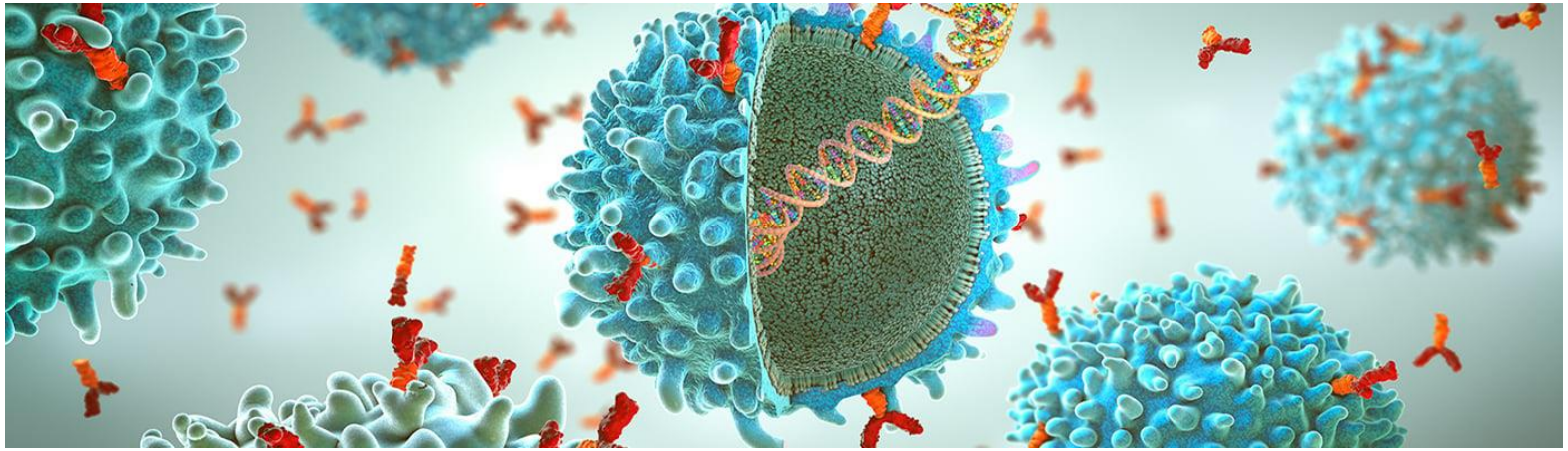
Foundations in Cancer Engineering



Lecture 1: Introduction/Overview

September 29, 2025

Daniel A. Heller, PhD

Member, Molecular Pharmacology Program, Sloan Kettering Institute

Memorial Sloan Kettering Cancer Center

Outline

- A Theory of Cancer Engineering
- Problems in Need of Cancer Engineering
- Core Knowledge of Cancer Engineering and Some Rationale
- Feedback, Advice, Next Steps

A Theory of Cancer Engineering

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Why Create this (Sub-)Discipline?

A Perspective Piece:

Cancer Cell

CellPress

Commentary

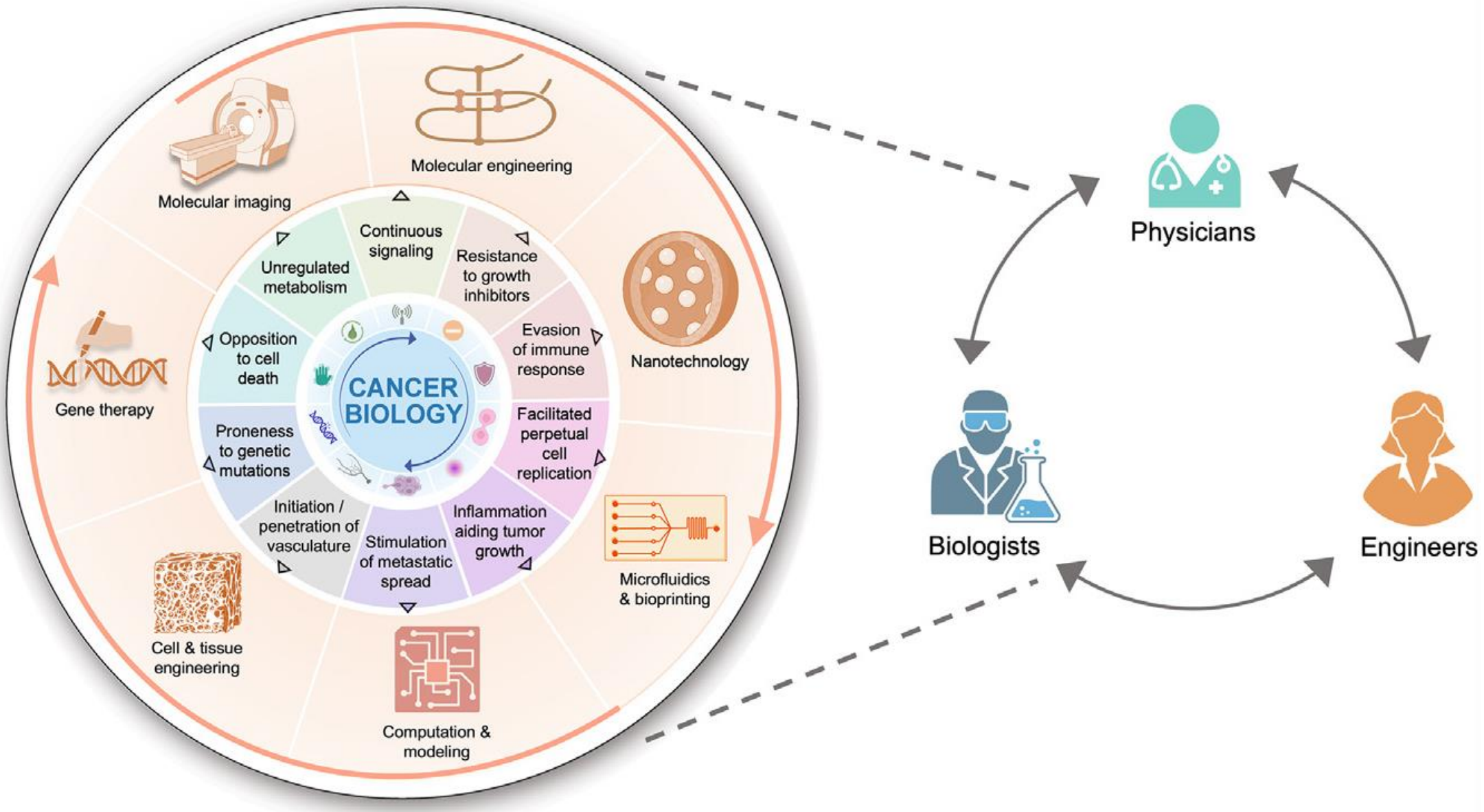
Engineering focusing on cancer

Kayvan R. Keshari,[1,2,4,5,*] Daniel A. Heller,[1,4,5,*] Rostislav Boltyanskiy,[5] Hedvig Hricak,[1,2,4,5] Thomas Magaldi,[4] and Michael Overholtzer[3,4,5,*]

[1]Molecular Pharmacology Program, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[2]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[3]Cell Biology Program, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[4]Gerstner Sloan Kettering School for Biomedical Sciences, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[5]Center for Molecular Imaging and Bioengineering, Memorial Sloan Kettering Cancer Center, New York, NY, USA
*Correspondence: rahimikk@mskcc.org (K.R.K.), hellerd@mskcc.org (D.A.H.), overholm1@mskcc.org (M.O.)
https://doi.org/10.1016/j.ccell.2024.04.013

Cancer Cell (2024), https://doi.org/10.1016/j.ccell.2024.04.013

Cancer Engineering



"A schematic representation of the elements of cancer engineering that are built on the needs and unique features of cancer biology" *Cancer Cell* (2024), https://doi.org/10.1016/j.ccell.2024.04.013

Some Potential Types/Goals of Technologies in Cancer Engineering

- Therapeutic technologies
- Diagnostic technologies
- Tools/methods for cancer biology research
- Tools/methods for clinical research
- Tools/methods for drug discovery

Some Disciplines Not Often Included in Bioengineering/Biomedical Engineering

- Pharmacology
- Drug discovery and development
- Biomarker discovery
- Clinical diagnostics
- Imaging probes
- Chemical biology

Another Perspective: Engineering and Biology are Verbs

- Engineer:
  - A tool
  - A method
  - A technology

- Biology:
  - To study
  - To ask a question
  - To assess a therapeutic action

Some Problems in Need of Cancer Engineering

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- Problems in Need of Cancer Engineering
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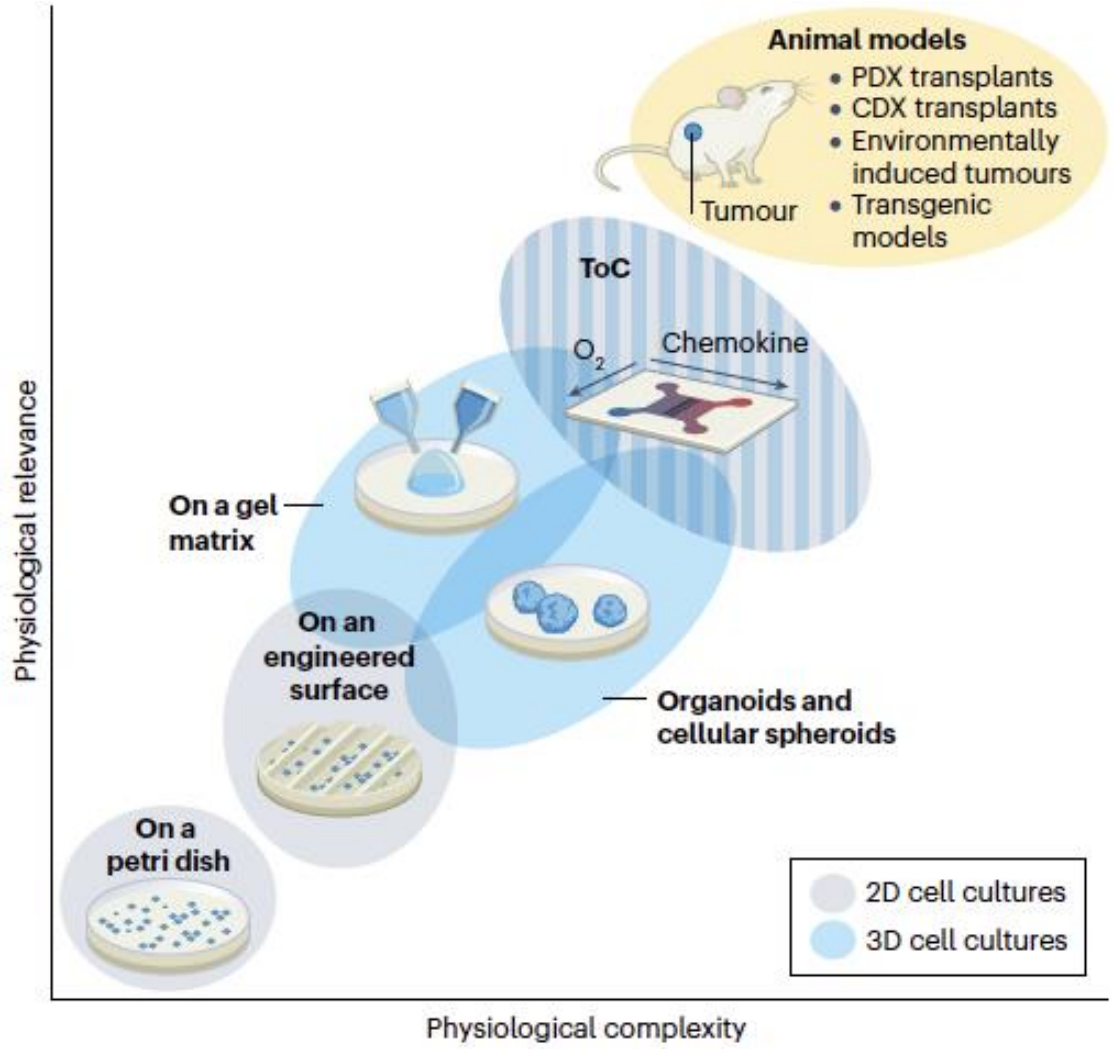
Better Cancer Models

- Many in vivo cancer models do not represent the human cancers well, including:
  - Tumor microenvironment (vasculature, stroma, immune microenvironment)
    - Leaky vasculature
    - Types/ratios of stroma/immune cells present
- 2D cell culture models lack many features of tumors that can be improved/modeled:
  - Mechanical properties (substrate, flow of blood/lymph)
  - Cell types present
  - Nutrient/oxygen gradients

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8212826/

Using Engineering Approaches for Cancer Modeling (Some Examples)

- Surface mechanical properties
- Shear forces
- Chemical gradients
- Tumor spheroids (cancer cells)
- Organoids (multiple cell types)
- Cell-derived xenograft (CDX)
- Patient-derived xenograft (PDX)
- Organoid-based xenograft
- Transgenic mouse models



Kim et al., Nat Rev Cancer (2023)

Measuring Analytes in Situ

- Detecting nutrients, lipids, chemokines, cytokines, hormones, etc.
- Quantifying amounts and changes, dynamics, and gradients
- Measuring in different locations of the tumor (microenvironment), and other areas of the body (regional, distant organs, immune system, blood, etc.)
- For studying disease biology as well as for tumor detection (screening, diagnosis, prognosis, for improving decisions about treatment).

Improved Bench/Mechanistic Biology/Drug Discovery Methods

- Assays for disease/mechanistic targets
- High-throughput assays for drug/activity screening
    - Tumor cell death
    - Tumor proliferation
    - Target engagement
    - Modulation of a pathway
    - Changes in metabolism

Earlier Cancer Detection/Screening, Better Treatment Decisions

- Minimally-invasive tests
- Inexpensive, rapid detection for cancer screening
- Better diagnostic/prognostic biomarkers
- Biomarkers that help decisions about cancer treatment
  - How to tell when a particular drug/immunotherapy might work for a patient?

Core Knowledge in Cancer Engineering and Some Rationale

- A Theory of Cancer Engineering
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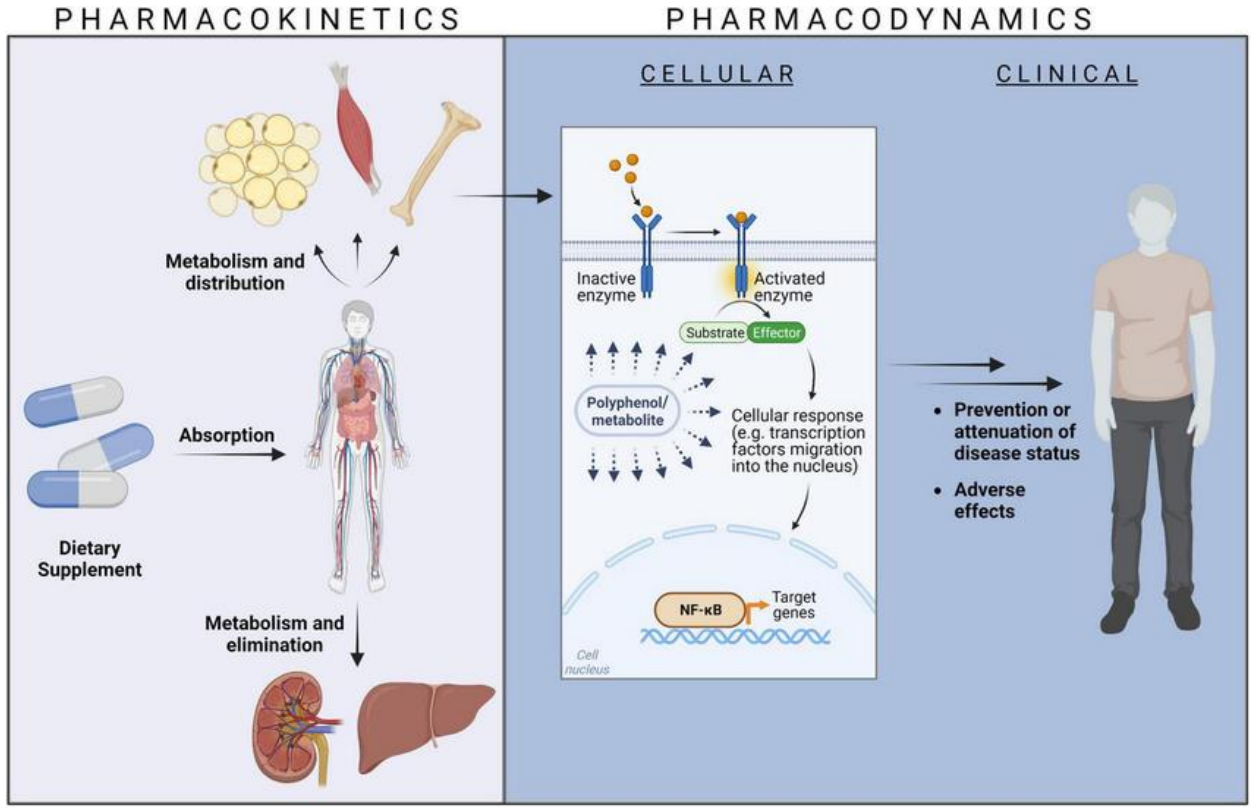
Core Knowledge in Cancer Engineering and Some Rationale

- Foundations in Cancer Engineering
- Imaging
- Genetic Engineering

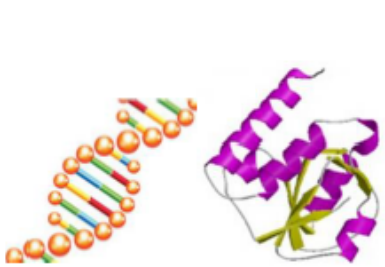
Pharmacology

Pharmacology is the science of drugs and medications, including a substance's origin, composition, pharmacokinetics, pharmacodynamics, therapeutic use, and toxicology. More specifically, it is the study of the interactions that occur between a living organism and chemicals that affect normal or abnormal biochemical function. If substances have medicinal properties, they are considered pharmaceuticals.



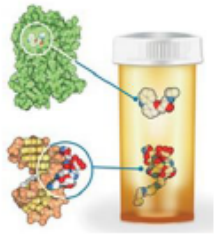
https://en.wikipedia.org/wiki/Pharmacology
DOI:10.3389/fnut.2024.1389422

Drug Development

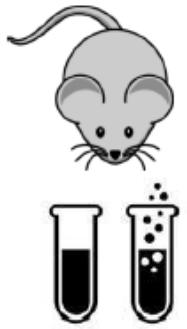


Gene

Protein Target



Lead Identification and Optimization

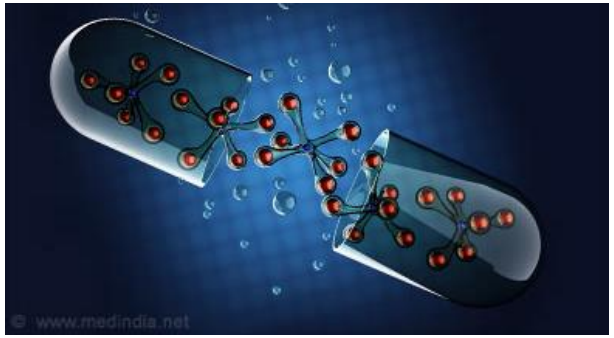


Non-Clinical Safety

Clinical Development

Drugs: Small Molecules and Antibodies

- Organic Compounds (chemotherapies + precision medicines)
  - Cytotoxic drugs
  - Inhibitors
  - Degraders

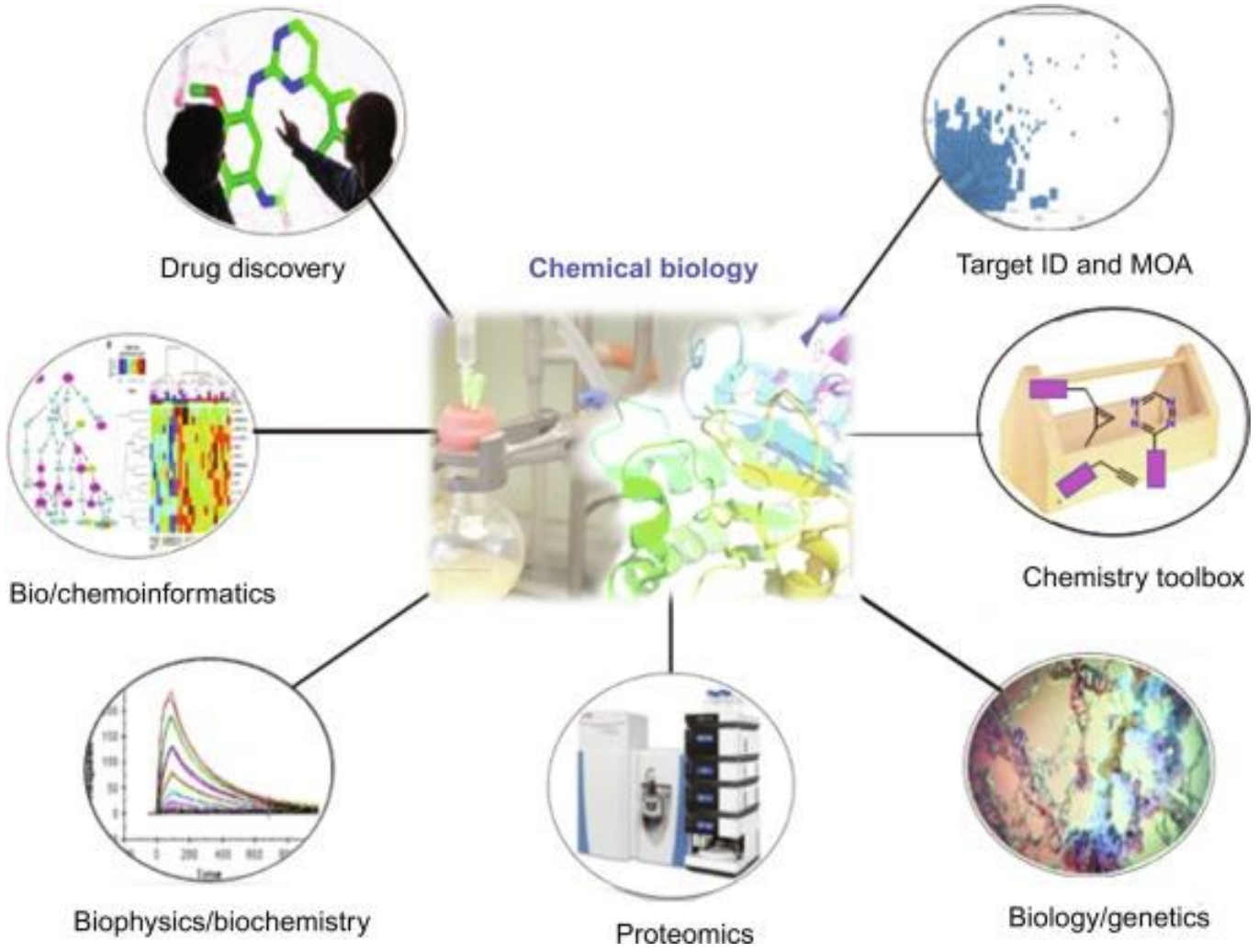


- Antibody Drugs
  - Inhibitors
  - Antibody-drug conjugates
  - Molecular imaging probes

Chemical Biology

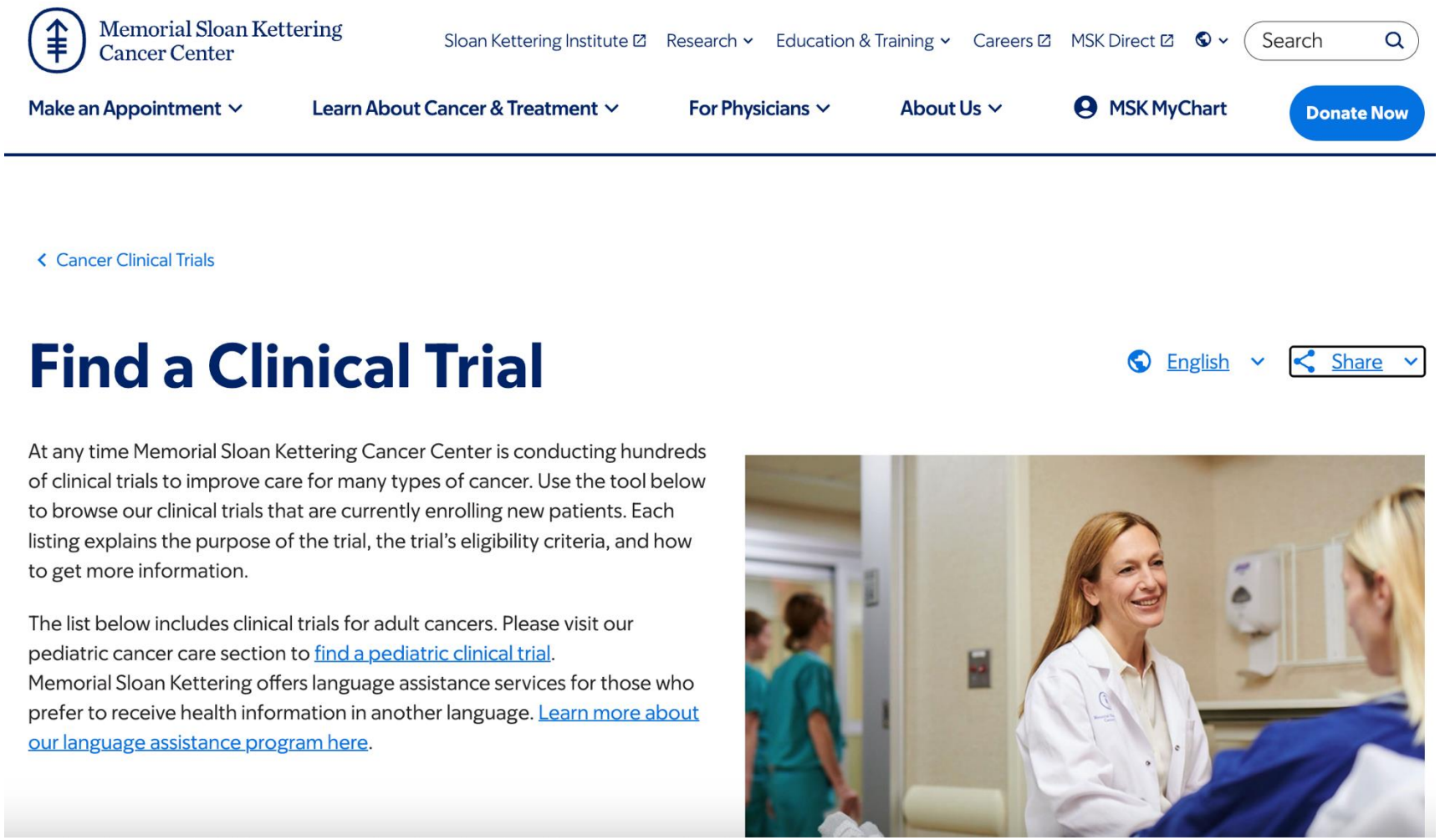
The application of chemical techniques, analysis, and often small molecules produced through synthetic chemistry, to the study and manipulation of biological systems.

An important department at MSK whose faculty often develop novel therapeutics.



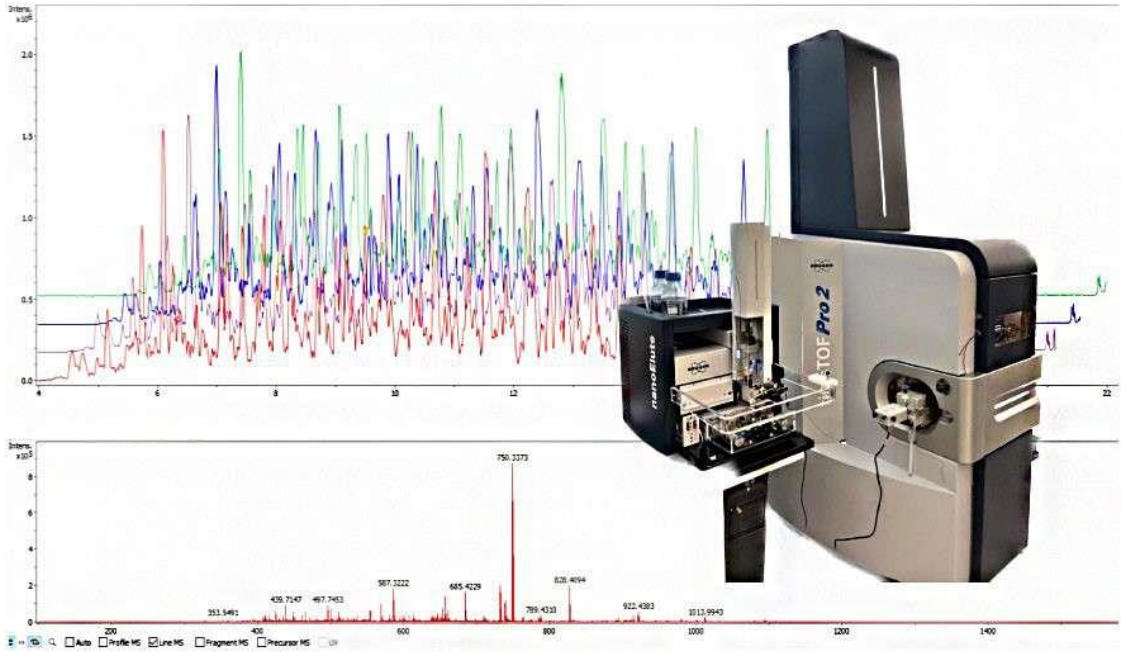
M. Paola Castaldi, et al., Annual Reports in Medicinal Chemistry 2017

Clinical Research at MSK & Early-Phase Clinical Development



Mass Spectrometry

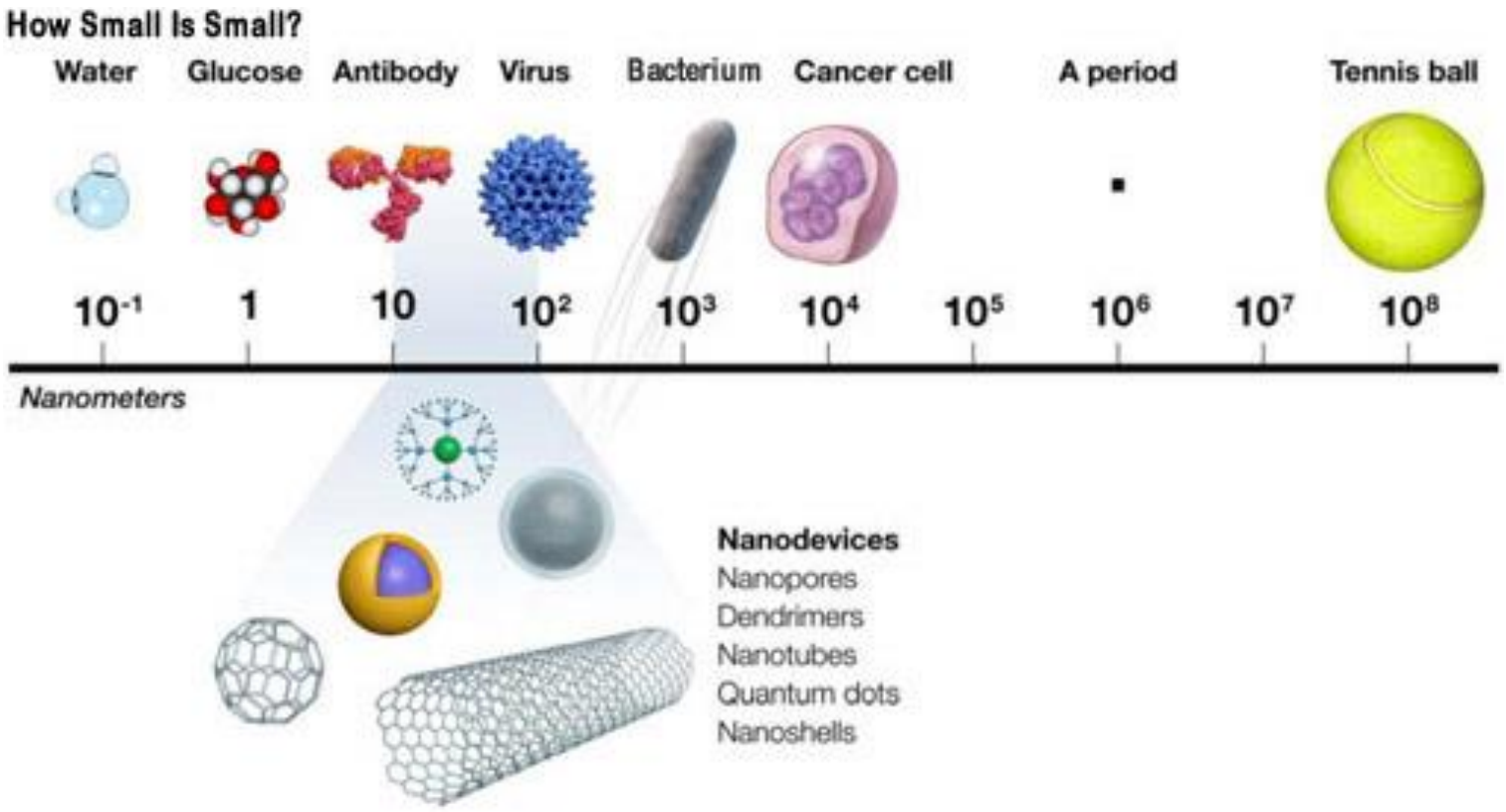
- Important for:
  - Chemistry and drug development
  - Pharmacology (measuring drug concentration and metabolism)
  - Drug delivery (quantifying drugs in different tissues)
  - Proteomics
    - Basic biological discovery
    - Target discovery
    - Diagnostics



https://wertheim.scripps.ufl.edu/cores-and-technologies/mass-spectrometry-and-proteomics/

Nanotechnology

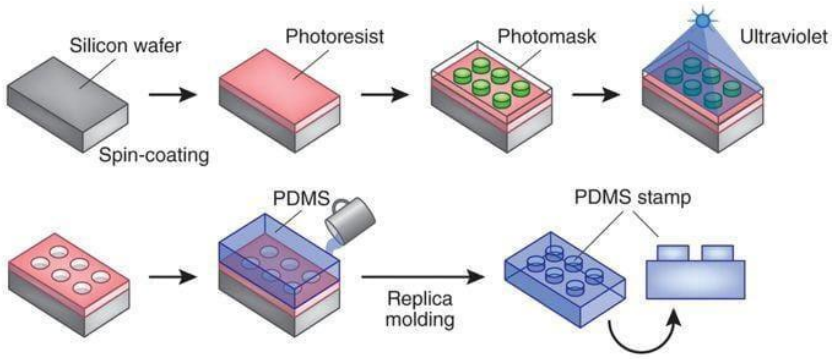
- Important for:
  - Drug delivery
  - Imaging
  - Sensors
  - (Biological measurement)

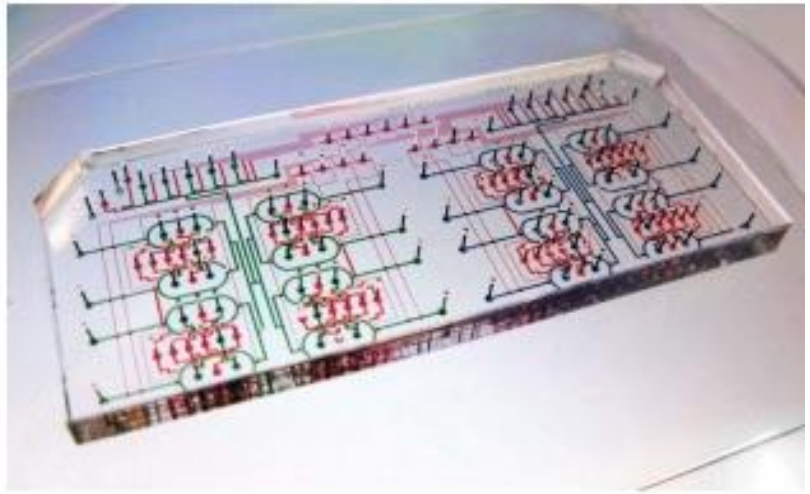


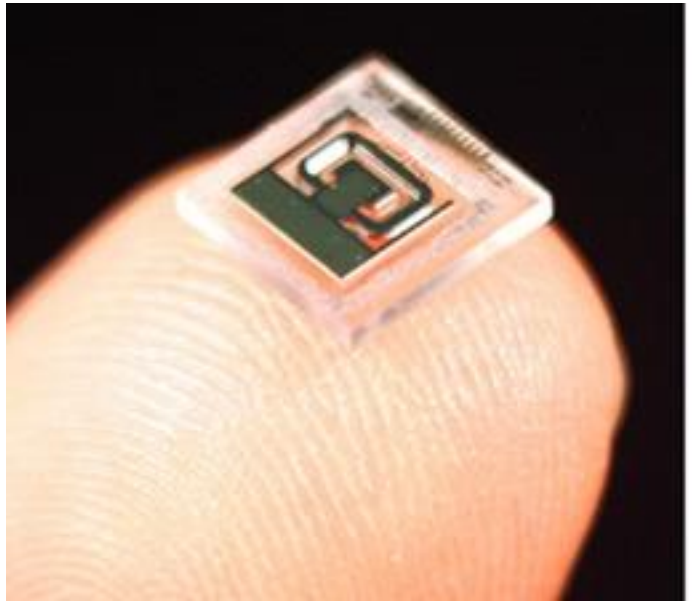
Drug Delivery

The goal of **drug delivery** is to control/alter the pharmacokinetics of a drug. Drug delivery systems may be medical devices, excipients (inactive ingredients/vehicle), drug carriers (like nanoparticles).

Fabrication and Fluidics





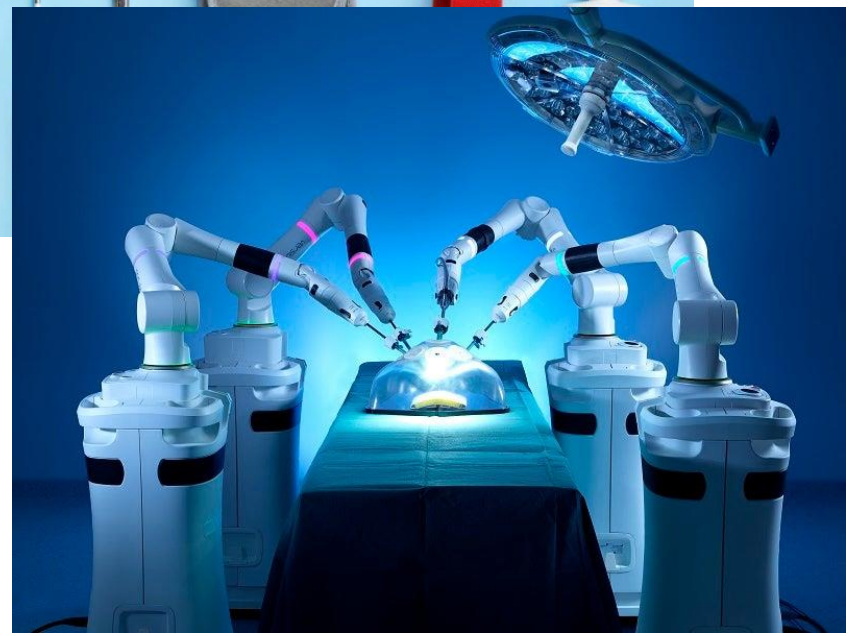


Microfluidic Devices:
Assays/microarrays
Control of cell environment
Single cell measurements
Drug screening
Drug (protein) delivery

https://www.advancedsciencenews.com/the-success-of-plasma-for-microfabrication/

Medical Devices

- Surgical devices
- Medical implants
- Drug delivery devices
- Anesthesia
- Measurement devices
- Point-of-care diagnostics



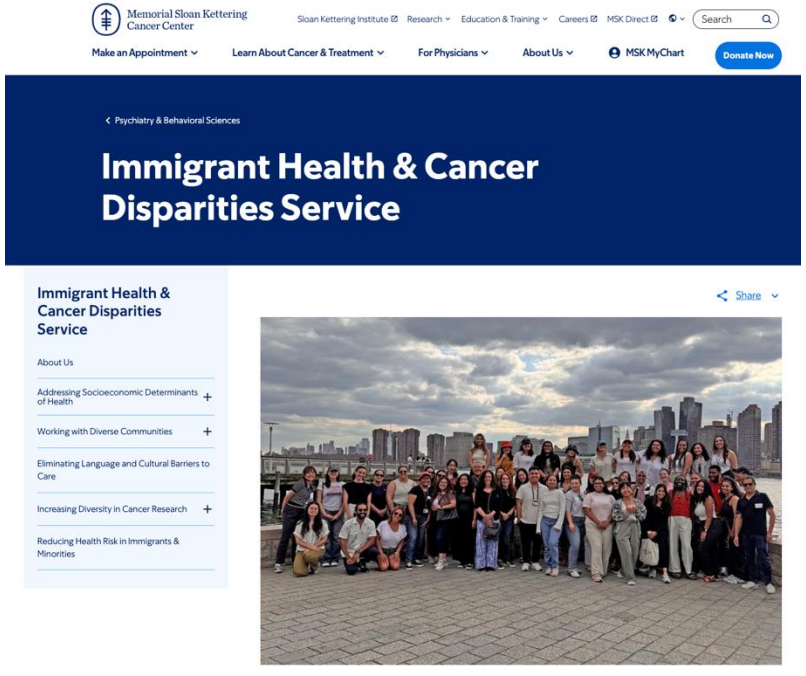
https://highpowervtls.com/2024/06/the-different-classes-of-reusable-medical-devices/
https://www.medicaldevice-network.com/features/da-vinci-surgical-robot-competitors/

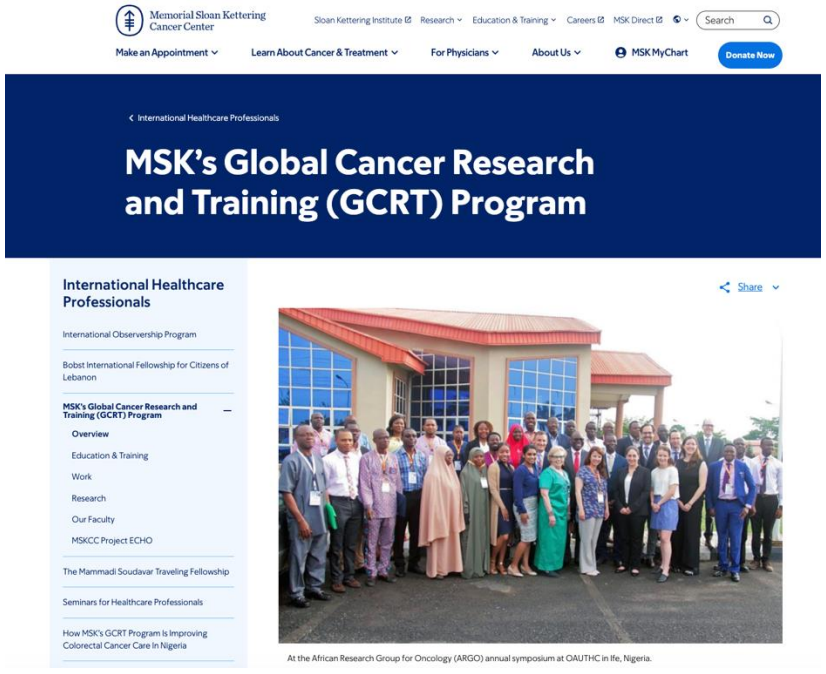
Laboratory Diagnostics and Biomarkers

- Laboratory medicine = information from blood (and other body fluids)
  - Chemistry
  - Hematology
  - Immunology
  - Microbiology
  - Transfusion medicine
  - Toxicology
  - Molecular diagnostics
- Biomarkers = molecules that give information about health and disease

Global Health and Underrepresented Populations

- Disparities - cancer diagnosis and treatment in:
  - Rural communities in the US
  - Cities in the US
  - Developing countries

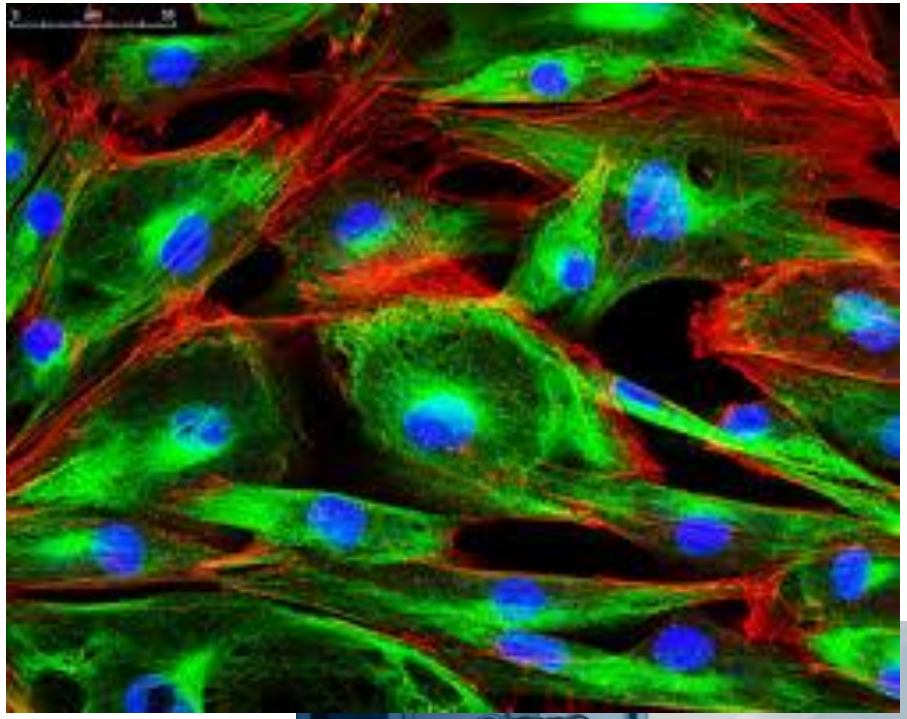




Imaging

- Pathology
- Cells
- Animals
- Whole body

- Optical imaging
- Pathology
- Nuclear imaging
- MRI
- PET
- Theranostics
- Molecular imaging probes



https://www.edmundoptics.com/
https://www.aps.org/careers/advice/medical-clinical-physicist

Genetic Engineering

- Gene engineering methods
  - CRISPR/CAS9
- Genome editing and chromosomal engineering
- Human genetics
- Genetic screening

https://www.pirbright.ac.uk/engage-with-us/science-case-studies/genetic-engineering

Protein, Cell and Tissue Engineering (Genetic Engineering Course)

- Protein engineering – designing proteins that do what you want
- Stem cell engineering – making cells that can differentiate into desired cell types
  - Induced pluripotent stem cells (iPSCs)
- Cell therapy engineering
  - CAR T cells
- Tissue engineering
  - Organoids
  - Cancer models

https://www.quantamagazine.org/an-ethical-future-for-brain-organoids-takes-shape-20200123/

Feedback and Next Steps

- A Theory of Cancer Engineering
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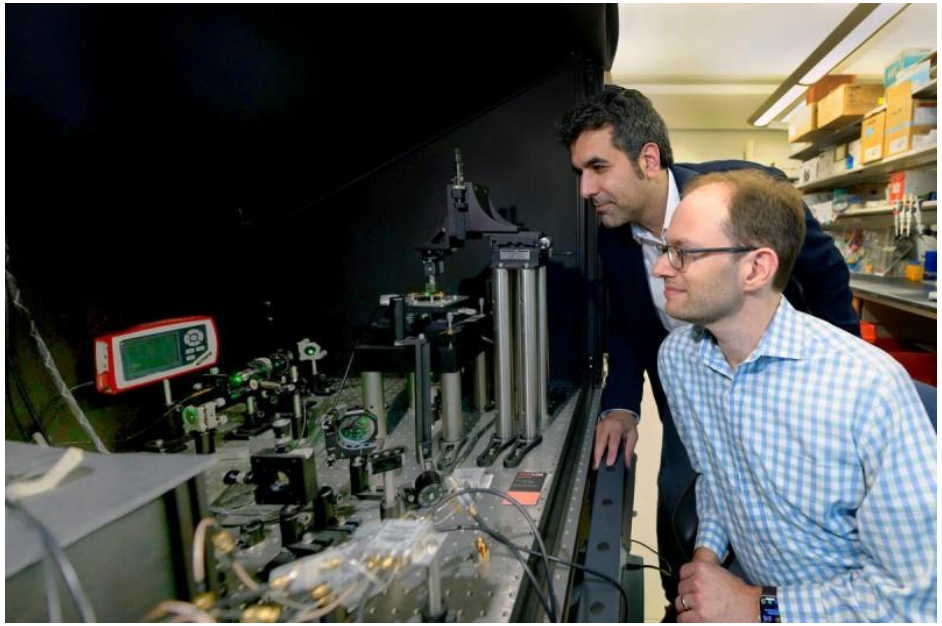
Feedback

- Cancer Engineering is a work in progress:
  - As a discipline
  - As a graduate program



Possible Next Steps

- A study – higher education research
- A new perspective/review article
- Symposia

Some Thoughts/Advice

- Learn about the MSK mission and the cancer patient journey
  - Meet physicians, patients, patient advocates, etc.
- Learn about the many different types of jobs and people who work here
  - In science, clinical, administrative, etc. roles
- Attend seminars outside of your field
- Don’t be shy about telling others about your research
- Make at least the first 30% of your seminar accessible to people outside of your field

Some Thoughts/Advice

- Learn about the opportunities and events at MSK/the Tri-I
  - Courses in: Drug development, entrepreneurship, biostatistics, etc. etc.
  - Lectures in science (seminars/works in progress) and medicine (grand rounds)
  - Continuing medical education (CME) activities
  - Entrepreneurship and company-related opportunities
  - Outreach opportunities
- Learn about opportunities and events in the NYC Area
  - New York Academies of Science/Medicine
  - NYU, Mount Sinai, Columbia, etc.
  - Outreach and entrepreneurship activities

One Opportunity – Sunday Oct 19

- ACS Making Strides Against Breast Cancer
- Central Park – 8:00 am – 12:00 noon
- Research Tent
- Ask Annie