding of the science and status of cancer research



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Cancer Declining for Some Cancers – But Numbers of U.S. Cases Projected to Increase Significantly

- In 2018, there will be an estimated 1,806,590 new cancer cases diagnosed and 606,520 cancer deaths in the United States
- Cancer risk increases significantly beyond age 50, and half of all cancers occur at age 66 and above (10,000 baby boomers turn 65 every day)
- Estimated cost of cancer care in the U.S. for 2017 was \$147.3 billion in direct medical costs
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Today's Agenda

- A brief look at some of the big focus areas in cancer research (some are in your questions; others are areas to look for as you virtually join sessions in the Annual Meeting)
- Why is the Annual Meeting so important in terms of assessing the state of cancer research?
- How do we navigate such a big meeting – and what might really help

Some homework to bring some organization to your thinking as you organize your approach to the Annual Meeting

- A Look at the Annual Meeting Program
- The questions



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What Areas are Going to be Featured in Research Reported at the Annual Meeting? A few examples!

- *Precision medicine*
- *“Big data” and new approaches to analysis (including RWE)*
- *New models for studying cancer including mathematical models and artificial intelligence*
- *Immunotherapy*
- *Innovation across the entire field of cancer research*
- *Some other critical areas: Evolution in cancer; the physics of cancer; clinical trials; biomarkers; cancer causation; survivorship.....*



What is cancer

Very simply cancer is the name given to a group of diseases that are essentially characterized by their ability to grow out of normal control. Cancers can be benign or malignant (invade neighboring tissues or leave the original tumor and travel to distant sites through the blood or lymph system.

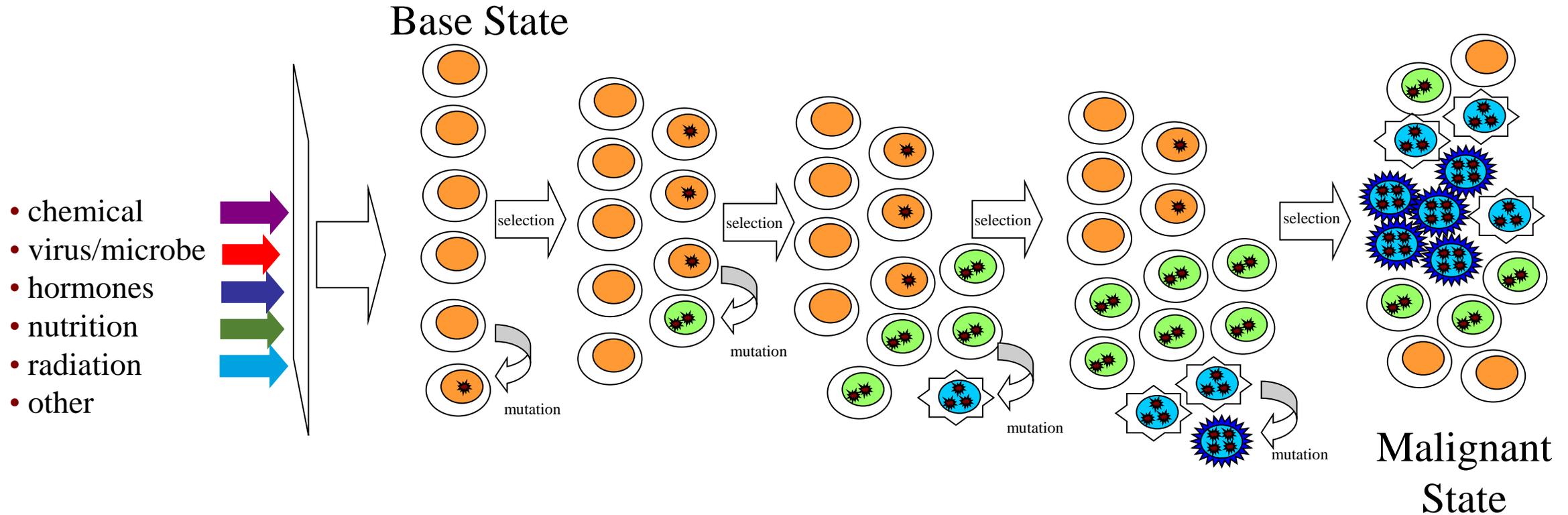
We often say that cancer is a disease of the genes – dysfunctional genes to be more specific. Identifying these genomic changes at every level of the genome to protein translation – and changes effected by the transcriptome are all important in dysregulating cells.

Identifying these changes via genome sequencing has become a foundational element of precision cancer medicine today.



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The Current Genome “Omics” Centric Focus of Cancer



Cancer occurs as a consequence of co-evolution of information-driven communication between cancer cells (in network subsystems) and their environment (context) across scales

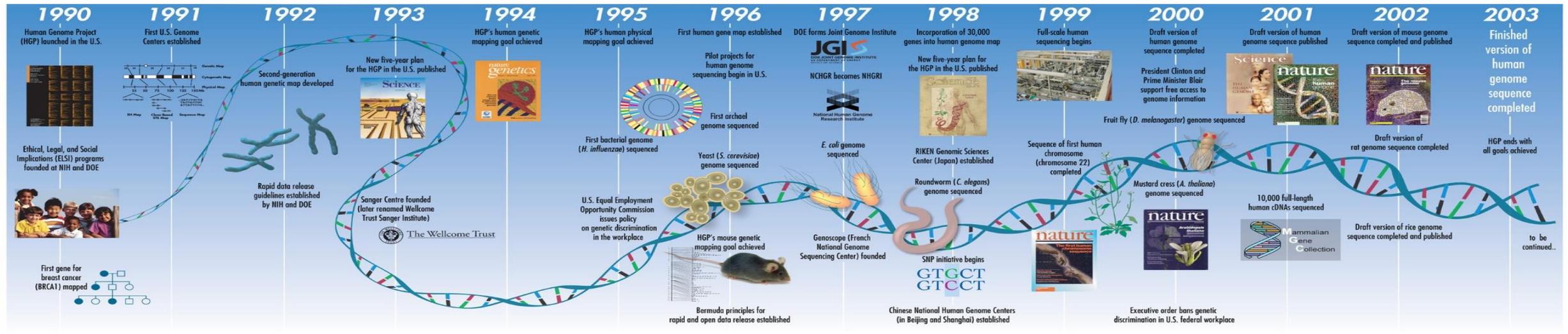


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“OMICS”: The Focus of Cancer Research Today – Is this Precision Medicine?

Vision: understanding genomic (omics) changes will enable targeted intervention

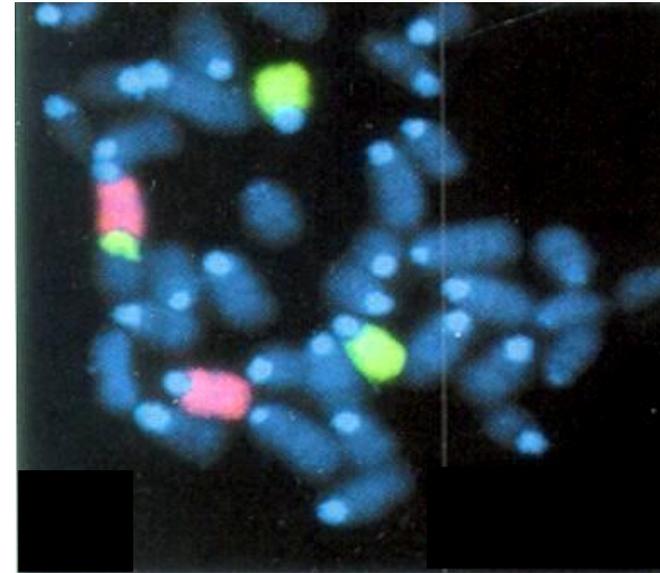
- **Since 2003: Sequencing costs fell from ~\$ 1.0 million in 2001 to less than \$500 - 1000 (an going down)**
- **Estimated that more than 500,000 genomes have been sequenced to date – but who knows**
- **Patient sequencing could approach 1000 PB per year at maturity**



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TCGA Scientific Rationale

- Biological significance of understanding genomic changes in cancer:
 - Copy number changes
 - Point Mutations
 - Transcriptome changes
 - Protein changes
 - Epigenomic changes

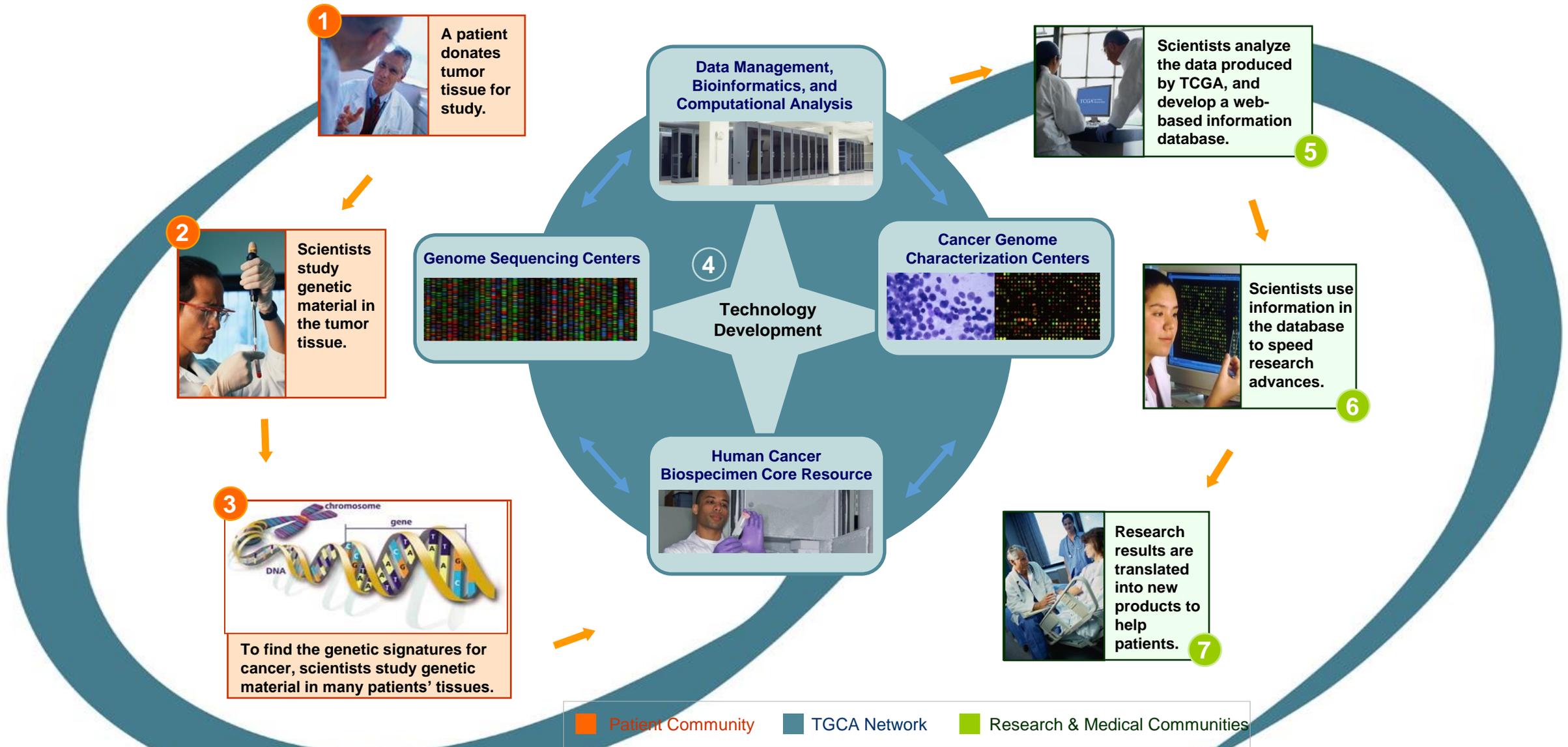


*Cancer is a disease of genomic alterations – **identification of all genomic changes would enable defining cancer subtypes** – potential to transform cancer drug discovery, diagnostics and prevention*



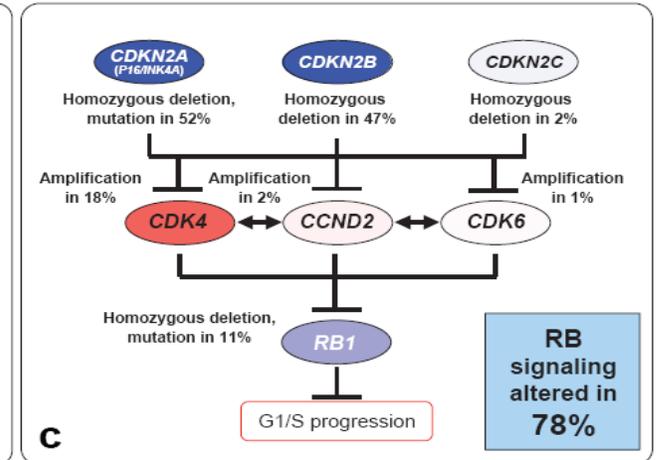
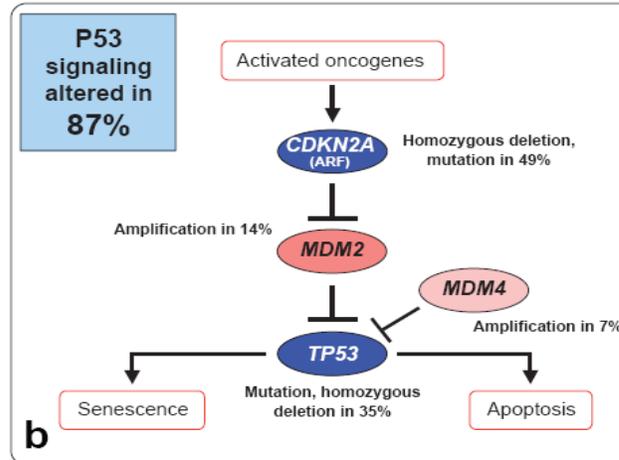
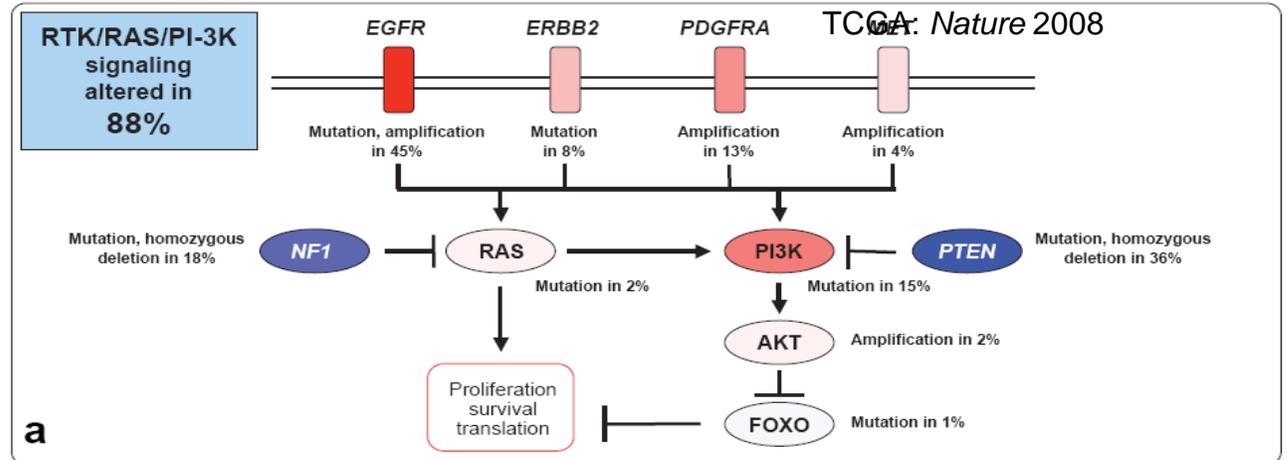
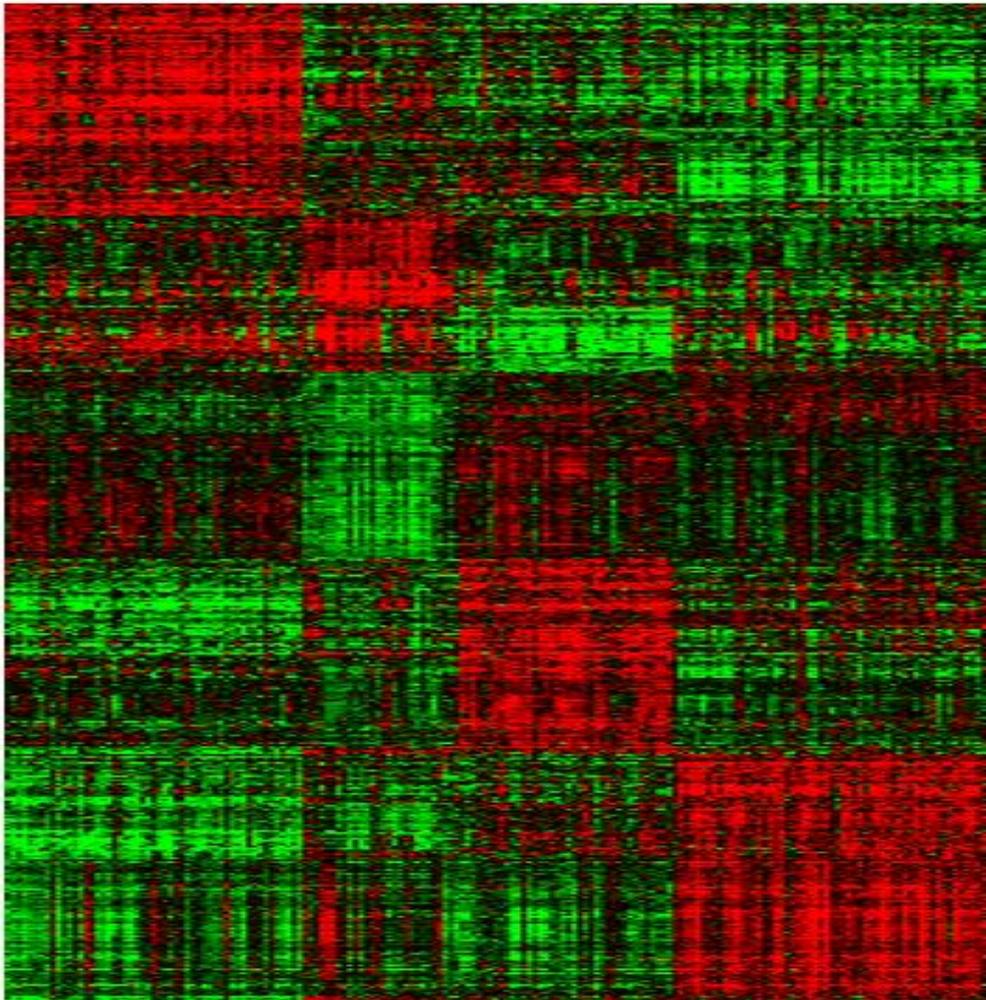
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The Cancer Genome Atlas – NCI-NHGRI



The Cancer Genome Atlas (TCGA): High Quality Molecular Profile for GBM

Proneural Neuronal Classical Mesenchymal



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What is a Biomarker?

“A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are examples of biomarkers. A biomarker is not an assessment of how a patient feels, functions, or survives.”

Joint FDA-NIH Working Group Definition



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Vision for Biomarker-Centric Precision Medicine

Today's Medicine

- Healthcare spending in 2017 - \$3.5 trillion
- Expected to continue to rise 4% per year for the foreseeable future
- Currently represents 18% of GDP – total rise to \$5.7 trillion by 2026
- Direct costs of cancer treatment in the U.S. last year was ~ \$90 billion

21s Century Medicine

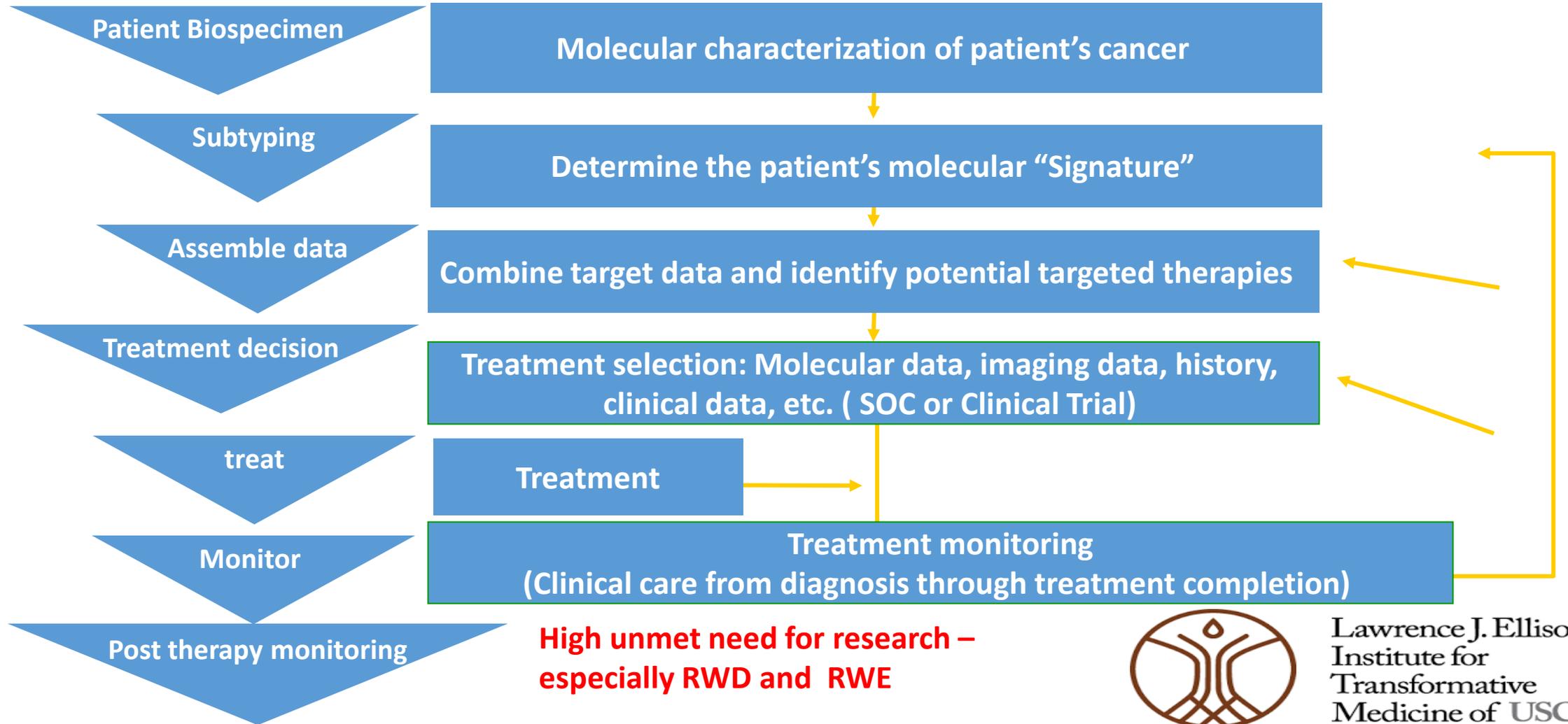
- Focus on molecular (**multi-omics**) and all patient data (**phenotype**) to support early detection and targeted therapies
- Molecular characterization and phenotyping of patients = **emerging “big data” and advanced analytics (AI) to identify biomarkers**
- **Innovative clinical trials (e.g., adaptive platform trials)** to test new generation of drugs/biologics
- Healthcare learning systems, successful trials of better drugs targeted to individual patients' **biomarkers**

21st Century Medicine – Individually Targeted Interventions Based on Patient's Biomarkers (Molecular/Clinical Profile). Current Drug Development Market = \$100 Billion



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Vision: 21st Century Precision Cancer Medicine (An Evolving “Ideal”)



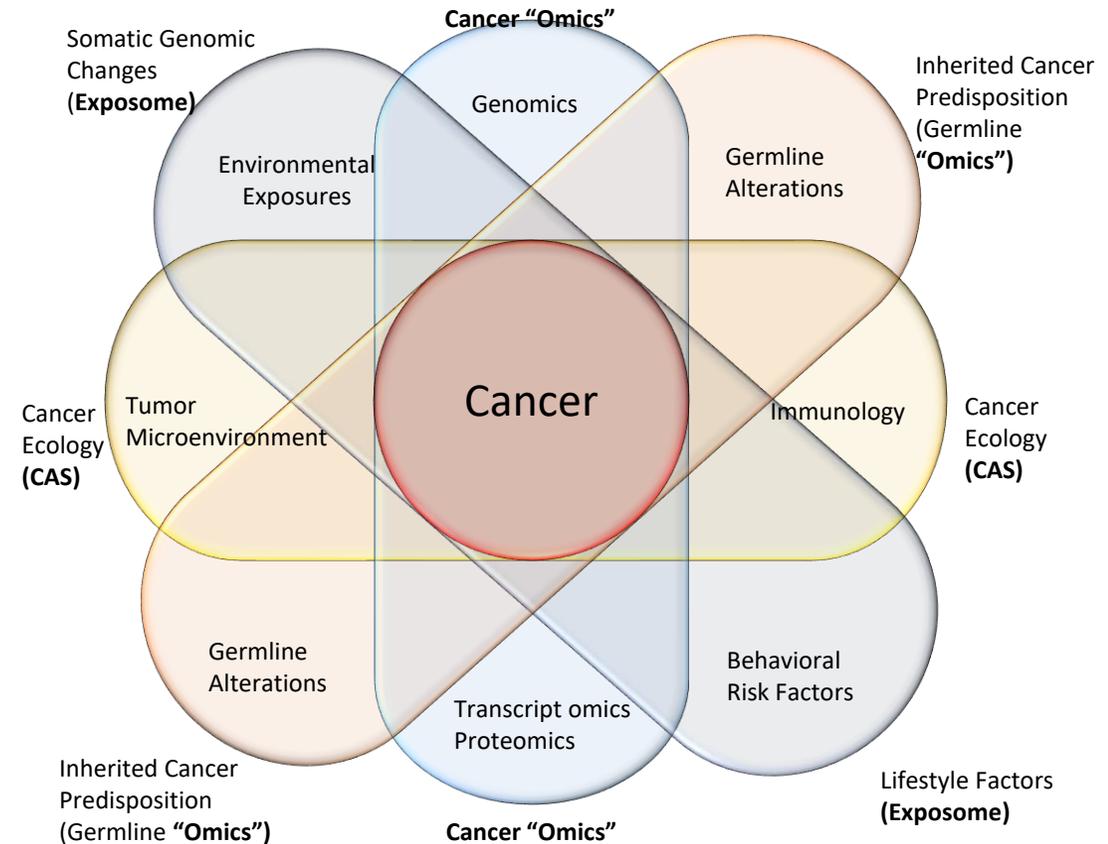
Why just studying the “omes” (genomes, transcriptomes, proteomes, epigenomes – and combinations) is not enough!



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Studying the “Parts”

- **We are currently defining the “parts” and producing a data “Tsunami” – data are not information.**
- A single cancer patient can generate nearly one terabyte of biomedical data, including routine diagnostic and clinical data.
- Genomics based research generates about one exabyte (10^6 terabytes) of data annually.
- Biomedical big data is complex and it is not always clear how the variables are affecting outcomes.
- Due to its complexity, the ability to accumulate biomedical big data has largely outpaced our capacity to analyze it.
- The presence of copious amounts of noisy or “scruffy” data further complicates analyses.
- **Isolated understanding of “parts” is helpful, but cancer is a complex adaptive (evolving) system (CAS).**
- <https://www.canwlivebetter.bayer.com/innovation/finding-cure-cancer-big-data-solution>



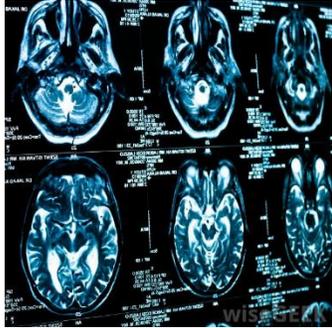
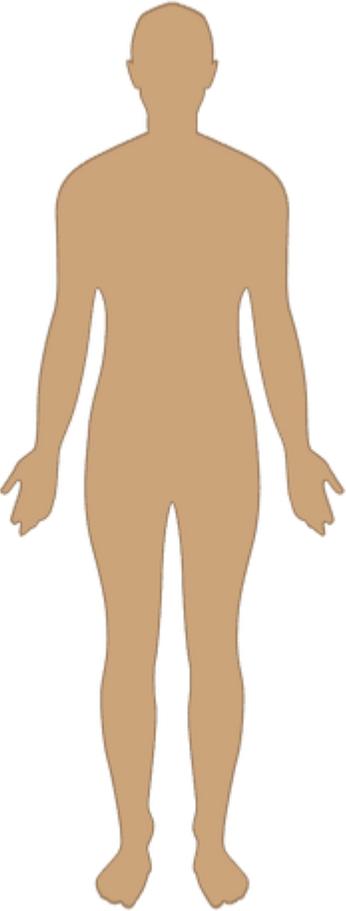
Developing the Molecular Profiles (OMES) of Patients was Step 1 – It's Now About Patient Data

Individualized, Targeted Cancer Care



**Single Patient Data X
Populations =
New Data Centric
Complex Systems
Models for
Prevention,
Diagnosis, Treatment
and Survivorship**

The Future – We need Useful Biomarkers – and they Need to be Complex Are Almost Always (Biology Is Complex)

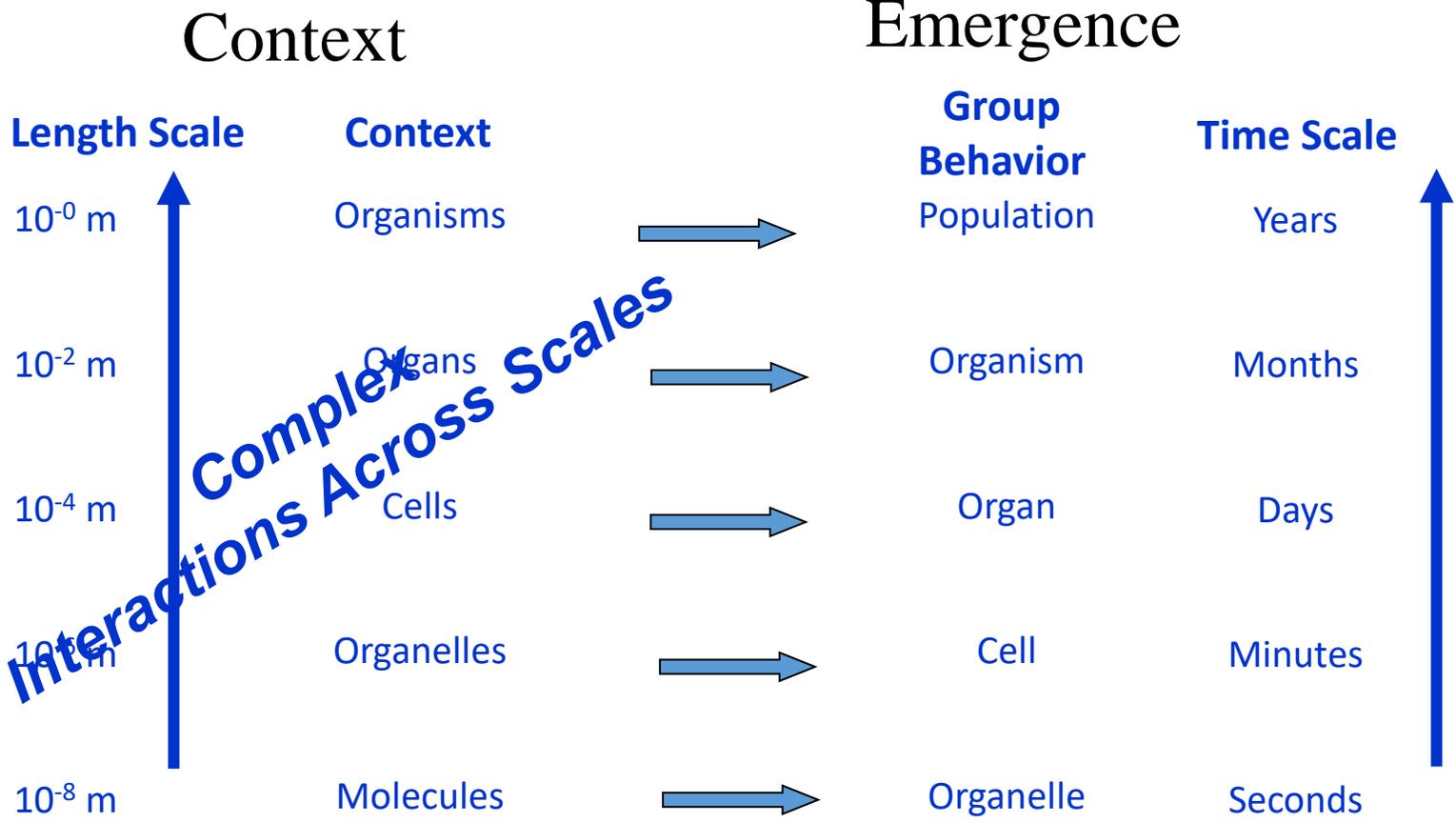


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Scale (and Emergence) is Critical in “Understanding” and Managing Cancer



- Emergence in biological CAS (cancer) highlights the importance of **integrating information across different scales of space and time.**
- Genomic alterations **(information)** drive the development of new information that enables the emergence of cancer.
- **Cancer emerges as a result of the interactions of the organism’s systems/subsystems across scales.**

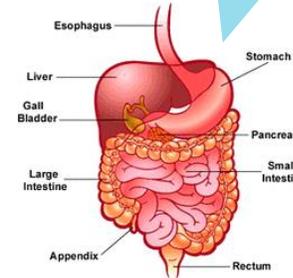
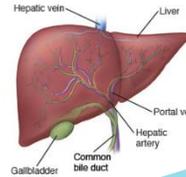
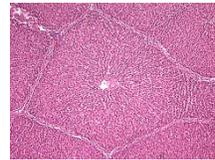
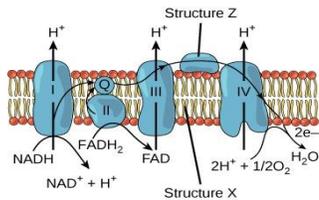


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Biomarkers are Measures of Integrative Information in Context Across Scales

← “PHENOTYPES” →

GENOTYPES

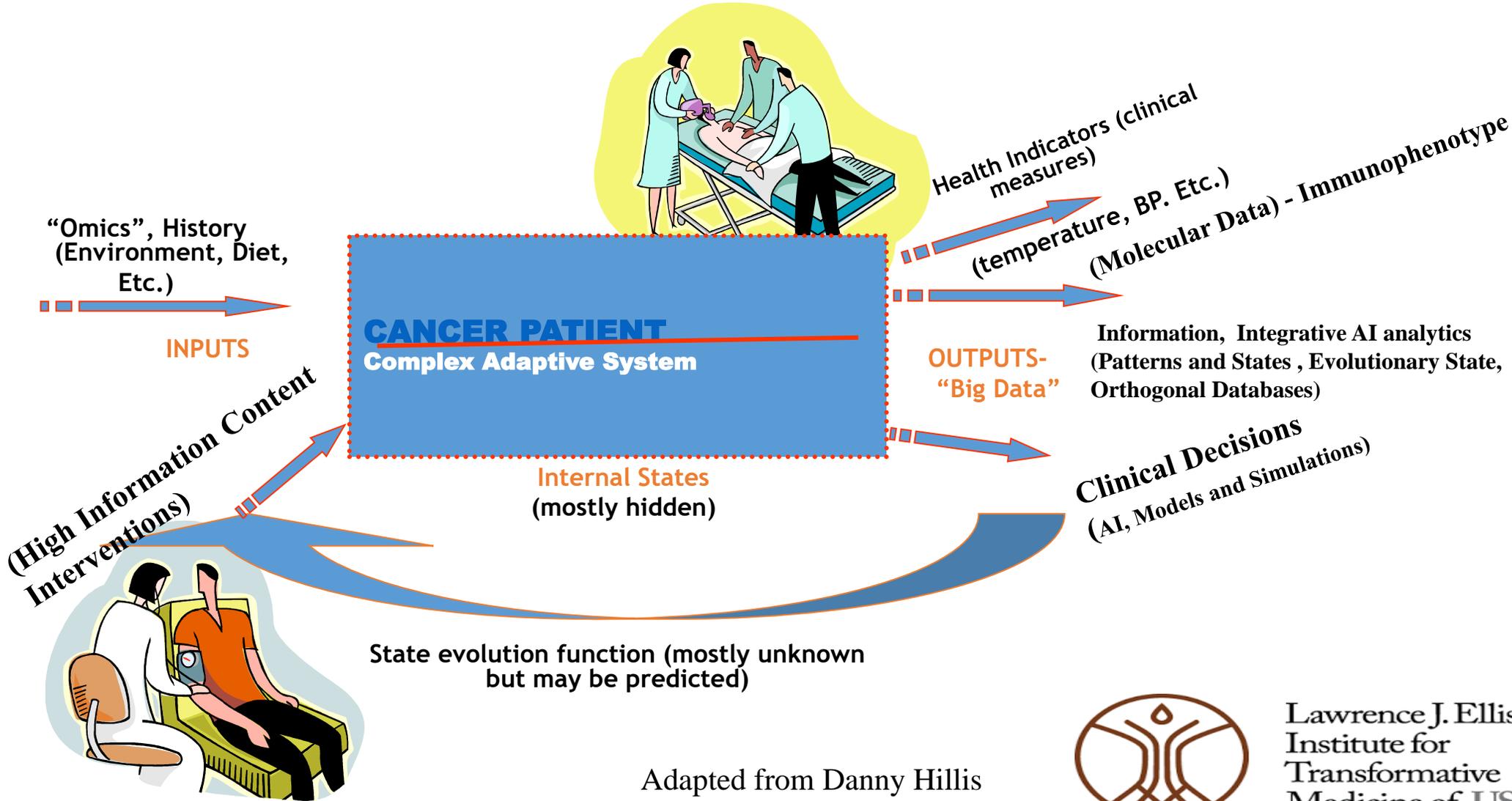


Biomarkers Must Reflect Complex Information Across Scales



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Managing Cancer as an Emergent Complex Adaptive System



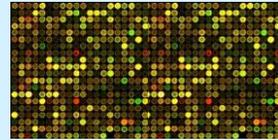
Adapted from Danny Hillis



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The Future: What If – Every Patient Received Precision Medicine and Precision Care Throughout their Entire Journey

Patient Information



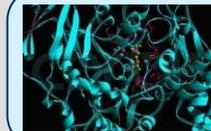
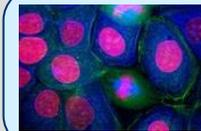
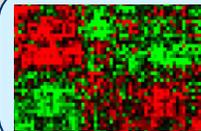
Current Approach



A Future Where Advanced Digital Technologies, RWD, RWE, PROs are All used to Enhance Patient Care

- Differential diagnosis (liquid biopsy, full molecular profile)
- Optimization of therapy based on selection of agents (likely combinations) informed by RWE
- Real-time therapeutic responses are measured longitudinally
- All patient data is collected throughout treatment in high quality RWD database – data used to adjust doses, targets, etc.. In real time
- After care occurs as part of a continuum _ONS TREATMENT SUMMARY AND CARE PLANS
- Monitoring for recurrence, long term toxicities, comorbidities, etc.
- Digital devices enable patient real time patient reporting
- Research and care would merge

Molecular Based Diagnostics and Treatments – Enabling Prevention



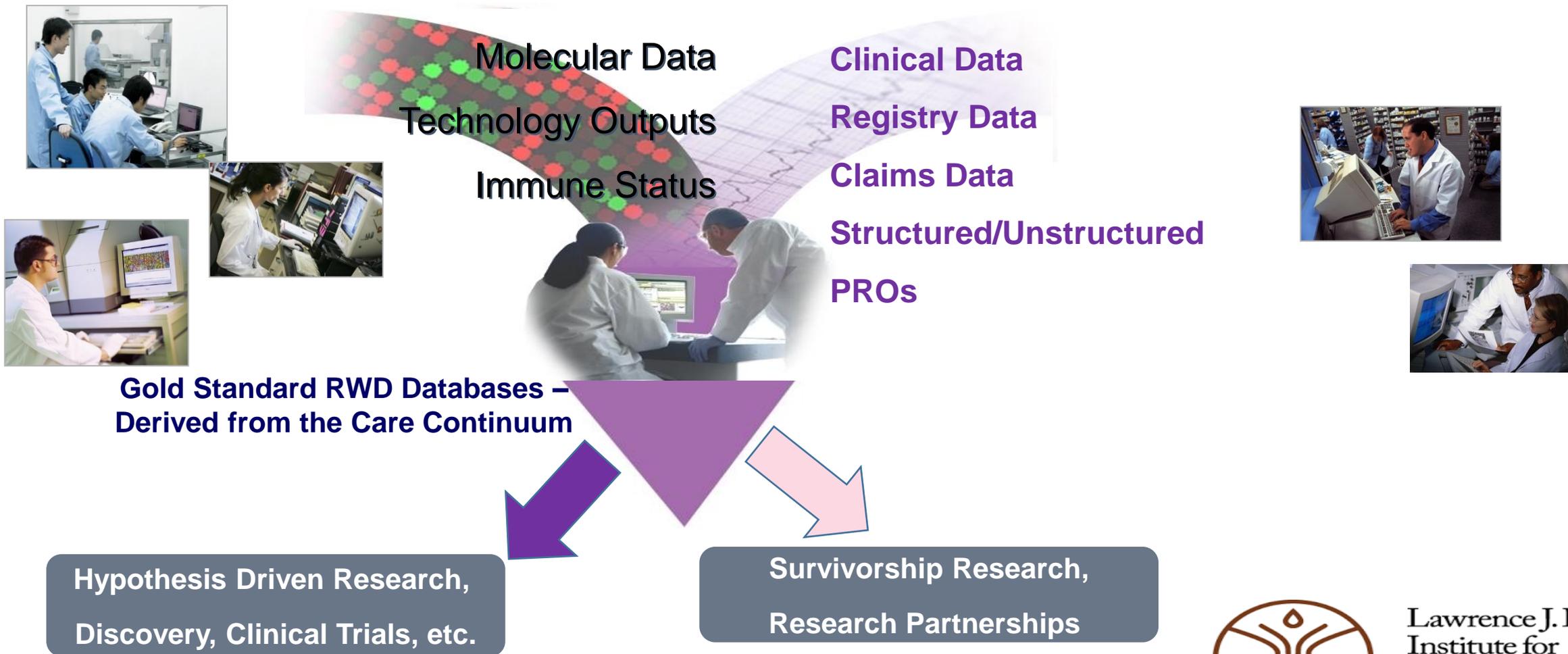
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Some other areas of focus relative to your questions!

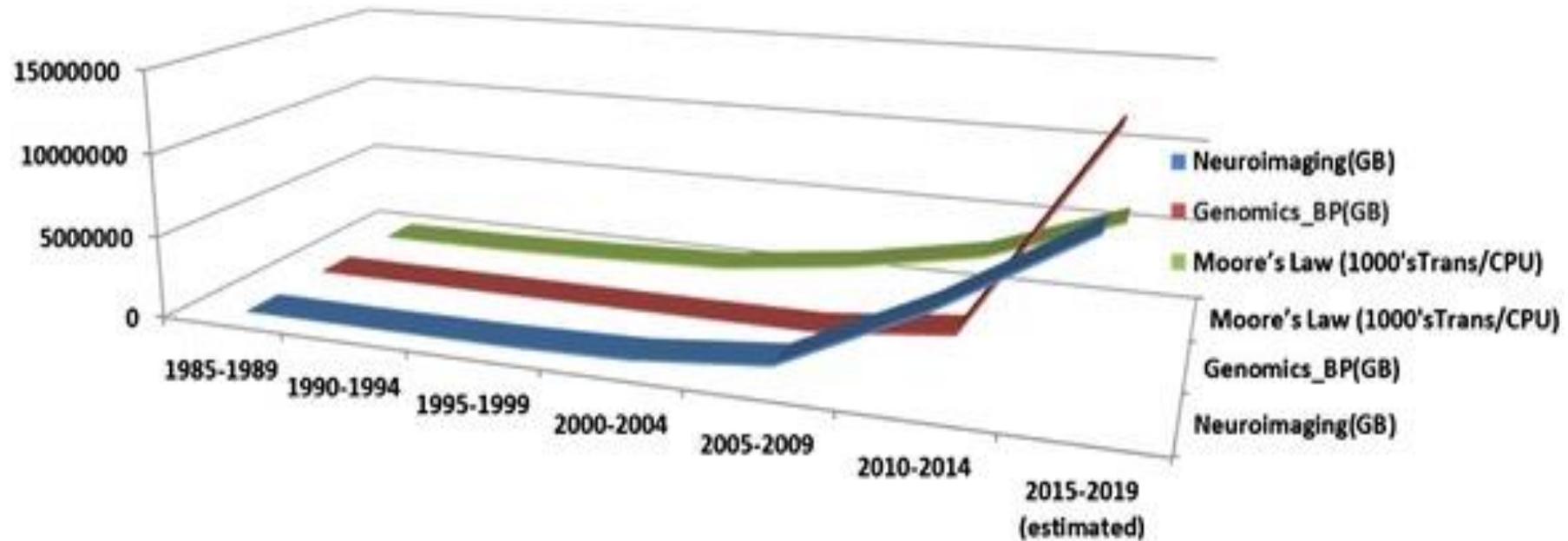


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Data are Coming from Many Sources



Ninety Percent of the Data in Biomedicine Created in the Past 2 Years Across All Fields – 1% Analyzed!!



“(Kryder’s law) Exponential growth of neuroimaging and genomics data, relative to increase of number of transistors per chip (Moore’s law)” (Image and Caption from Toga & Dinov, 2015).



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“The data that we now generate overwhelm our abilities of interpretation, and the attempts of the new discipline of “systems biology” to address this shortfall have to date produced few insights into cancer biology... So, perhaps ironically, we have come full circle, beginning in a period when vast amounts of cancer research data yielded little insight into underlying mechanisms to a period (1980–2000) when a flurry of molecular and genetic research gave hope that cancer really could be understood through simple and logical reductionist thinking, and finally to our current dilemma....we can’t really assimilate and interpret most of the data that we accumulate.”

Robert Weinberg

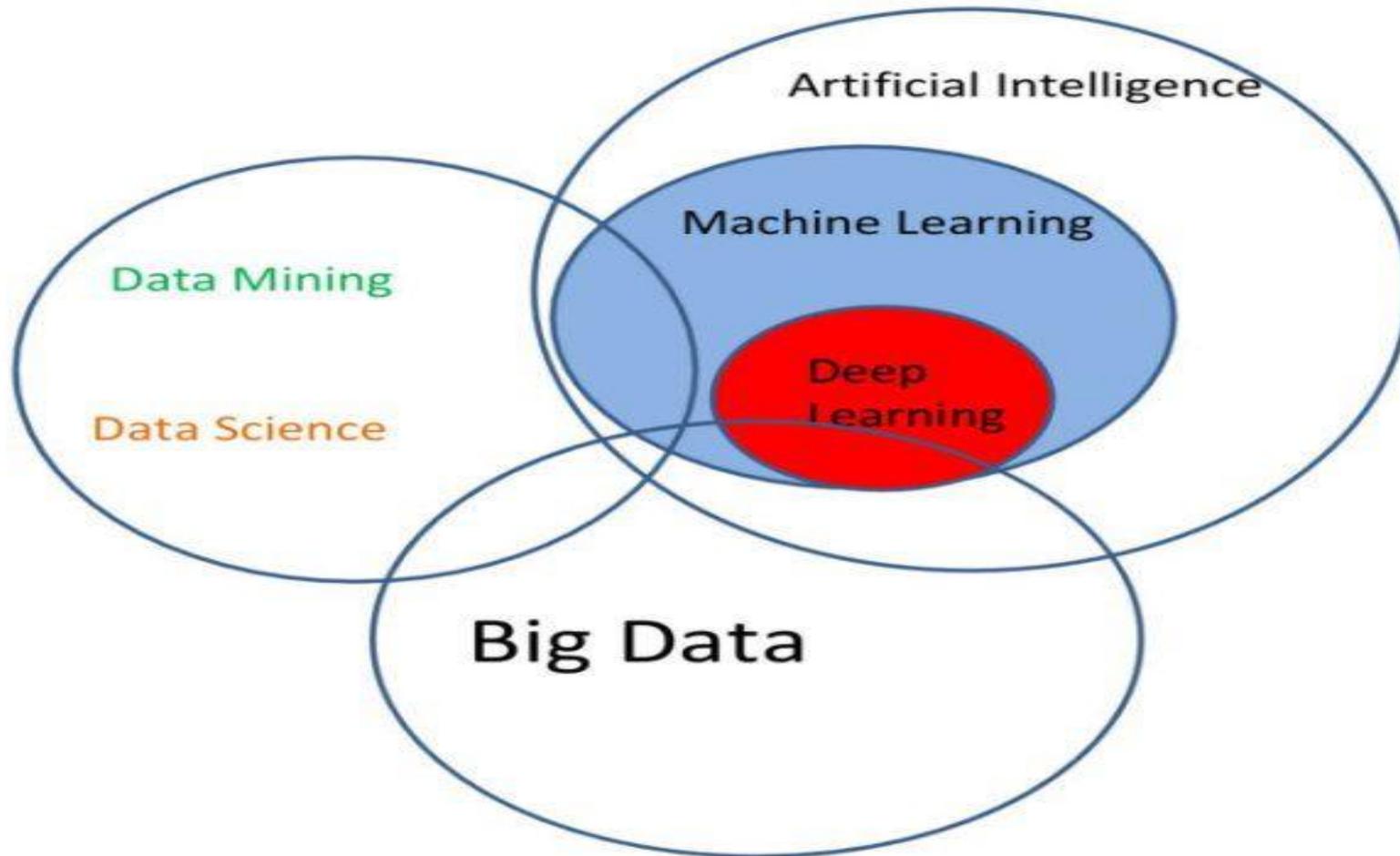
“Coming full circle—from endless complexity to simplicity and back again”

Cell. 2014 Mar 27;157(1):267-71

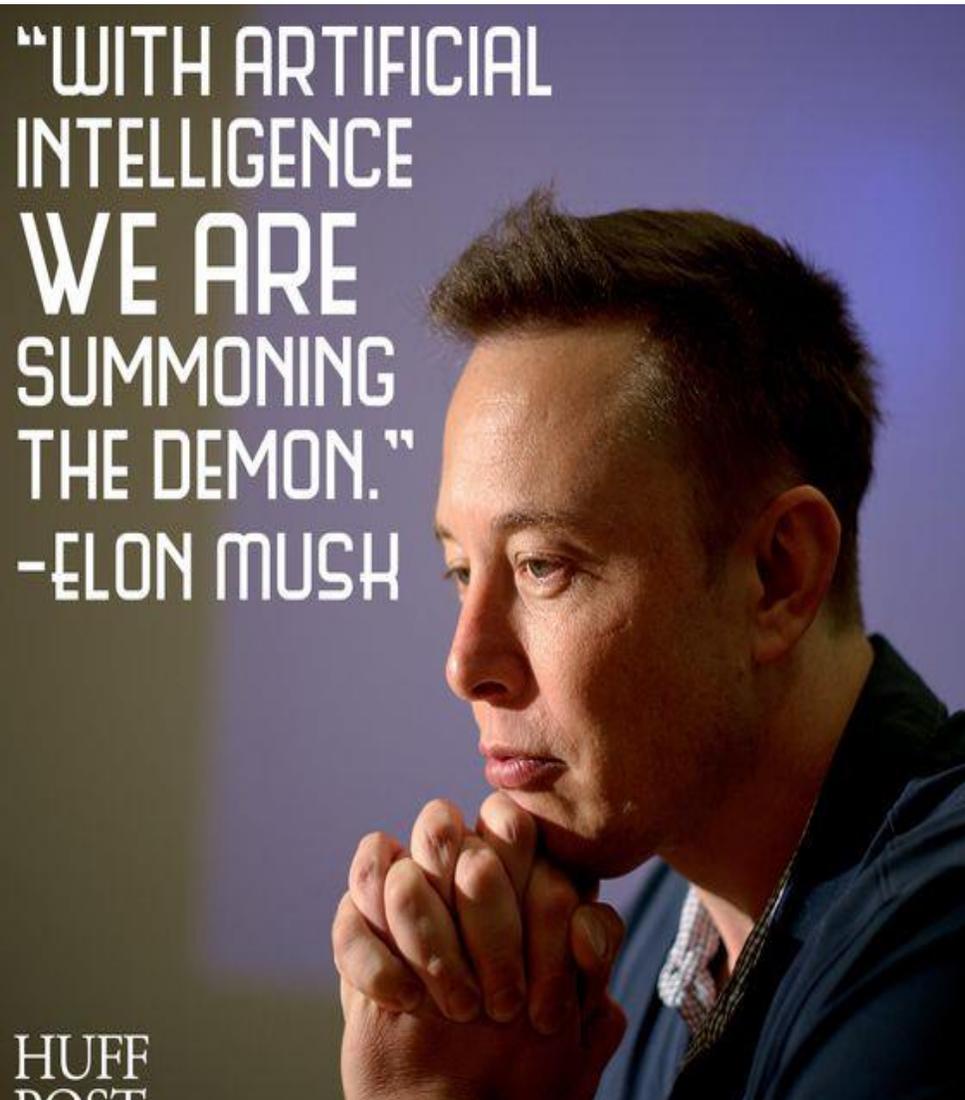


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The Future of Data Analysis



Elon Musk Is Worried – Some Profound Questions



- We will not know what questions that AI driven computers will be asking - what questions they are asking
- Human intuition will generally disappear from biomedical research – is that bad?
- Is AI the only hope to find real answers to our questions in the irreproducible complexity of biology?
- Will humans understand what AI may find – will it be the “black box” often predicted? Faith in the predictions – because it’s just too complex?
- Should we worry that E. Musk is Right? Man has never feared the future – is this different?

Immunotherapy essentially harnesses specific parts (or all) of the immune system to kill cancer cells. Immunotherapies come in many forms – antibodies to specific targets; vaccines; adoptive cell transfer, checkpoint inhibitors, cytokines – and many others. You will see a lot of sessions at the meeting on many types of immunotherapy – most will reference checkpoint inhibitors or CAR-T cells.



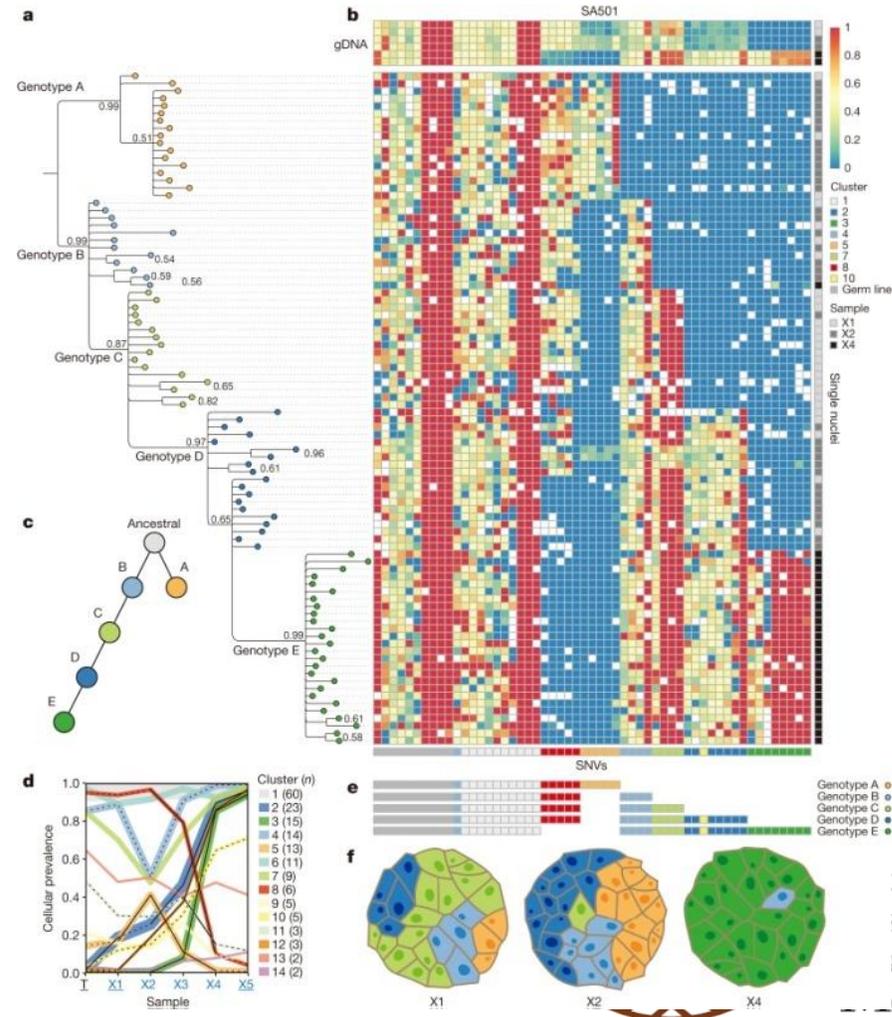
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Why is Immunotherapy Different? It Targets a Complex Adaptive

System vs. Cancer Cells

- Complicated, but also complex
- Cancer is a diverse collection of different molecular diseases composed of hundreds of alterations that vary individual to individual even within an organ site
- Tumors are molecularly heterogeneous within an individual and change over time in response to changing system circumstances
- The immune response is an interconnected, self-regulating, multicomponent system that responds and adapts to changing circumstances

Ken Buetow, ASU



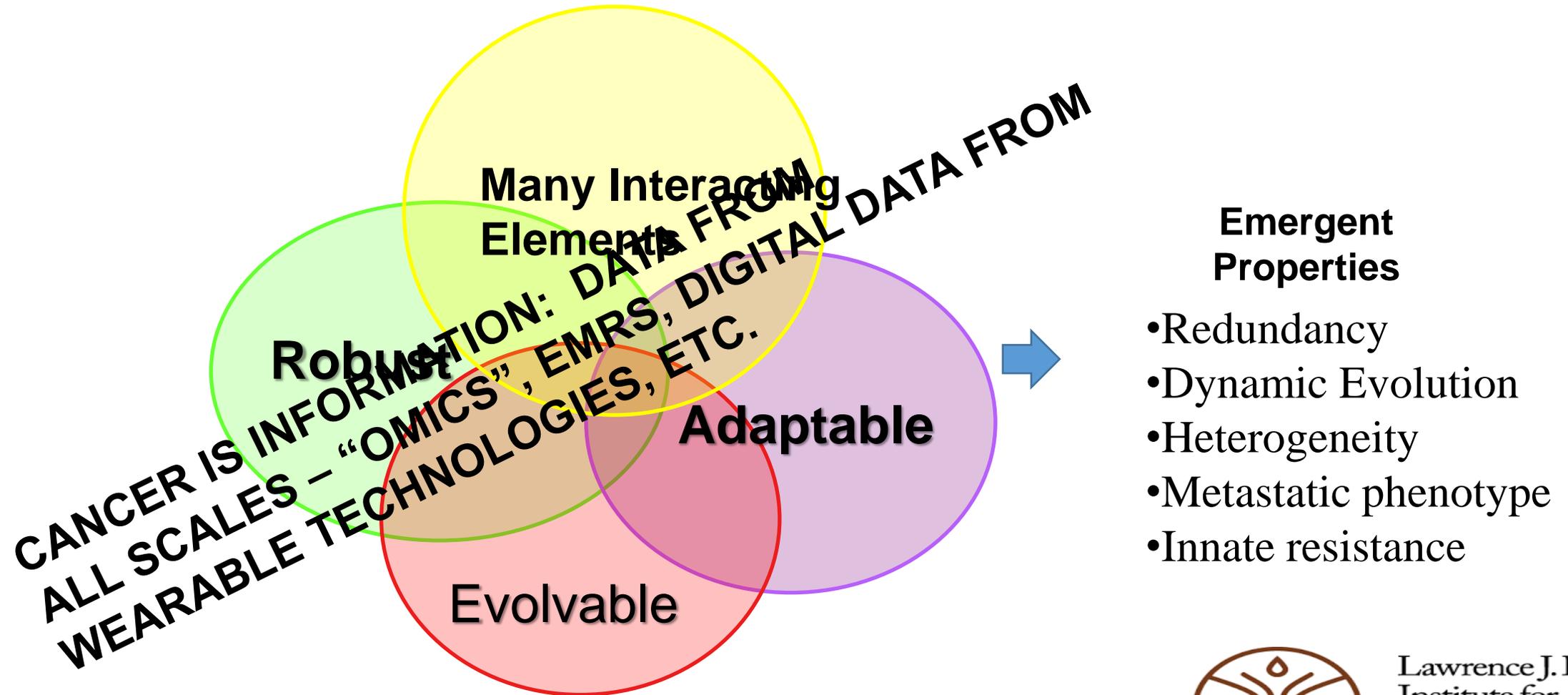
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Cancer Evolution !



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Biological Systems (Cancer) are Complex Adaptive Systems



Evolution: stochastic, unpredictable – incredibly diverse



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NAVIGATING THE ANNUAL MEETING



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Evolution Drives Heterogeneity – and Resistance to Treatment – Future Must Engage Evolutionary Models

- **Focus on understanding malignant tumors through characterization of targeted clones and fitness landscapes**
- **Identify what the selection pressures are – and where they have impact**
- **If it makes sense – de-convolute the role of the numbers of types of mutations in different clones – and how they interact**
- **Tumors are organ specific – and malignant clones find their way to specific organs – determine if the fitness programmed in the organ, the cancer cell, or both**
- **Design cancer therapies to take into account selection pressures**
- **Test combinations of agents that are designed to address evolution and associated changes in ecosystems**
- **Develop biomarkers as predictive/prognostic/surrogate biomarkers to aid in addressing these issues**



What makes you **wonder**? Ideate/Speculate? What defines Innovation

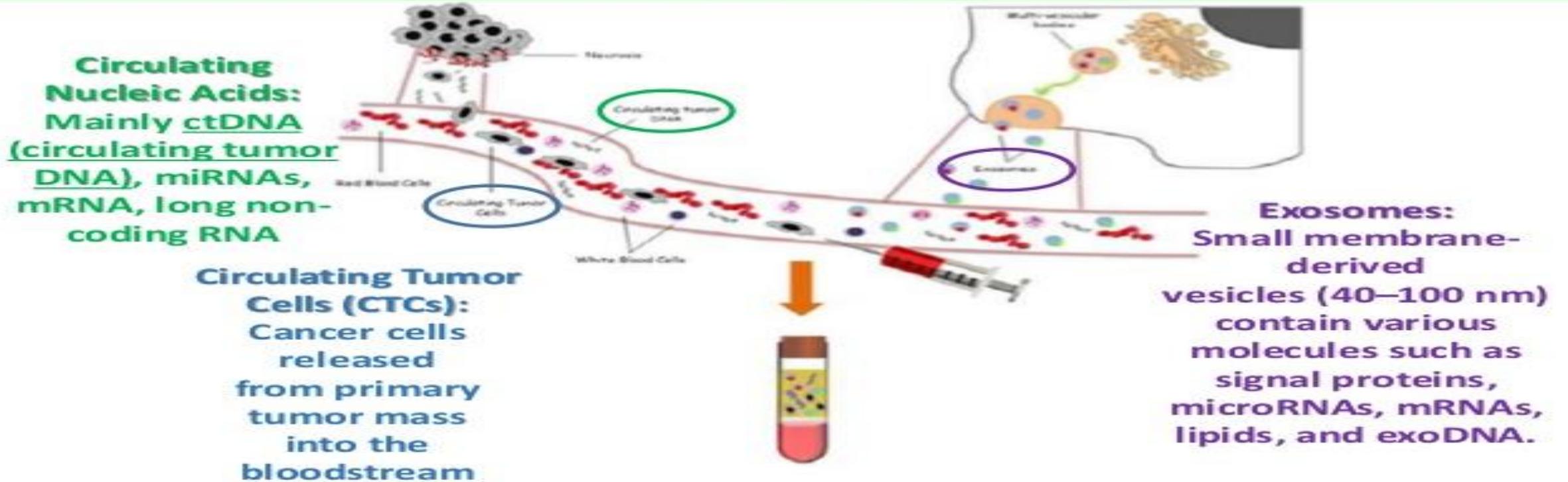
- Is it a **new** question?
- Is it a new **idea**?
- Is it a **unique insight** at the
“intersection” of
fields/technologies?
- Does an idea/insight **combine**
solutions/methods from **unrelated**
fields?
- Is it **disruptive** to current dogma?
- Does it **challenges assumptions**?



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The Liquid Biopsy: Is this Approach an Innovation that is Bringing Change to Cancer Medicine?

Liquid biopsy



C. Rajb et al. / Biochimica et Biophysica Acta 1846 (2014) 539–546



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Some Suggestions for Navigating the Virtual AACR Annual Meeting

- Build a “Curriculum” – based on days and sessions/workshops, etc.
- Try to attend as many types of sessions as possible – don’t just do the “easy stuff”
- There are no dumb questions! You can ask questions in the chat box
- Get to know the class
- Identify the “should not miss” sessions
- Select sessions that are not focused just on a single cancer (even it is your diagnosis – pan cancer studies increasingly show as many similarities as differences)



Get the Most Possible out of Everything You Attend – Make a ScheduleG

- **Do what it takes to identify the major events you want to attend – and Find Them**
- **Ask questions**
- **Learn the lingo – you too can speak in acronyms**
- **Connect the dots – across topics – sessions – posters etc. (understand the continuum)**
- **Think carefully about how you can integrate what you learn – and transfer information to your “constituents”**
- **Combine your interests with the questions we have posed**



The Homework: To Gather and Integrate Information – Understand a “Field” of Research -

- Look at the question – seek clarification
- Attend sessions, etc. – gather information – integrate into “answer(s)”
- Get some email addresses and talk together on Zoom to compare notes and improve your scope of learning (make up some slides)
- Organize your information – and ask questions in our upcoming Zoom session
- You will have the opportunity to submit a summary of what you learned about the 4 questions that were posed
- Let the questions help you to look for the current state of the science in a number of areas – there are many more than 4 – but these 4 are highly integrative of a lot of research



Scientist - Survivor Program “Where You Can Make a Difference”

- **Biospecimens**
- **Precision /Personalized Medicine**
- **Bioethics - Privacy Issues**
- **Conflict of Interest – Mutually Beneficial Solutions**
- **Clinical Trials – (Enrollment, Education, Patient Reported Outcomes)**
- **Education Period!**
- **Patient Centric Drug Development**
- **Addressing Regulatory Barriers**
- **Expect no demand – Innovation – if “same old” isn’t working try something!**

