

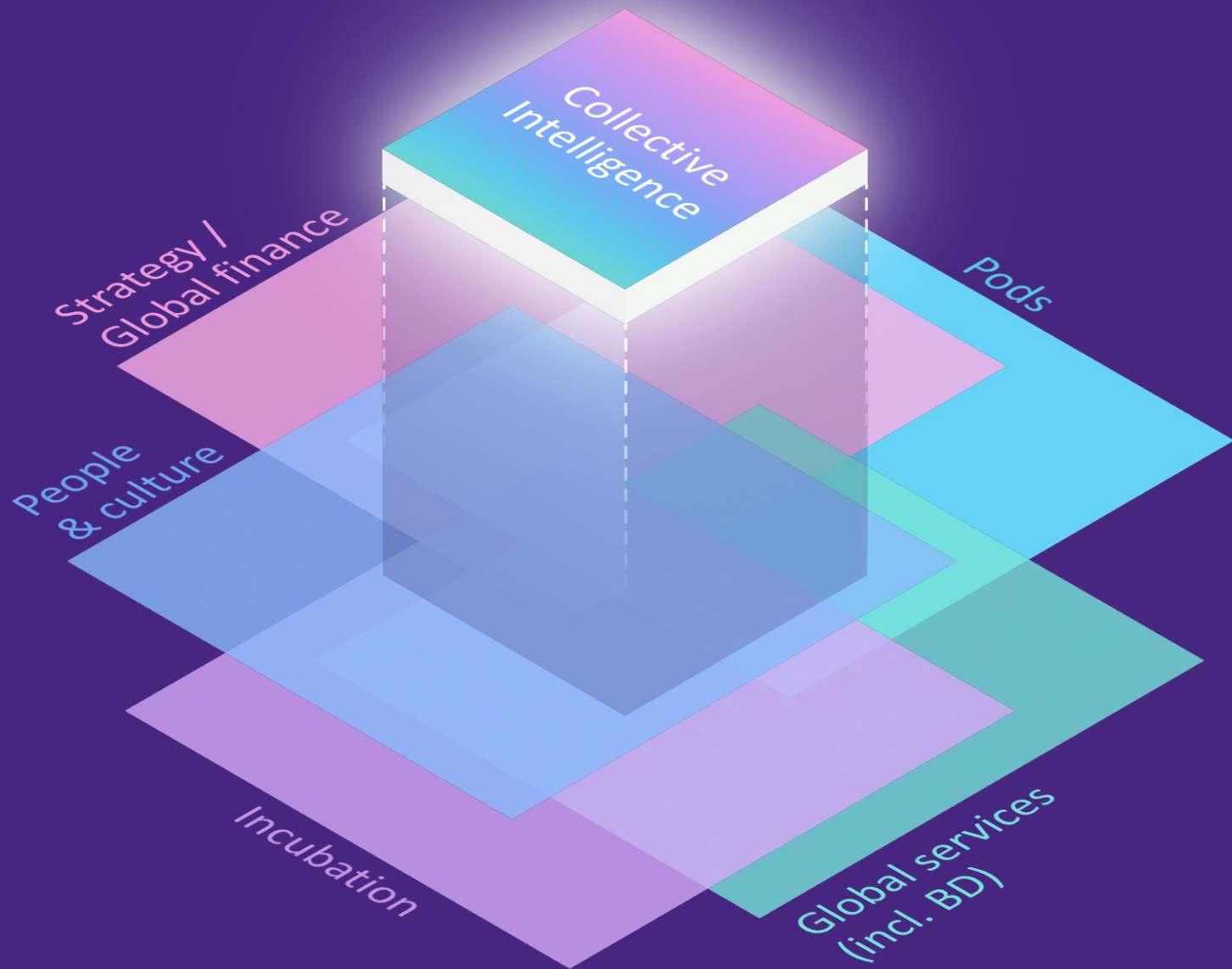
# Towards integrating precision medicine in clinical trials using AI

Danish Memon, PhD  
Team Lead Bioinformatician

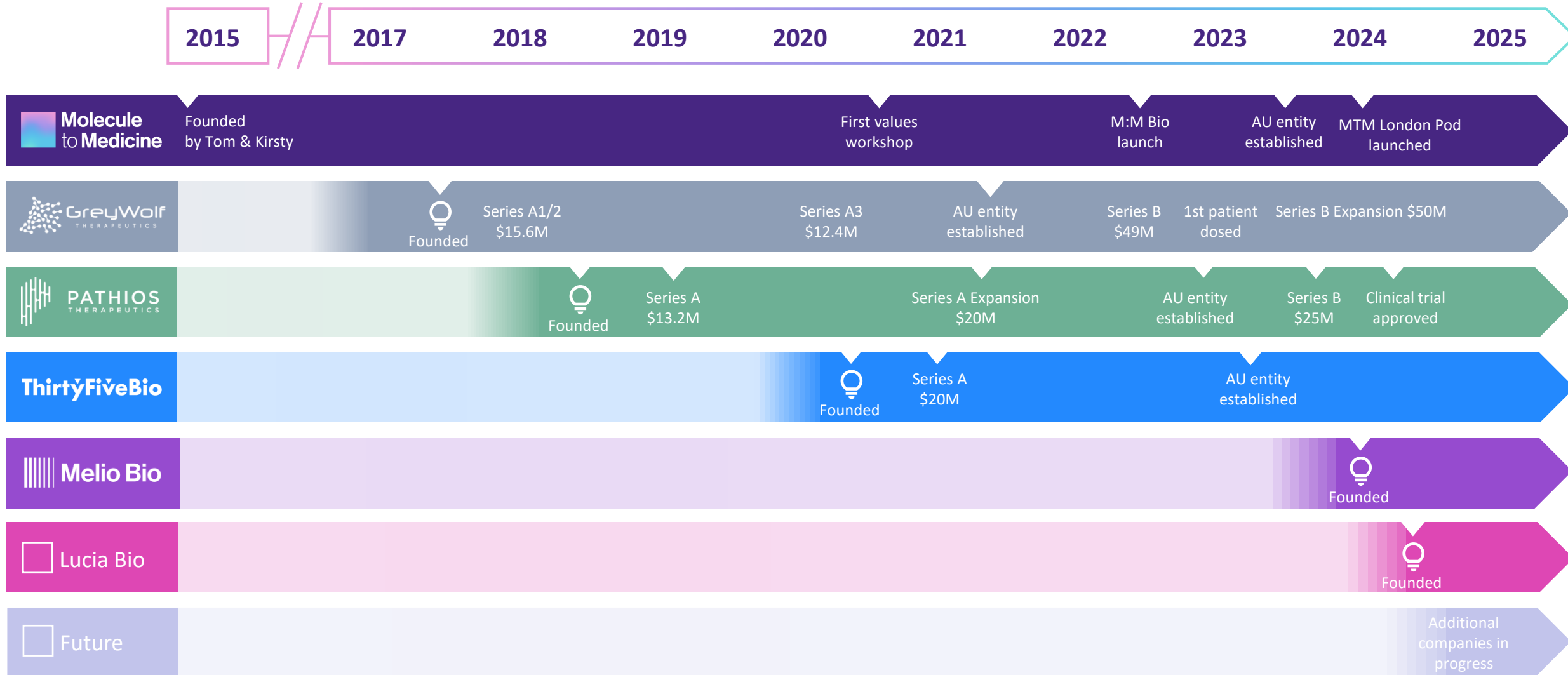
Life Sciences Conference,  
14<sup>th</sup> November 2024



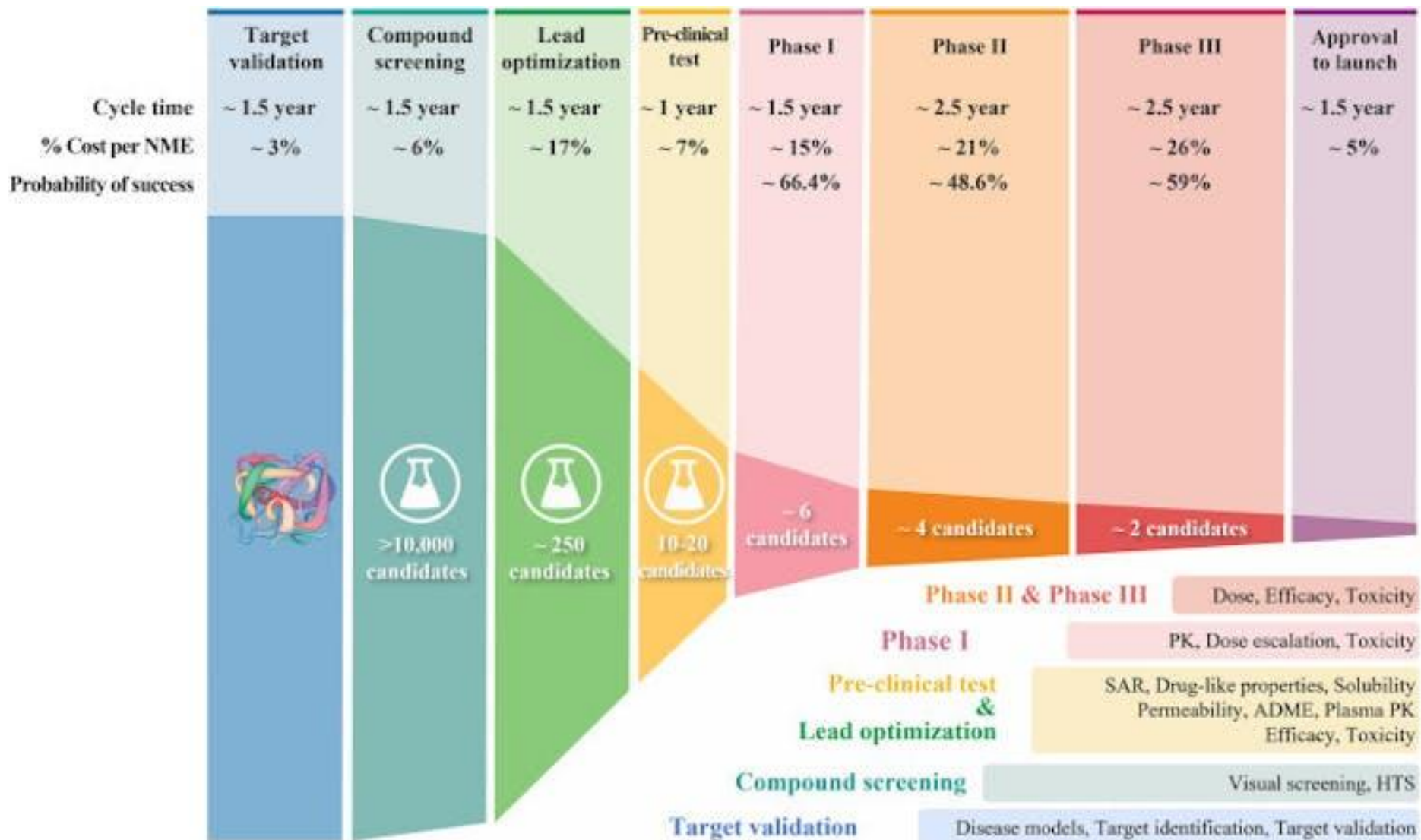
Our future is a place where collective intelligence sustains an ecosystem that transforms molecules to medicines



# A Rapidly Expanding Ecosystem...

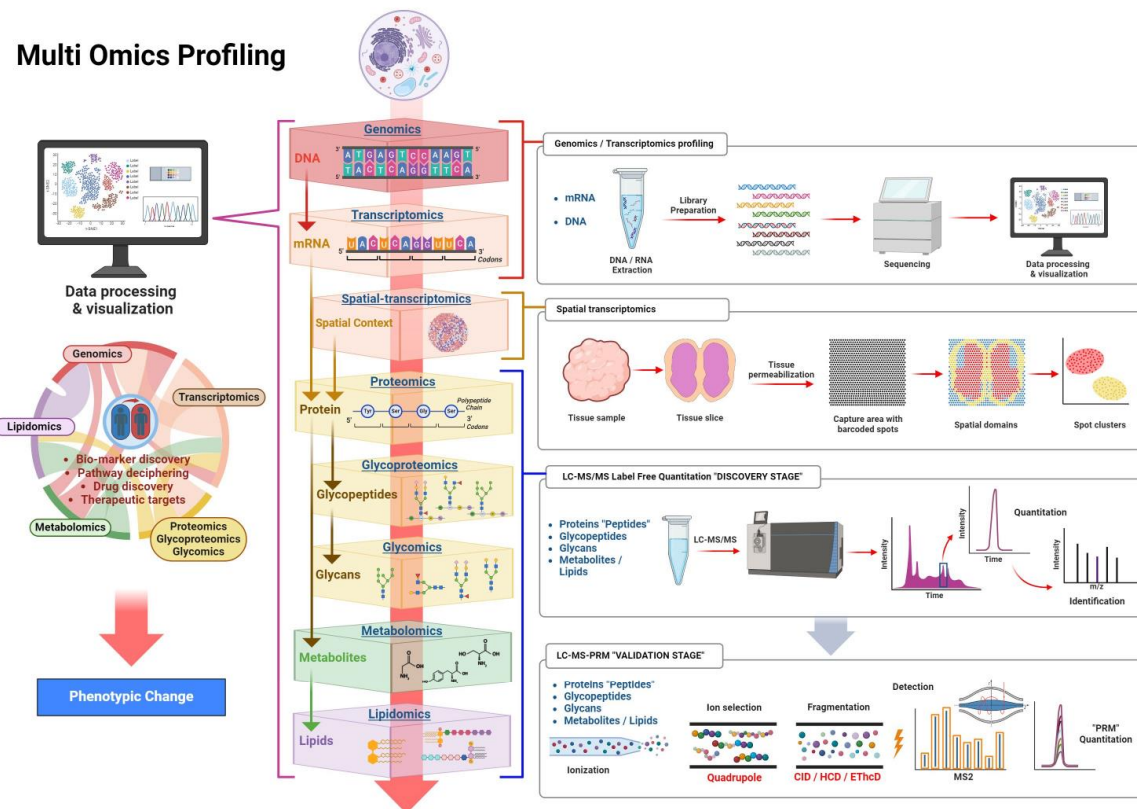


# Clinical trials are long, expensive and have high failure rates



# 1. Good time for AI in clinical research - why?

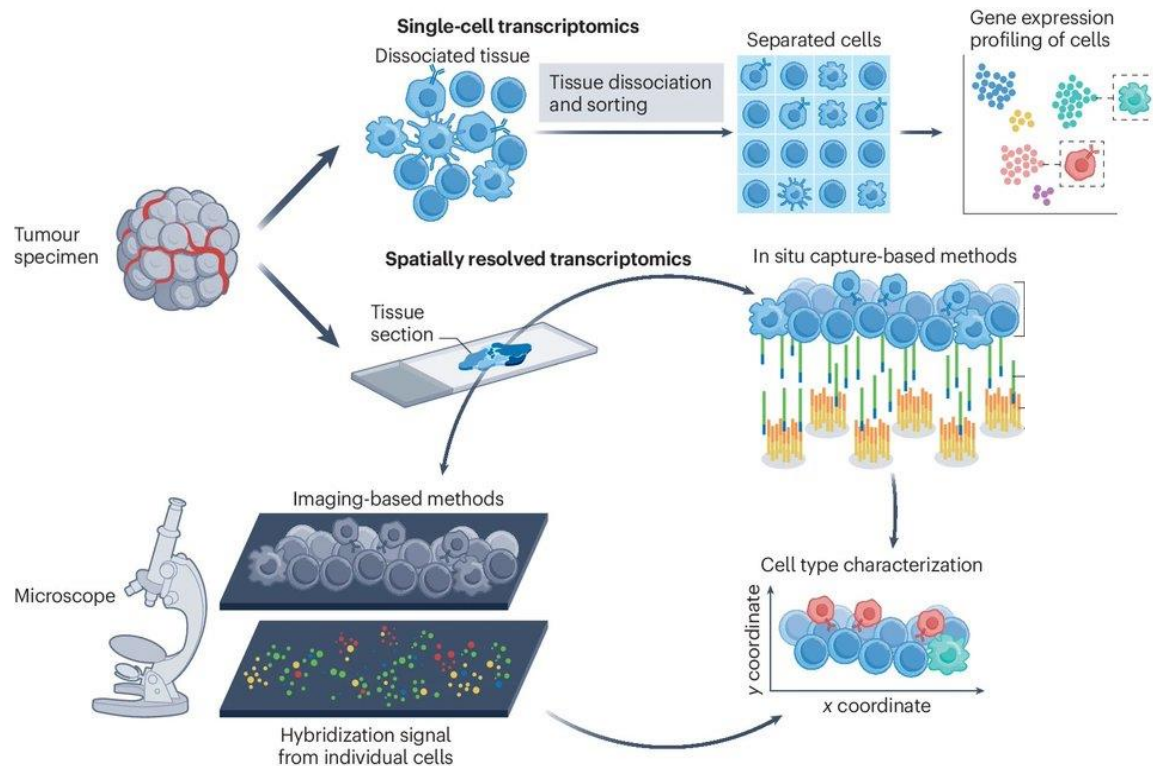
Increasingly diverse biological datasets:  
genomics, transcriptomics, proteomics,  
lipidomics.....



Source: <https://www.mdpi.com/1467-3045/46/6/345>

# 1. Good time for AI in clinical research - why?

## Increasingly high-resolution biological datasets: single cell, spatial transcriptomics and imaging data



Source: Chen *et al.*, 2024



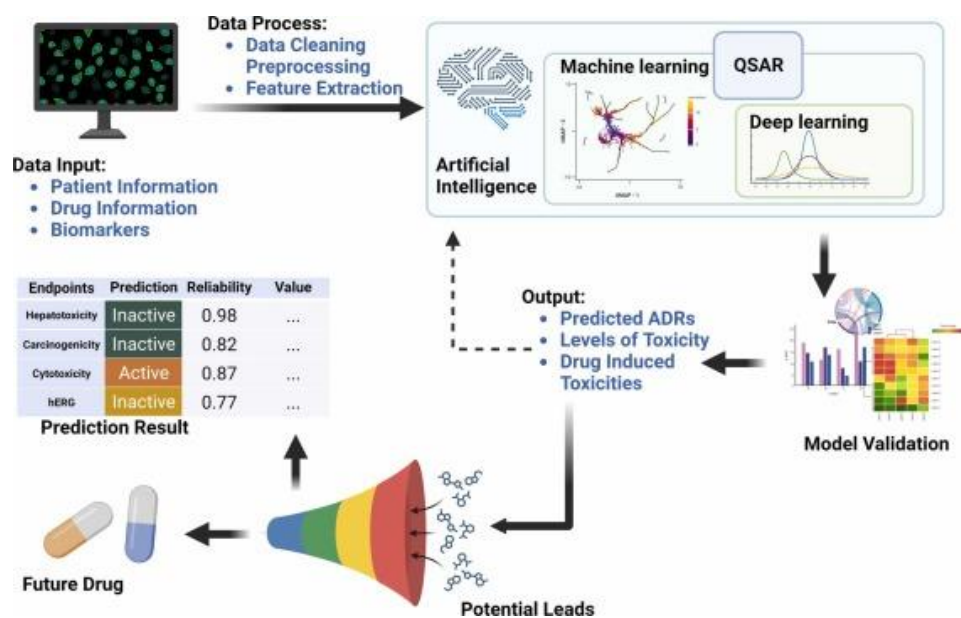
## 2. Where do we see AI in clinical research?

- Diagnosis (Imaging, blood, urine)
- Protocol writing
- Trial recruitment / site selection
- Trial simulations + digital twin approaches...

**Makes the process faster but not all of them will help make effective drugs!**

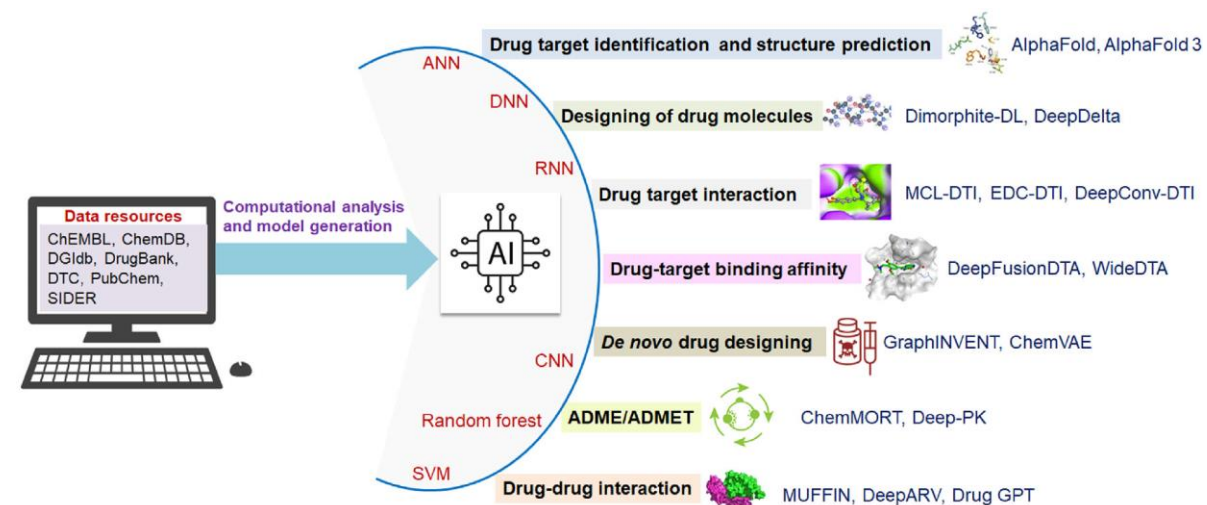
# 3. Opportunities to use AI ahead of clinical trials?

## More accurate drug toxicity predictions



Source: Yang *et al.*, 2023

## Better designing of drug molecules



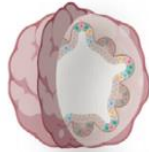
Source: Chakraborty *et al.*, 2024

# 3. Opportunities to use AI ahead of clinical trials?

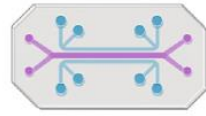
## Exploiting better preclinical models



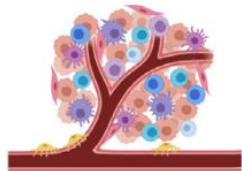
3D *in vitro* models



Organoids



Microphysiological systems



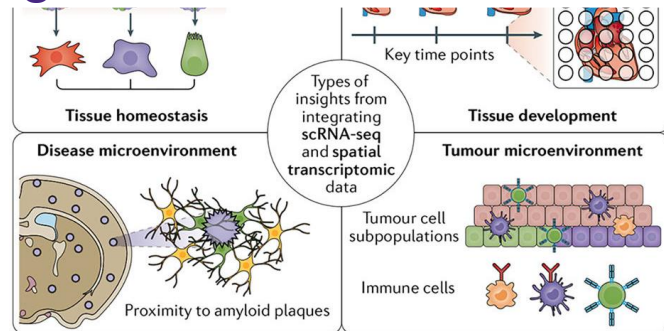
Vascularized *in vitro* models



Chimeric animal models

Source: Khalil *et al.*, 2020

## Integrating advanced perturbation technologies



**b** Identification of cell subpopulations  
scRNA-seq

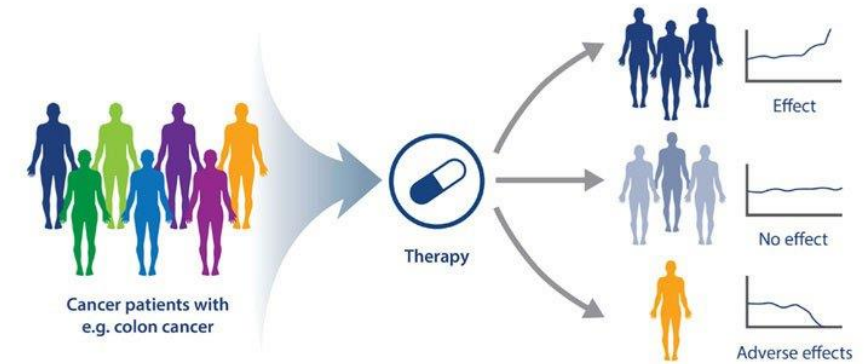
**c** Physical localization of cell subpopulations in tissue



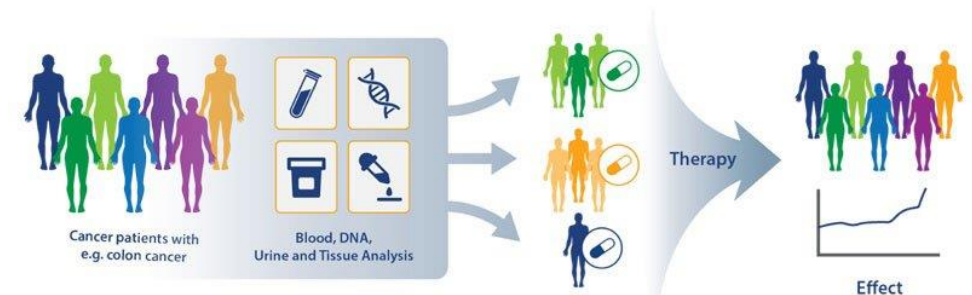
Source: Longo *et al.*, 2021

## Integrating precision medicine in clinical trials

Traditional Medicine  
One Treatment Fits All

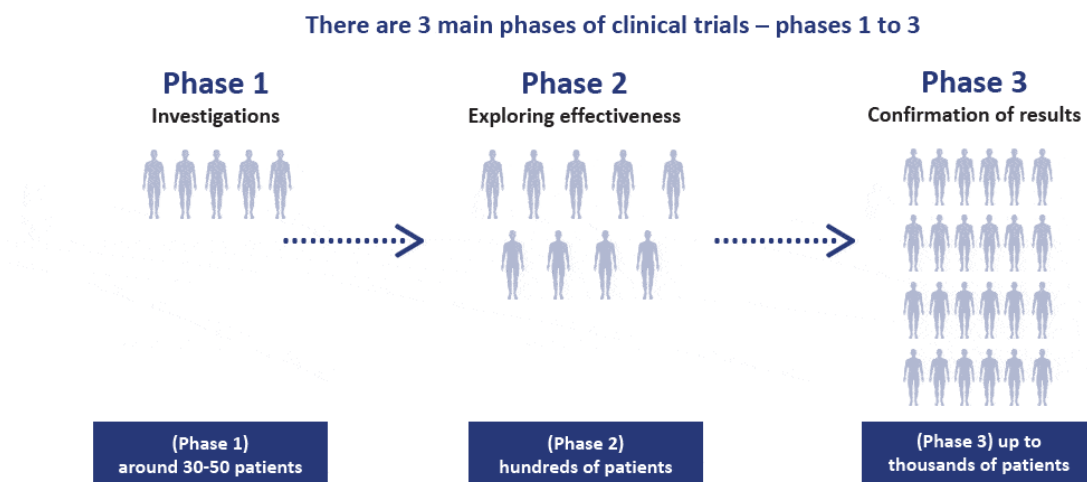


Precision Medicine  
More Personalized Diagnostics



## 4. So why are there so few AI-driven patient selection criteria?

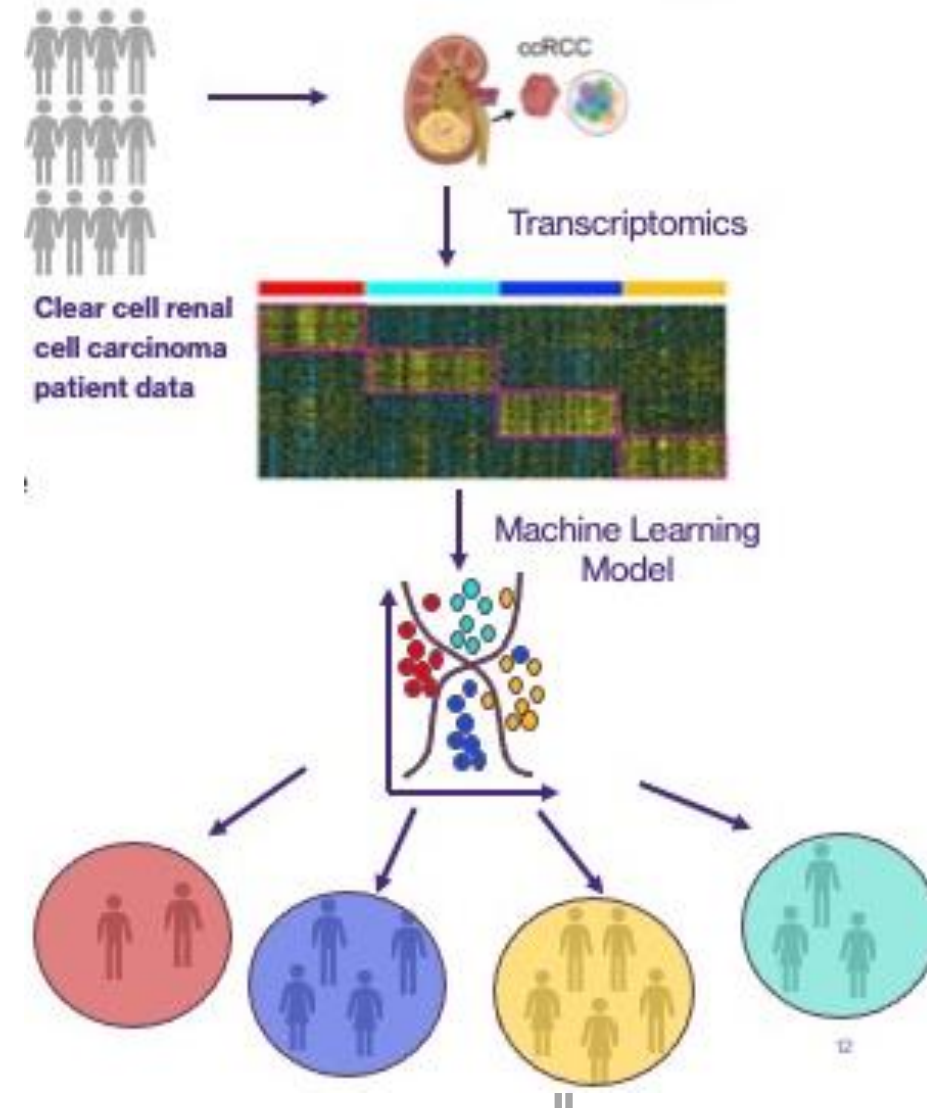
- Curse of dimensionality, i.e. very high-resolution datasets from relatively few patients who take specific novel therapy on trial
- Many more measurements and few patients.
- Too late in the day - we need to build patient selection classifiers ahead of trials not after them.
- Cost/time/ethics of obtaining data vs. familiar AI applications (shopping, finance, driving, etc.).
- Scientific Data is fragmented and siloed.



Source: <https://melanomafocus.org/melanoma-trialfinder/about-clinical-trials/>

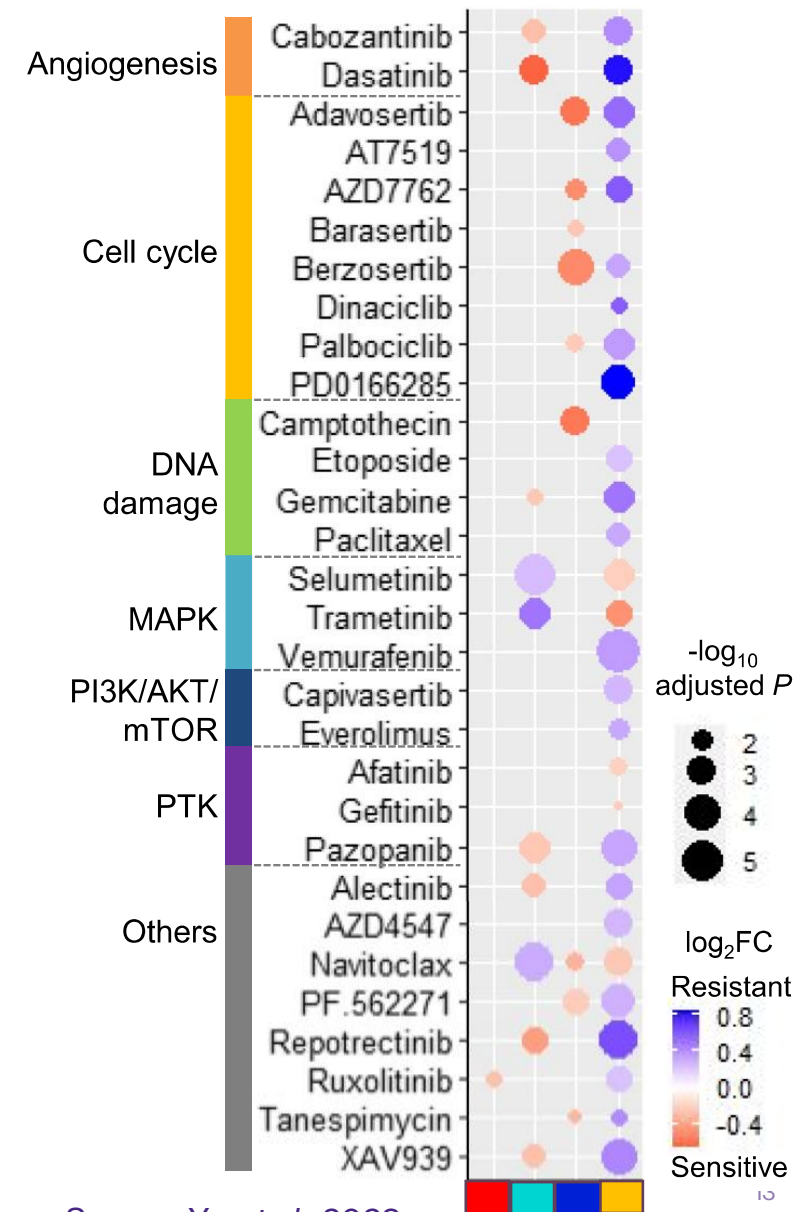
## 5. What can we do about it?

- MTM OncoSelect Grant funded by Innovate UK to build a platform that develops predictive biomarkers based on modeling of genomics and transcriptomics data in renal clear cell carcinoma.
- Explore disease first - identify and interpret patient subgroups in much larger disease cohorts instead of just patients who take one novel therapy on trial.



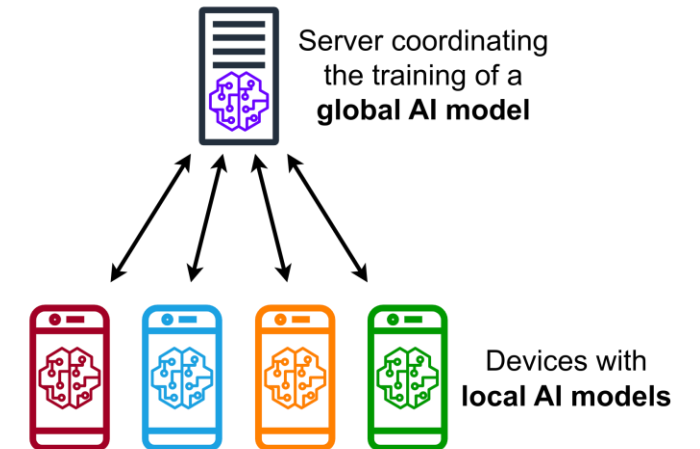
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- Explore disease first - identify and interpret patient subgroups in much larger disease cohorts instead of just patients who take one novel therapy on trial.
- Match (or even originate) novel therapeutic MoAs to specific patient subgroups so that selection classifiers may be validated (rather than originated) in early stage trials.
- As well as unsupervised learning and computational biology, foundation models used increasingly to encapsulate most relevant feature spaces for key disease characteristics and simulate patient cohorts/responses.



## 6. Challenges to new approaches (especially ones that legal minds can help to overcome)

- Need lots of data, and lots of patient samples/clinical data/RWE - who has it? where does it come from? how can we represent global patient diversity better?
- Would uniform ethical and regulatory consent frameworks help to fully leverage samples and data from different geographies? Or federated learning frameworks?
- Need proof that this approach is worth the effort - chicken & egg problem, who will fund/accept this type of approach 'up front' of pharma R&D?

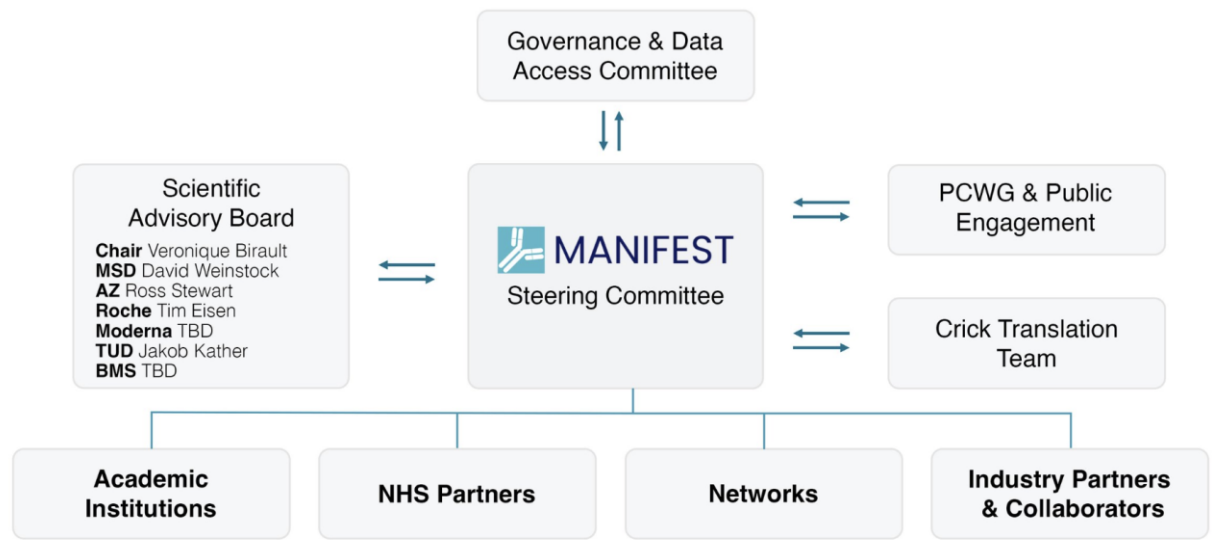
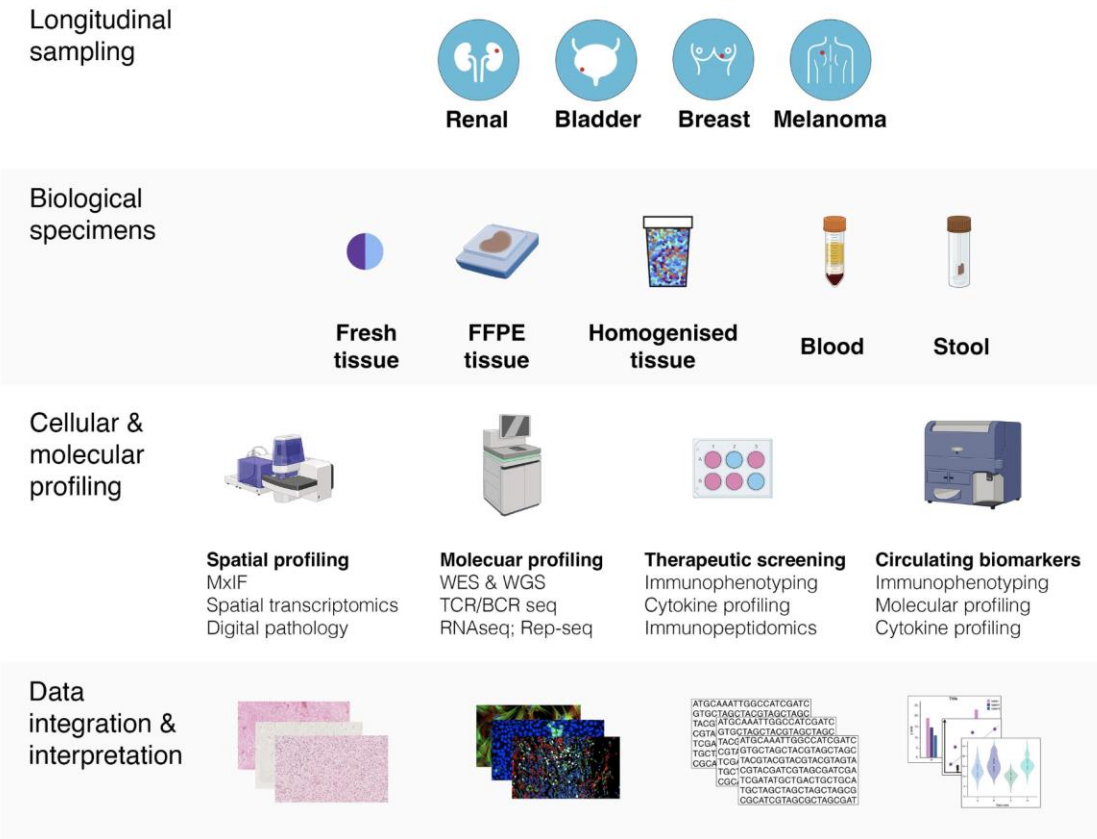


Source: <https://en.wikipedia.org>

# Multiomic ANalysis of Immunotherapy Features Evidencing Success and Toxicity (MANIFEST)

**Aims to predict how patients will respond to immunotherapy to enhance treatment precision and effectiveness.**

**The consortium is comprised of 14 leading academic institutions, 6 NHS trusts and 19 industry partners including MTM.**



# Acknowledgements

- Dr. Matthew Trotter - Ennuste Research