College of Pharmacy
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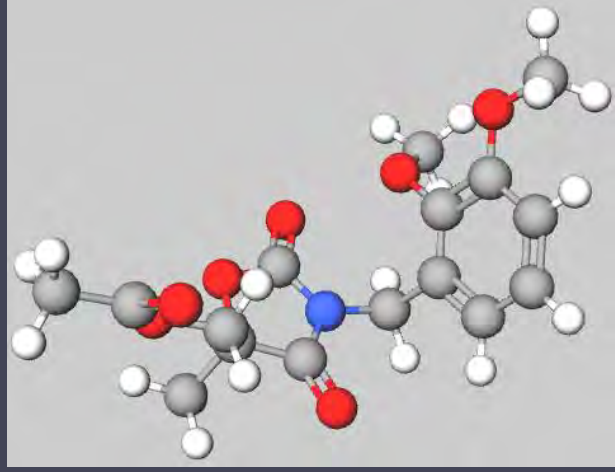

The Role of Medicinal Chemistry in Cancer Research

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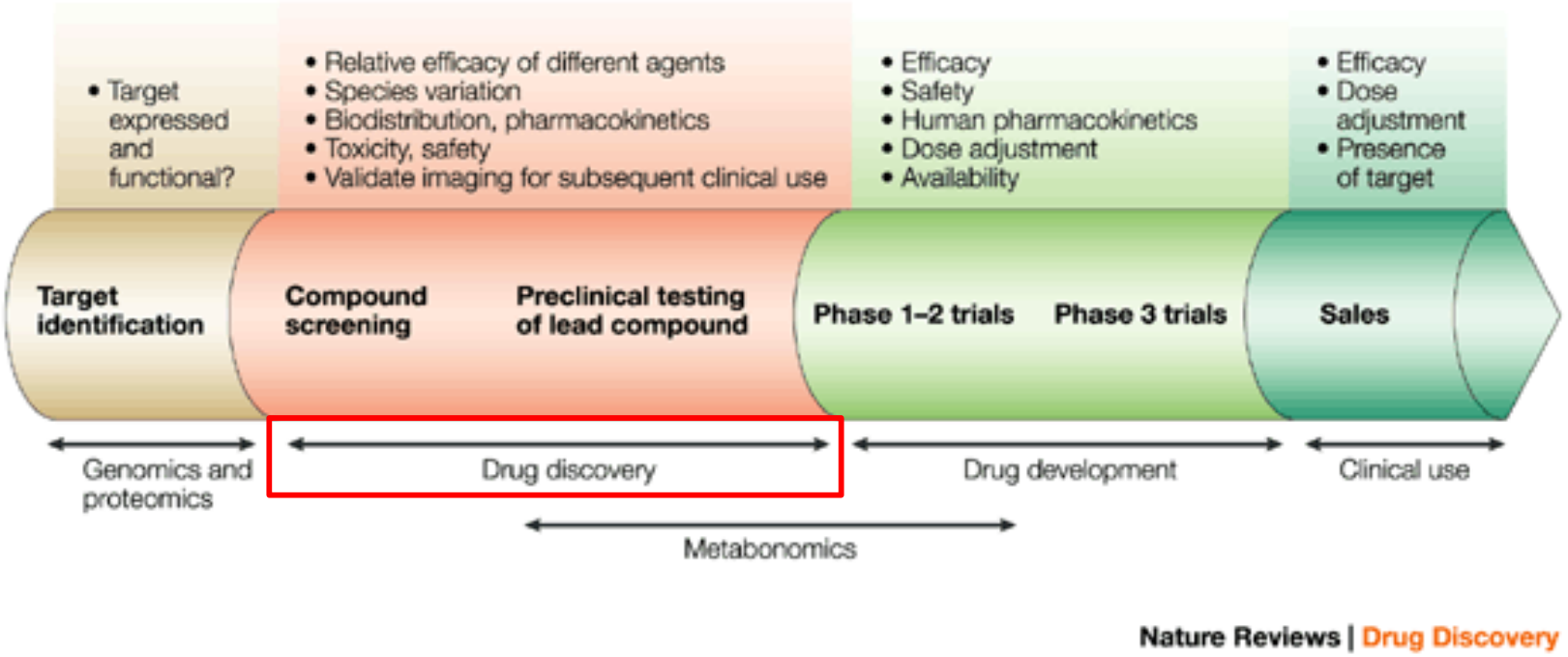
September 24, 2019


WHO
ARE
YOU

Learning Objectives

- Illustrate the role of medicinal chemistry in the drug discovery and development process.
- Define medicinal chemistry, including in practical terms.
- Analyze the breadth of chemistry of anti-cancer drugs.
- Consider a career path in medicinal chemistry

Drug Discovery and Development Process



Medicinal Chemistry

- As defined by IUPAC:

"Medicinal Chemistry" is a chemistry-based discipline, involving aspects of biological, medical and pharmaceutical sciences. It is concerned with the invention, discovery, design, identification and preparation of biologically active compounds, the study of their metabolism, the interpretation of their mode of action at the molecular level and the construction of structure-activity relationships.

Medicinal Chemistry

Understanding the relationship of a drug structure with its:

- Physiochemical properties
- Pharmaceutical properties
- Pharmacological properties
- Toxicological properties

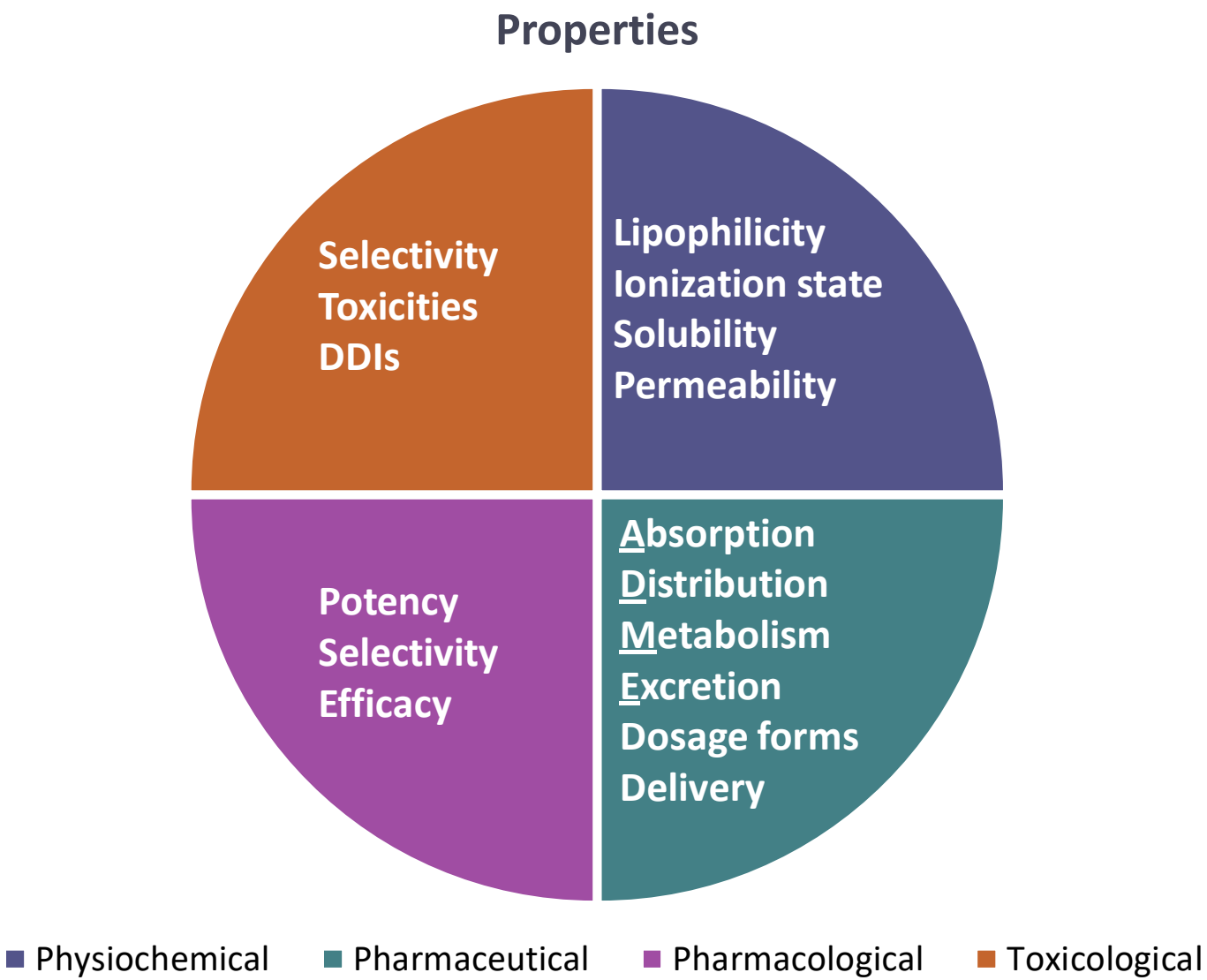
Medicinal Chemistry

Why its structure?

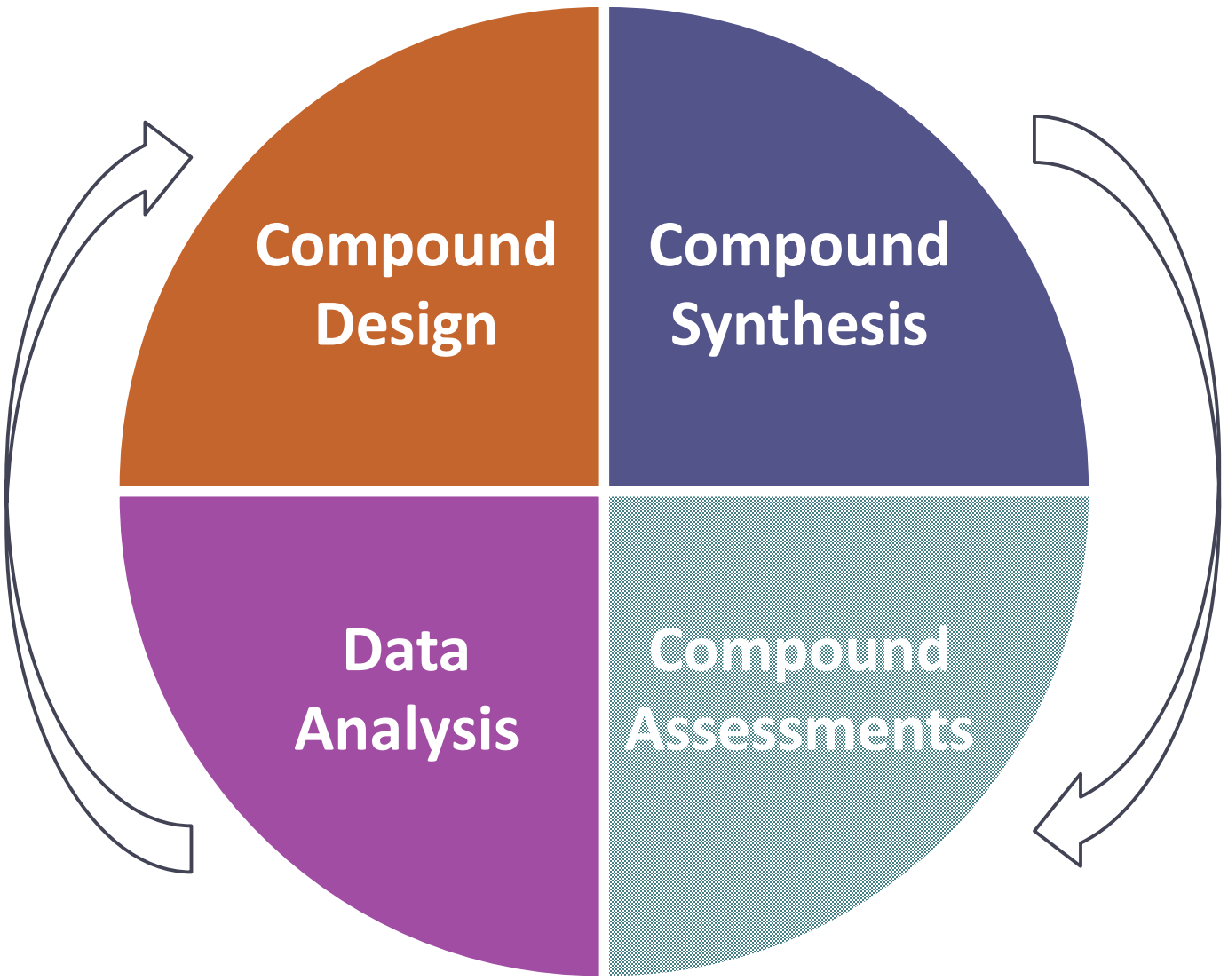
Almost all of the wanted and unwanted physiochemical, pharmaceutical, pharmacological and toxicological properties of a drug are dictated by its 3D structure.

E.g. The 3D display of functional groups and the interactions of the structure with its surroundings.

Medicinal Chemistry → Balance Properties

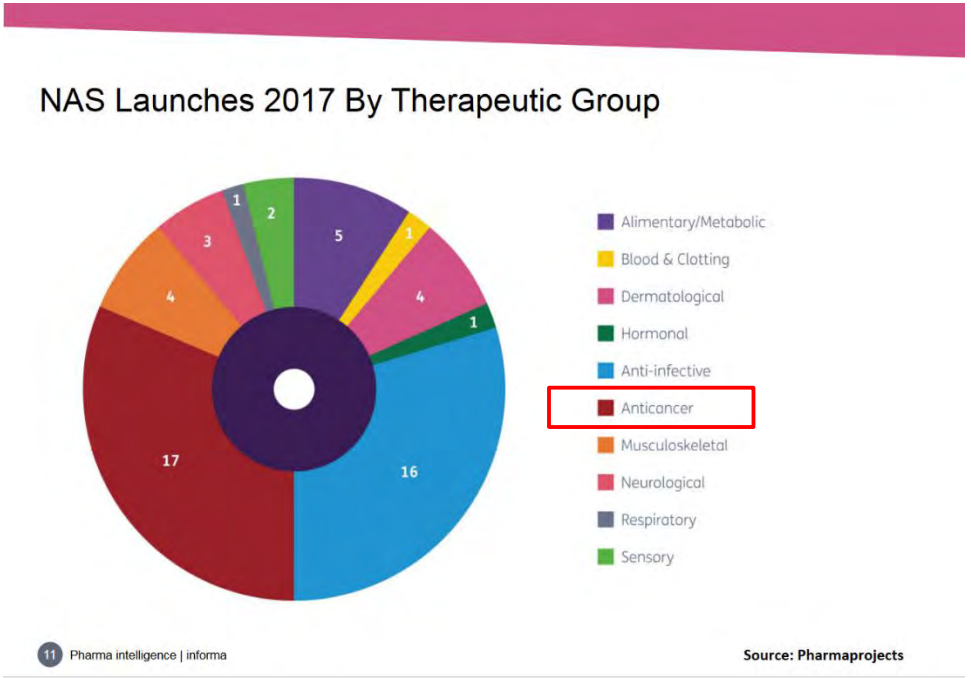


Practice of Medicinal Chemistry

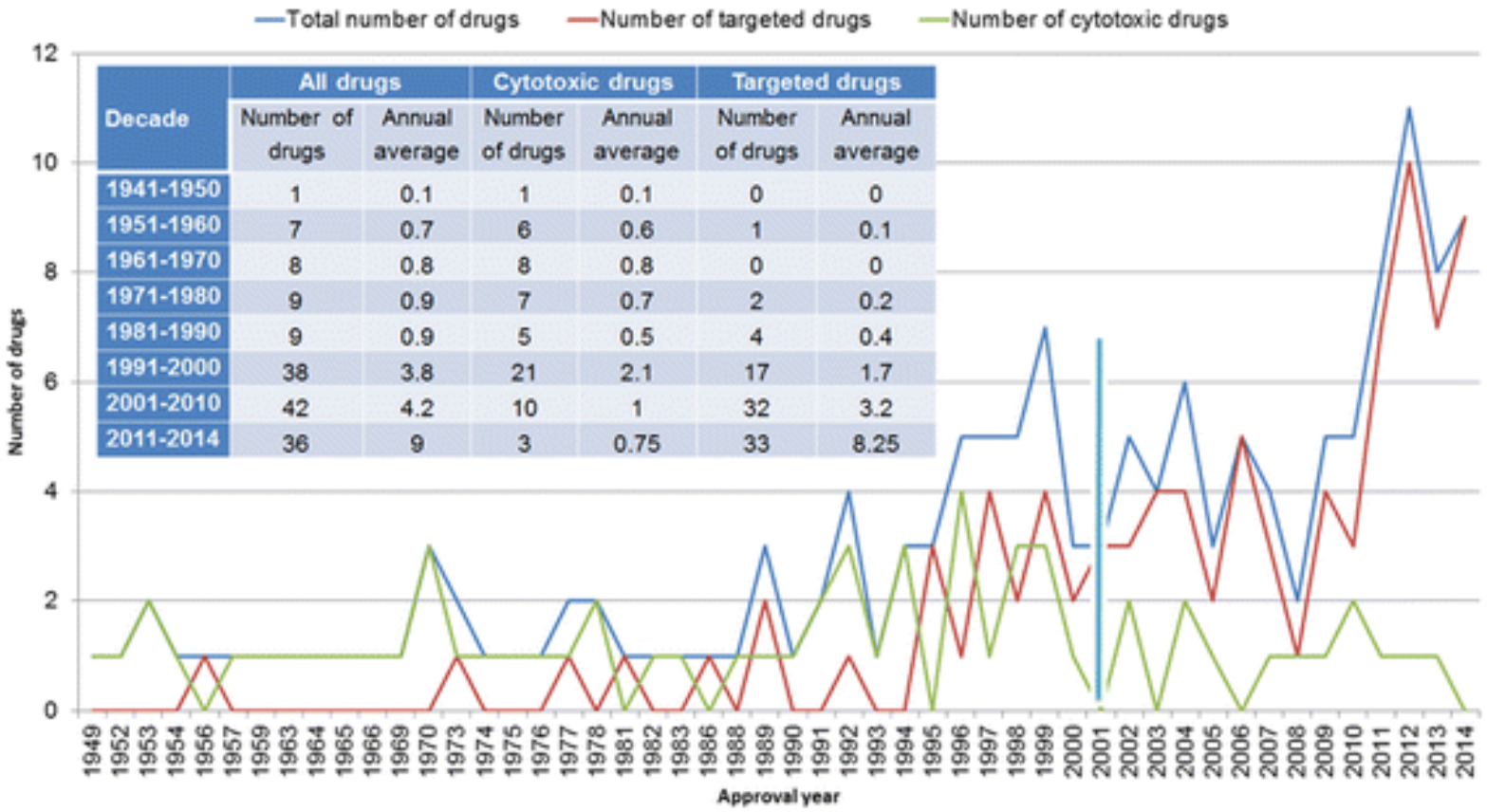


Medicinal Chemistry: Therapeutic Areas

- Generally, medicinal chemists are not trained based in a specific therapeutic area.
- Most medicinal chemists will work in multiple therapeutic areas throughout their career.



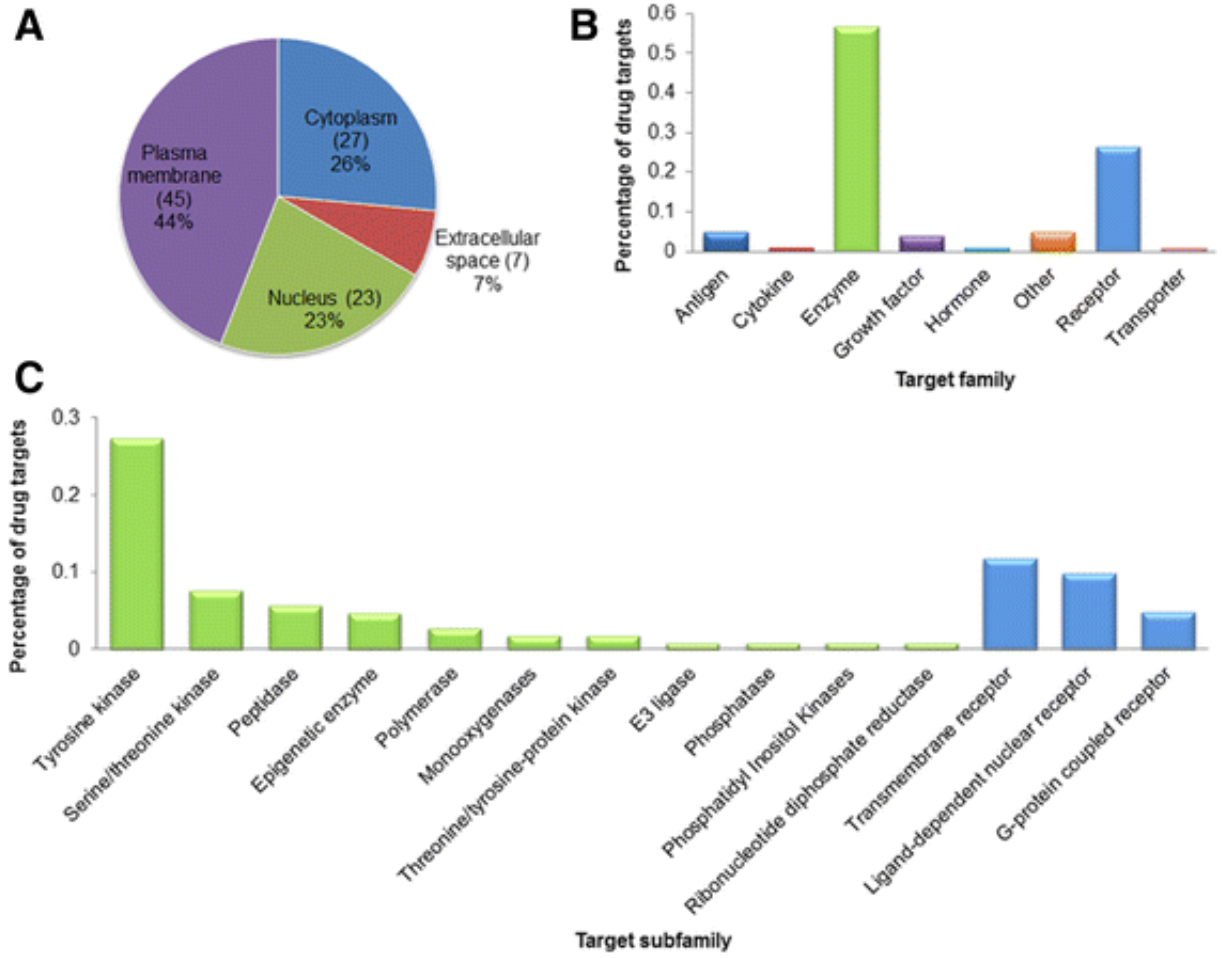
Medicinal Chemistry of Cancer Drugs



Decade	All drugs		Cytotoxic drugs		Targeted drugs	
	Number of drugs	Annual average	Number of drugs	Annual average	Number of drugs	Annual average
1941-1950	1	0.1	1	0.1	0	0
1951-1960	7	0.7	6	0.6	1	0.1
1961-1970	8	0.8	8	0.8	0	0
1971-1980	9	0.9	7	0.7	2	0.2
1981-1990	9	0.9	5	0.5	4	0.4
1991-2000	38	3.8	21	2.1	17	1.7
2001-2010	42	4.2	10	1	32	3.2
2011-2014	36	9	3	0.75	33	8.25

Sun, J., et al. *BMC Syst Biol* **2017**, *11(Suppl 5)*, 87

Medicinal Chemistry of Cancer Drugs

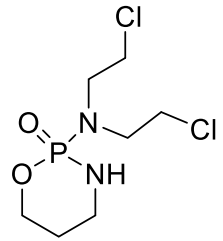


Sun, J., et al. *BMC Syst Biol* **2017**, *11(Suppl 5)*, 87

Medicinal Chemistry of Cancer Drugs

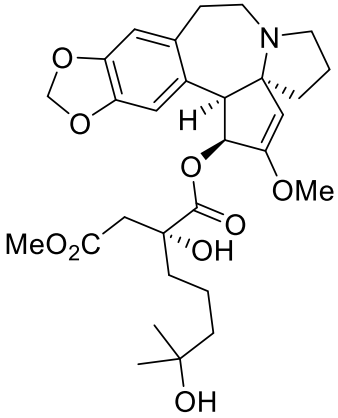
Cytotoxic Drugs

Reactive and non-reactive Small Molecules Targeting DNA/RNA and protein synthesis or cell division



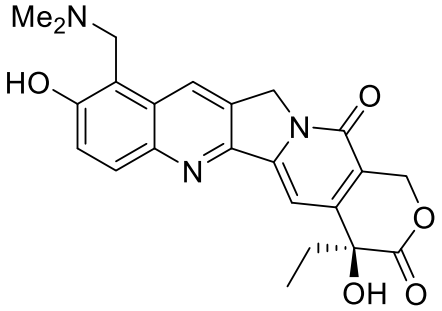
cyclophosphamide
(1959)

DNA synthesis inhibitor



omacetaxine
(2012)

Protein synthesis inhibitor

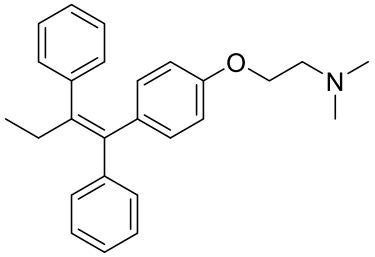


topotecan
(1996)

Topoisomerase inhibitor preventing DNA replication

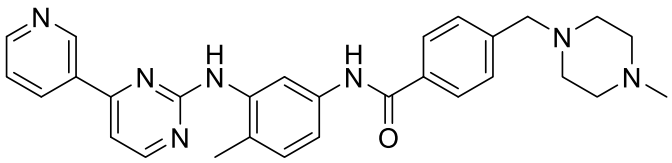
Medicinal Chemistry of Cancer Drugs

Targeted Drugs
Non-reactive
Small Molecules
and Proteins



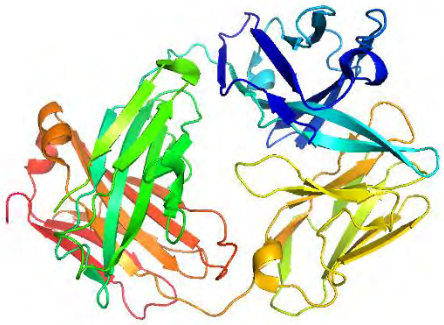
tamoxifen
(1977)

Selective estrogen receptor modulator



imatinib
(2001)

Bcr-Abl kinase inhibitor

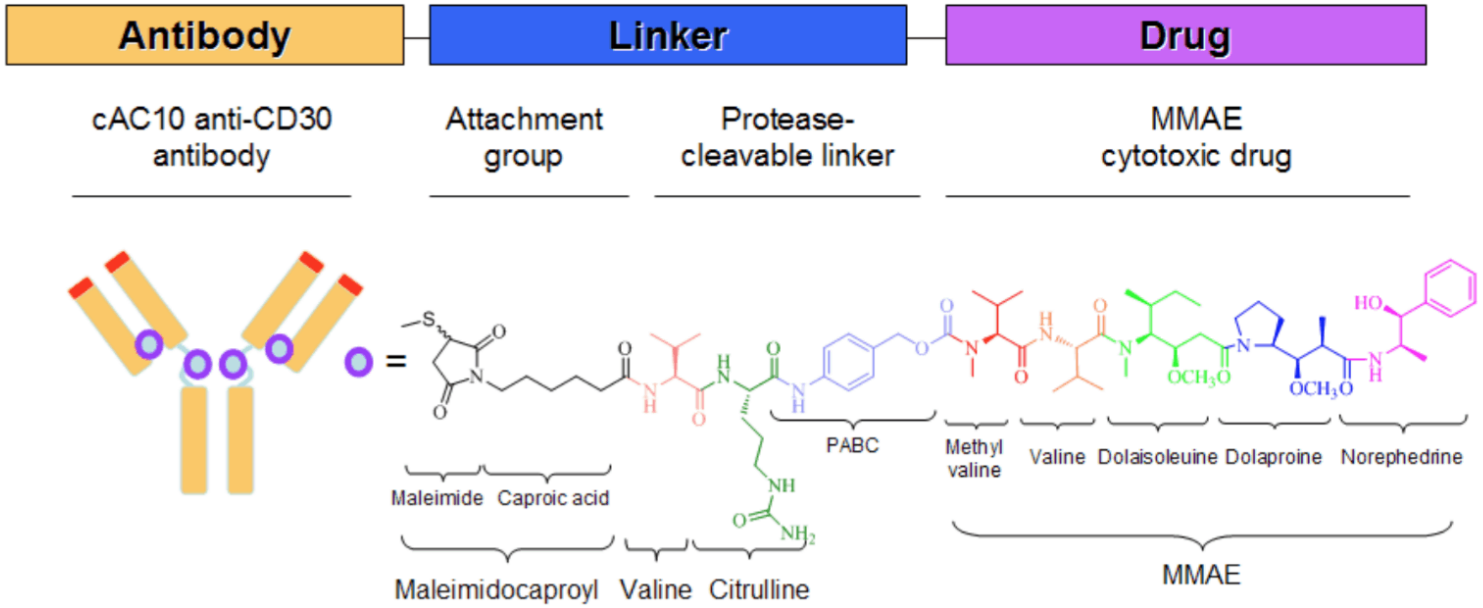


rituximab
(1997)

Chimeric mAb against CD20 on B cells triggers cell death

Medicinal Chemistry of Cancer Drugs

Targeted Drugs
Non-reactive
Small Molecules
and Proteins

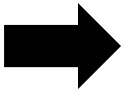


brentuximab vedotin
(2011)

Targeted delivery of a cytotoxin

Career Path in Medicinal Chemistry

Training:
BS/PhD in Organic or Medicinal Chemistry



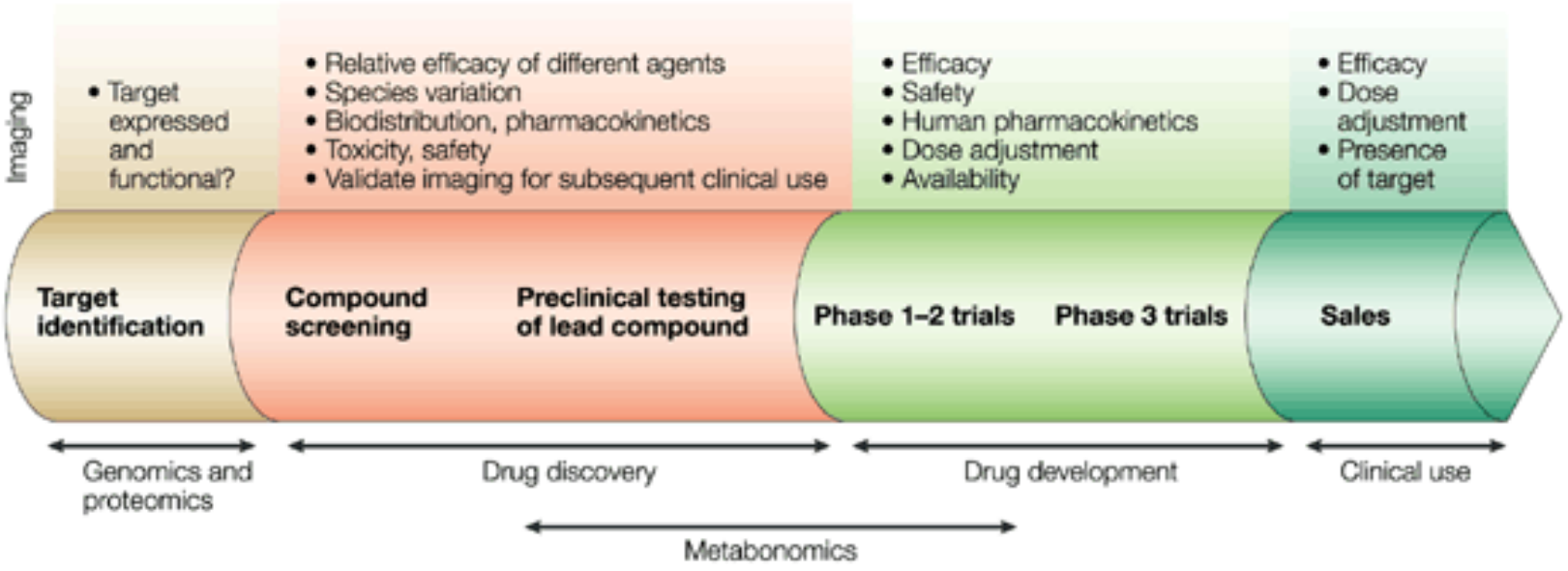
- Biopharmaceutical industry
  - Medicinal chemistry
  - Pharmaceutics
  - Regulatory affairs
- Academics
- Government
- Others (e.g. Consulting, Intellectual property law, etc.)

Chemical Sciences in the Drug Discovery and Development Process

Biochemistry
Chemical Biology

Medicinal Chemistry
Pharmaceutical Sciences

Process Chemistry
Chemical Engineering



Nature Reviews | Drug Discovery

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