A data-driven approach to assess technologies for precision cancer medicine

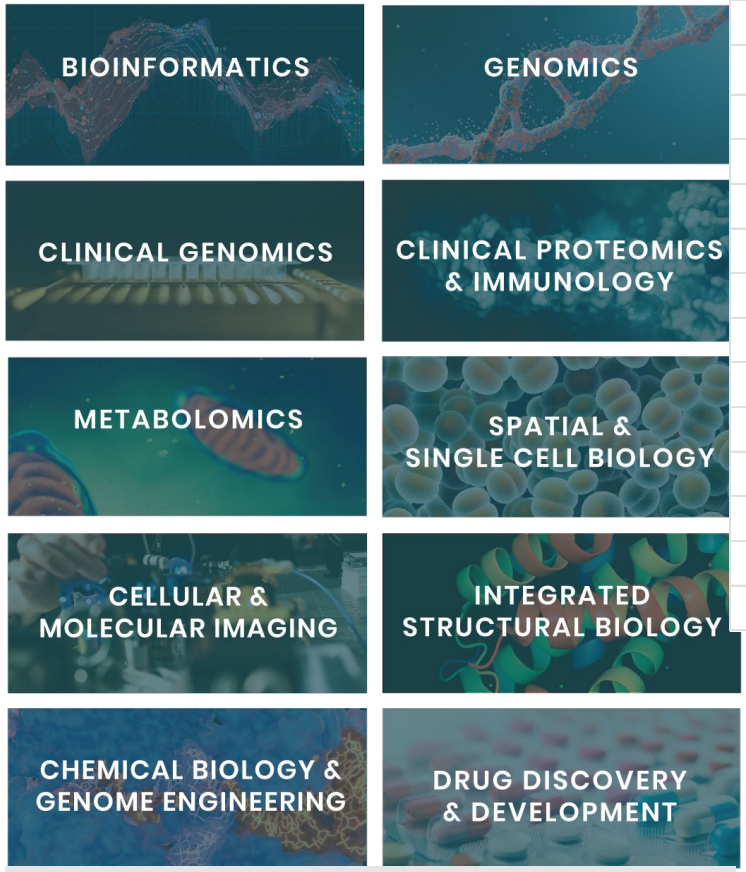
Olli Kallioniemi
Director of the KAW-SciLifeLab DDLS Program (40%)
Professor of Molecular Precision Medicine, KI

Mid 2024- > Research Program Director at FIMM (60%)

Disclosures

Board member Sartar Therapeutics
Advisory board: Novo Nordisk Foundation, Data Science Committee
Grant support and advisory role: Knut and Alice Wallenberg Foundation

SciLifeLab infrastructure - platforms and units: State of the art services provided for the research community



Nature Method of the Year

2022	Long-read sequencing
2021	Protein structure prediction
2020	spatial transcriptomics
2019	single-cell multimodal omics
2018	Imaging in freely behaving animals
2017	organoids
2016	Epitranscriptome analysis
2015	single-particle cryo-electron microscopy
2014	light-sheet fluorescence microscopy
2013	single-cell sequencing
2012	targeted proteomics
2011	genome editing with engineered nucleases
2010	Optogenetics

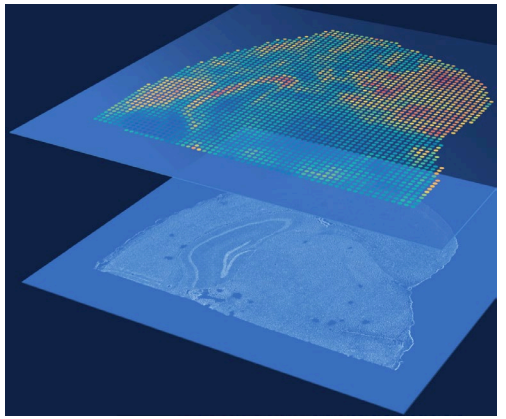
Technology Feature | Published: 06 January 2021

Method of the Year: spatially resolved transcriptomics

Vivien Marx

Nature Methods **18**, 9–14(2021) | Cite this article

23k Accesses | **6** Citations | **88** Altmetric | Metrics



2022 Ancient DNA

2022 Click chemistry

2020 Crispr-Cas

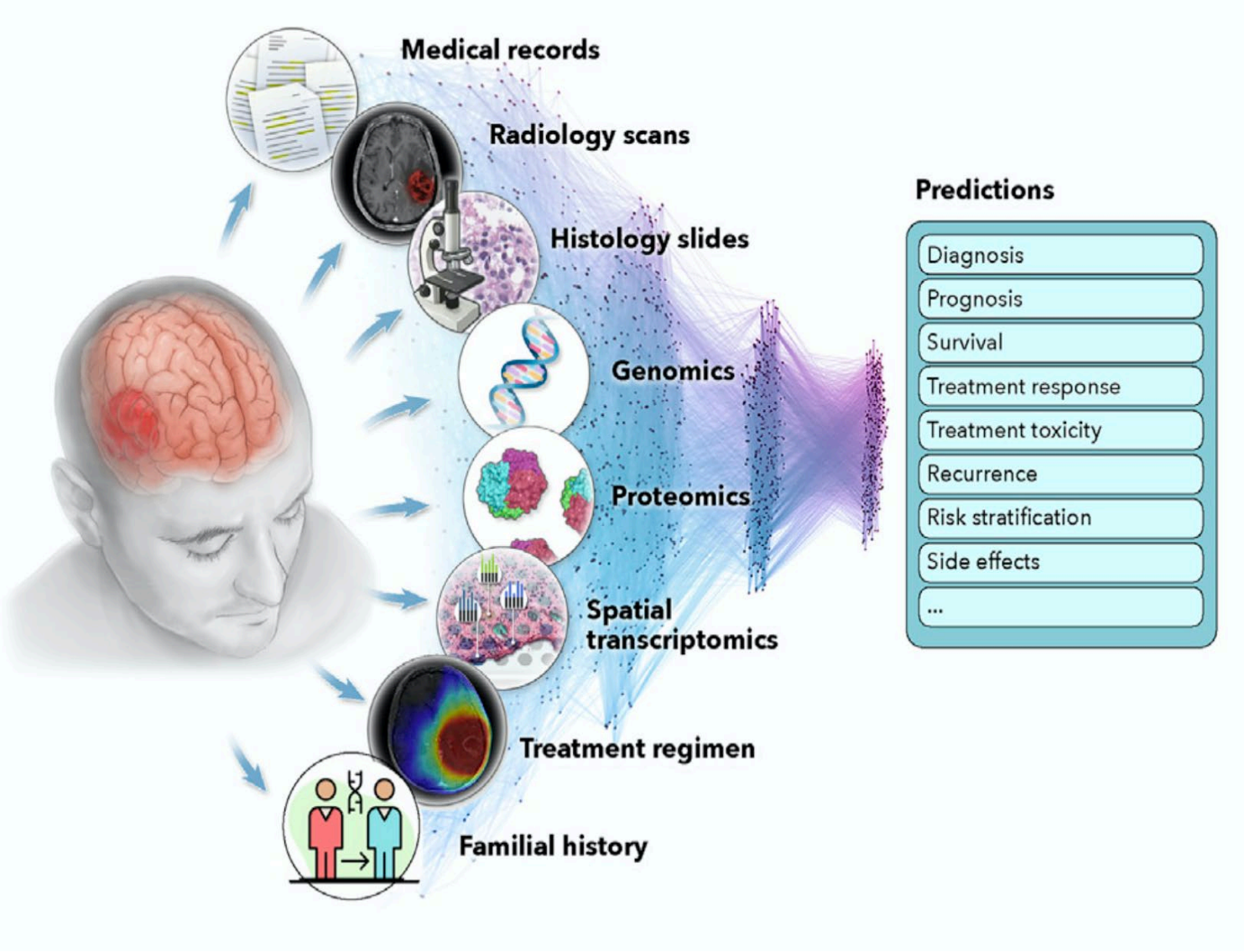
2018 Phage display

2017 Cryo-EM

2014 Super-res microscopy

Technologies awarded Nobel Prize applied at SciLifeLab infra (established before prize)

Data integration in multi-modal precision medicine



Review

Artificial intelligence for multimodal data integration in oncology

Jana Lipkova,[1,2,3,4] Richard J. Chen,[1,2,3,4,5] Bowen Chen,[1,2,8] Ming Y. Lu,[1,2,3,4,7] Matteo Barbieri,[1] Daniel Shao,[1,2,6] Anurag J. Vaidya,[1,2,6] Chengkuan Chen,[1,2,3,4] Luoting Zhuang,[1,3] Drew F.K. Williamson,[1,2,3,4] Muhammad Shaban,[1,2,3,4] Tiffany Y. Chen,[1,2,3,4] and Faisal Mahmood[1,2,3,4,9,*]

[1]Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[2]Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[3]Cancer Program, Broad Institute of Harvard and MIT, Cambridge, MA, USA
[4]Data Science Program, Dana-Farber Cancer Institute, Boston, MA, USA
[5]Department of Biomedical Informatics, Harvard Medical School, Boston, MA, USA
[6]Harvard-MIT Health Sciences and Technology (HST), Cambridge, MA, USA
[7]Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology (MIT), Cambridge, MA, USA
[8]Department of Computer Science, Harvard University, Cambridge, MA, USA
[9]Harvard Data Science Initiative, Harvard University, Cambridge, MA, USA
*Correspondence: faisalmahmood@bwh.harvard.edu
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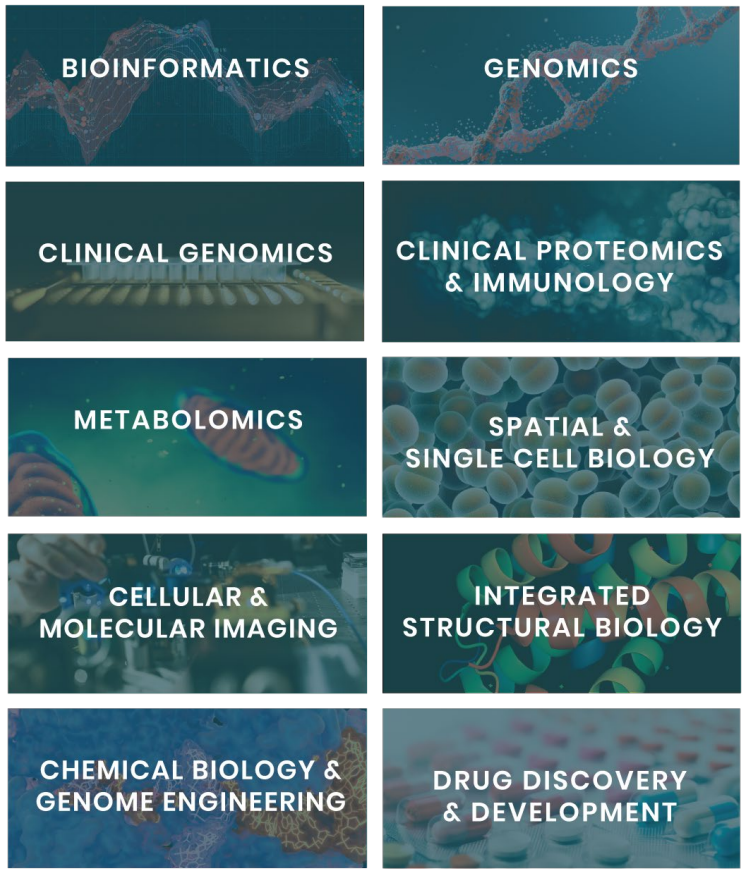
Molecular profiling technologies for precision cancer research

Every expert has good arguments that their favorite technology is the key to success in PM



Expensive
Time consuming
Sample requirements
Expertise required
Integration complicated
Prioritization
=> Difficult to translate

Prompt for GPT 4.0: How do you suggest that the field of functional precision cancer medicine will be developing. Will it eventually replace genomic precision medicine? What needs to happen for wide-spread clinical use?

1. Shift from Genomics-Only to Functional Approaches

2. Combining Functional and Genomic Approaches

3. Technology and Infrastructure Advancements

- **High-Throughput Screening**
- **Standardization**
- **Integration into Clinical Pipelines**

4. Challenges to Clinical Adoption

- **Clinical Trials and Regulatory Approvals**
- **Reimbursement and Cost**
- **Data Interpretation**

5. What Needs to Happen for Wide-Spread Attention and Use

- **Demonstrated Impact on Patient Outcomes**
- **Public and Professional Awareness**
- **Collaborations and Networks**

The field of functional precision cancer medicine (FPCM) is poised to complement, rather than fully replace, genomic precision medicine. Here's how FPCM may develop and what needs to happen for its widespread clinical adoption

Conclusion: Complementary, Not Replacing

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Apply Evidence-Based Approaches**
  - Conduct **comparative effectiveness research** (CER), we can determine under what circumstances one approach should be prioritized over the other, or where the combination is most effective. This can help avoid redundant testing
  - **Guideline-Driven Recommendations**: Medical societies and regulatory agencies should issue clear **clinical practice guidelines** based on robust clinical evidence. These guidelines should specify when genomic testing alone is sufficient, when functional assays add value, and when a combined approach is truly necessary.

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Targeted Patient Selection**
  - **Personalized Technology Application**:
    - Not all patients require both functional and genomic testing. Developing patient stratification models to identify who will benefit most from FPCM?
  - **Biomarker-Guided Decisions**:
    - Using biomarkers to identify specific subsets of patients who would benefit from one technology over another.
    - For example, patients with certain drug-resistant tumors or rare cancers might be prioritized for functional screening, whereas common mutations in other patients may allow genomic testing alone.

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Unified Data Platforms:**
  - Develop integrated data platforms where genomic, multi-omic, and functional assay data can be harmonized.
  - AI and machine learning tools can be used to predict when combining data streams to improve outcomes and when it is unnecessary.
  - The key is to only combine technologies when their integrated data provides added value.
- **Clinical Decision Support (CDS) Tools:**
  - Implementing CDS systems that automatically guide physicians based on patient profiles and previous outcomes can help ensure that the right tests are ordered in the right contexts

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Health Economics Evaluations:**
  - Performing cost-effectiveness analyses early in the clinical adoption process can help identify the most economically sustainable use cases for FPCM.
- **Value-Based Reimbursement:**
  - If functional testing demonstrates superior outcomes in specific cancer types or stages, then it will be reimbursed accordingly.
- **Phased Adoption:**
  - A phased adoption strategy based on evidence and cost-effectiveness in specific cancers or treatment-resistant cases can help mitigate unnecessary costs.

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Cross-Industry and Research Collaboration**
  - Co-Development of Standards: Academic institutions, regulatory agencies, industry, and clinical providers need to work together to set standards
  - Public-Private Partnerships: Encouraging public-private partnerships to pool resources and data can reduce redundant R&D efforts.

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Adopting a Tiered Testing Approach**
  - Developing tiered testing models or clinical decision trees can help minimize redundancy. For example, starting with genomic testing and only moving to functional assays when genomic data alone is insufficient can streamline care.
  - Predictive algorithms that assess the likelihood of genomic or functional test success for specific cancer types

GPT4.0: This is what often happens in medicine that we entertain complementary technologies, which then results in excessive costs and redundancy and poor market penetration and complex data interpretation. How can we avoid this?

- **Regulatory Pathways for Novel Technologies:**
  - Regulatory agencies can design pathways that incentivize the integration of complementary technologies only when there is clear added clinical benefit
  - Payer Alignment and Reimbursement Structures: Payers should reimburse based on demonstrated outcomes, not for performing more tests.

GPT 4.0: What are the top 10 latest technologies for precision cancer studies of predicting drug response in acute leukemias?

1. Integrated Single-Cell Multi-Omics with Functional Drug Response
2. Ex Vivo Drug Sensitivity and Resistance Testing (DSRT)
3. CRISPR-Based Functional Genomics
4. Organoids and 3D Cultures for Drug Sensitivity Testing
5. High-Content Imaging and Drug Sensitivity Assays
6. Phospho-Proteomics for Signaling Pathway Analysis
7. Metabolomics
8. Flow Cytometry-Based Functional Assays
9. Integrated Genomic and Epigenomic Profiling
10. Single-Cell Functional Assays

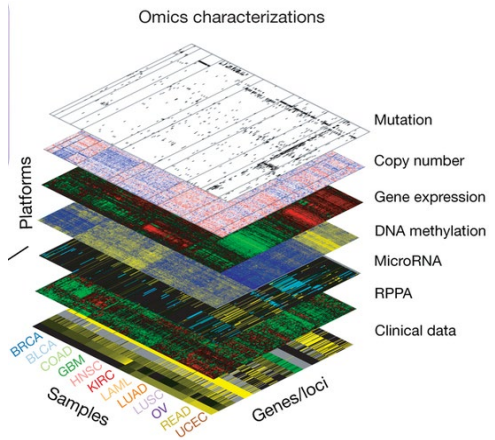
Precision medicine in AML: taxonomy, risk prediction and therapeutic allocations

Genomic Precision Medicine

+ Genotype

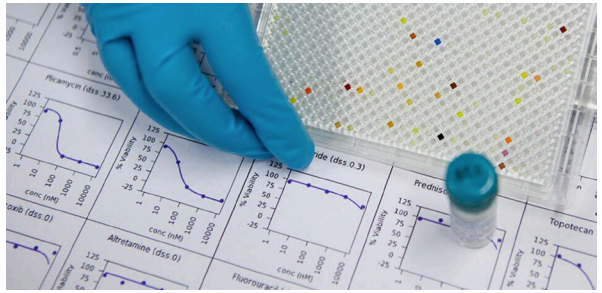
Molecular Precision Medicine

+ Phenotype



Functional Precision Medicine

+ Function



Data Integration

Integration and data-driven analysis

Molecular profiling technologies for cancer research

Every expert has good arguments that their favorite technology is the key to success in PM

- Cancer cells are driven by genetic alterations => You have to measure **genetics**, i.e. the cancer drivers

- Regulation and expression of genes critical, there are many epigenetic drugs => Apply **transcriptomics and epigenetics**

- It is the proteins that function in cells and most drug targets are proteins => You have to measure **proteins**

- Cancer cells have metabolic alterations, therapeutic vulnerabilities => you need to understand **metabolism**

- Cancer tissues have many different cell types => you will need to measure properties of **single cells, in the spatial context**

- You will need to measure blood to follow patients: Measure CTCs, ctDNA, secretome and other **blood biomarkers**

- Direct functional test ex-vivo on drug efficacy, cause-effect relationships => **functional assays** are key

Expensive
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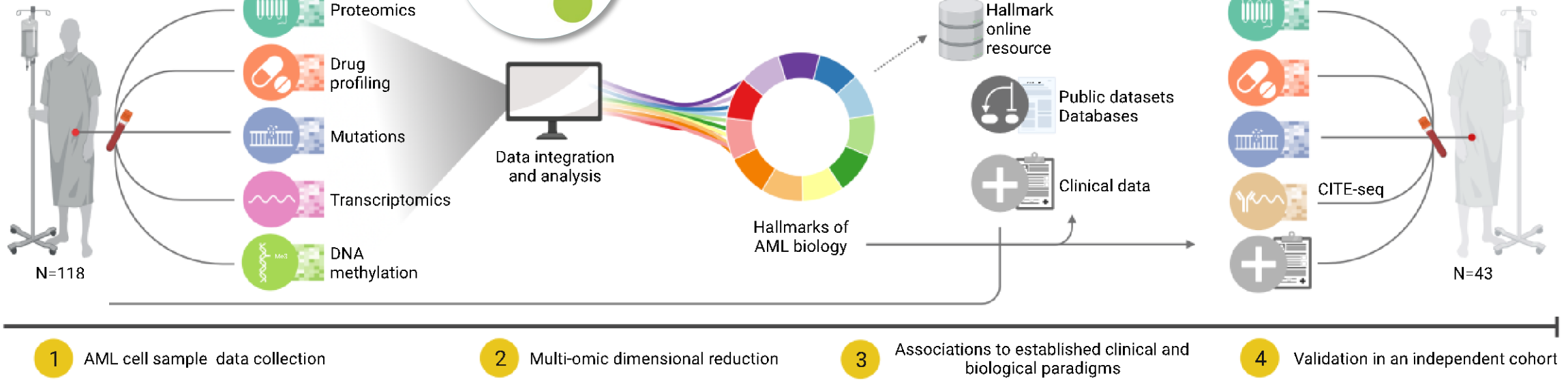
The challenge of translation to the clinic in the era of big data: Tom Erkers' paradigm

SciLifeLab

Tom Erkers

90 million datapoints on functional and omics data in AML

Systems Biology for AML
Sören Lehman (UU)
Janne Lehtiö (KI)
Yudi Pawitan (KI)
Olli Kallioniemi (OK)



→ 90 M datapoints condensed to
11 data-driven hallmarks of AML

Tom Erkers | Nona Struyf | Cornelia Arnroth | Franscesco Marabita | Tojo James

In preparation Erkers T., et al.

Which tech platform is most informative?

- Cancer cells are driven by genetic alterations => You have to measure **genetics**, i.e. the cancer drivers

- You have to understand the regulation and expression of genes => Apply **transcriptomics and epigenetics**

- It is the proteins that function in cells and most drug targets are proteins => You have to measure **proteins**

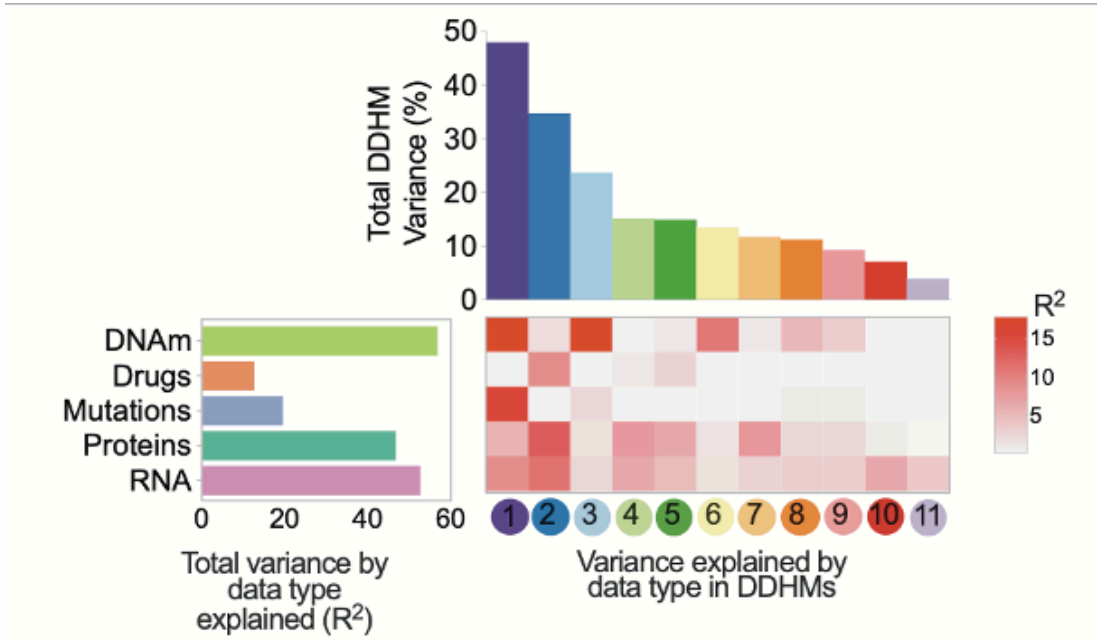
- Cancer cells have metabolic alterations, hence => you need to understand **metabolism**

- You will need to measure blood to follow patients: Measure CTCs, ctDNA, secretome and other **blood biomarkers**

- Cancer tissues have many different cell types => you will need to measure properties of **single cells, in the spatial context**

- You need to establish functional evidence, cause-effect relationships => **functional assays** are key

Which platforms contribute to which data-driven hallmark?



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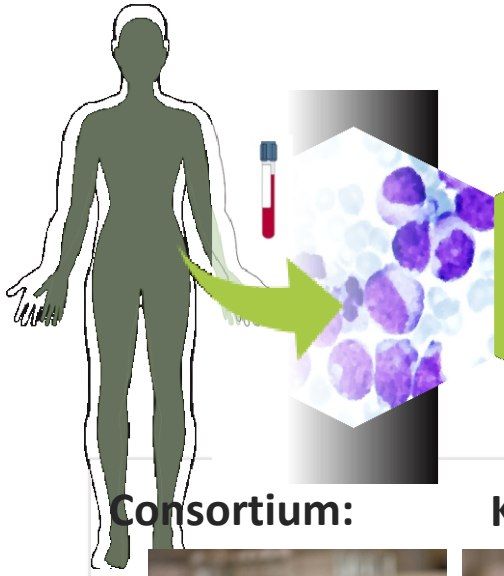
90 M datapoints? → Measure 11 data-driven hallmarks

In preparation Erkers T., et al.

Systems precision medicine for AML



Phenomics

Drugs

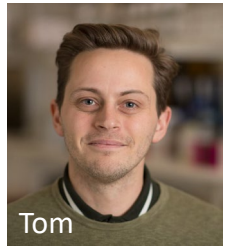
Clinical data

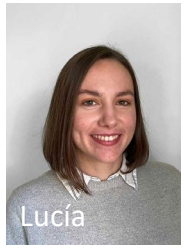
AIM:

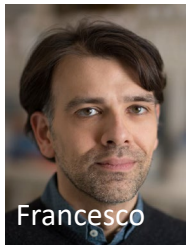
- Can we predict prognosis?
- Can we predict response to drugs?
- Can we find effective drug combinations?
- Can we generate useful informatic models?

Consortium:

Kallioniemi

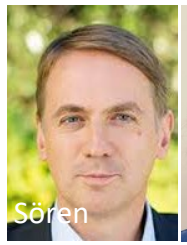


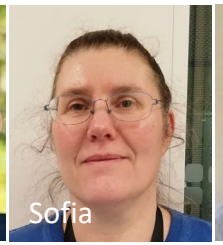




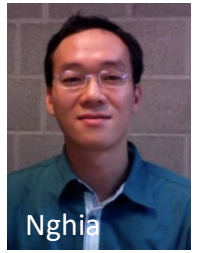
Lehtiö

Lehmann





Pawitan



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