

Cancer: how to deal with it?

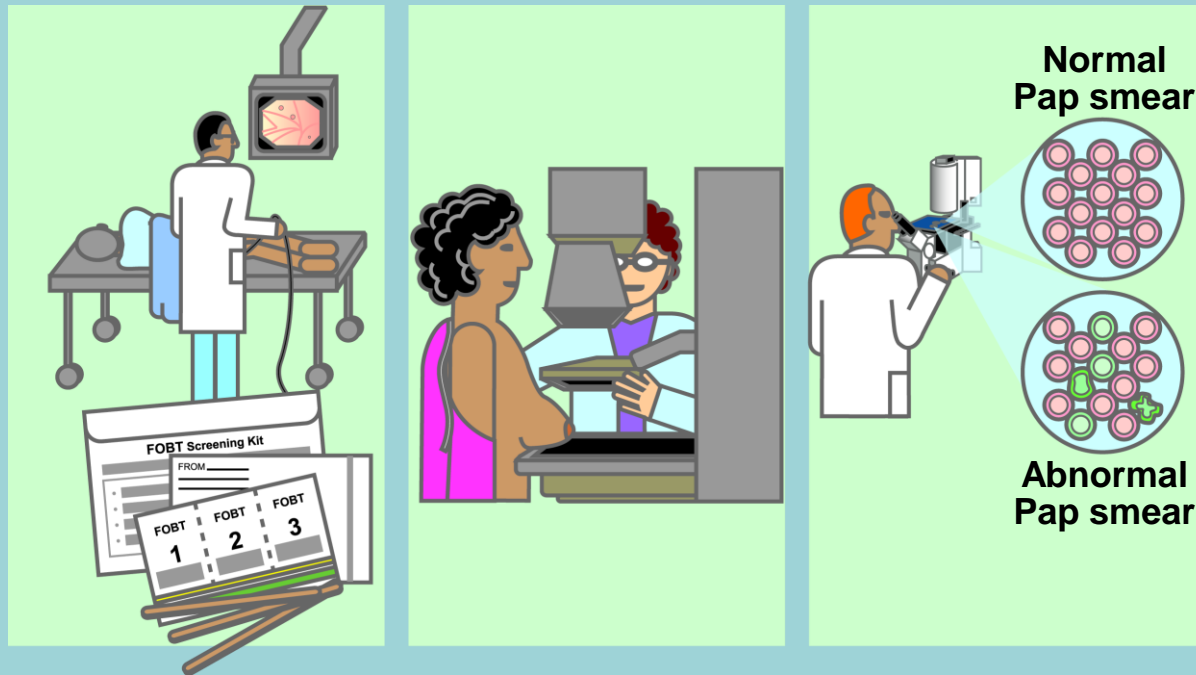
Diagnostics (*in vitro*, *ex vivo* & *in vivo*) to know what is going on

Therapy (systemic & targeted) to inhibit it

Surgery (conventional & fluorescent-assisted) to eradicate it

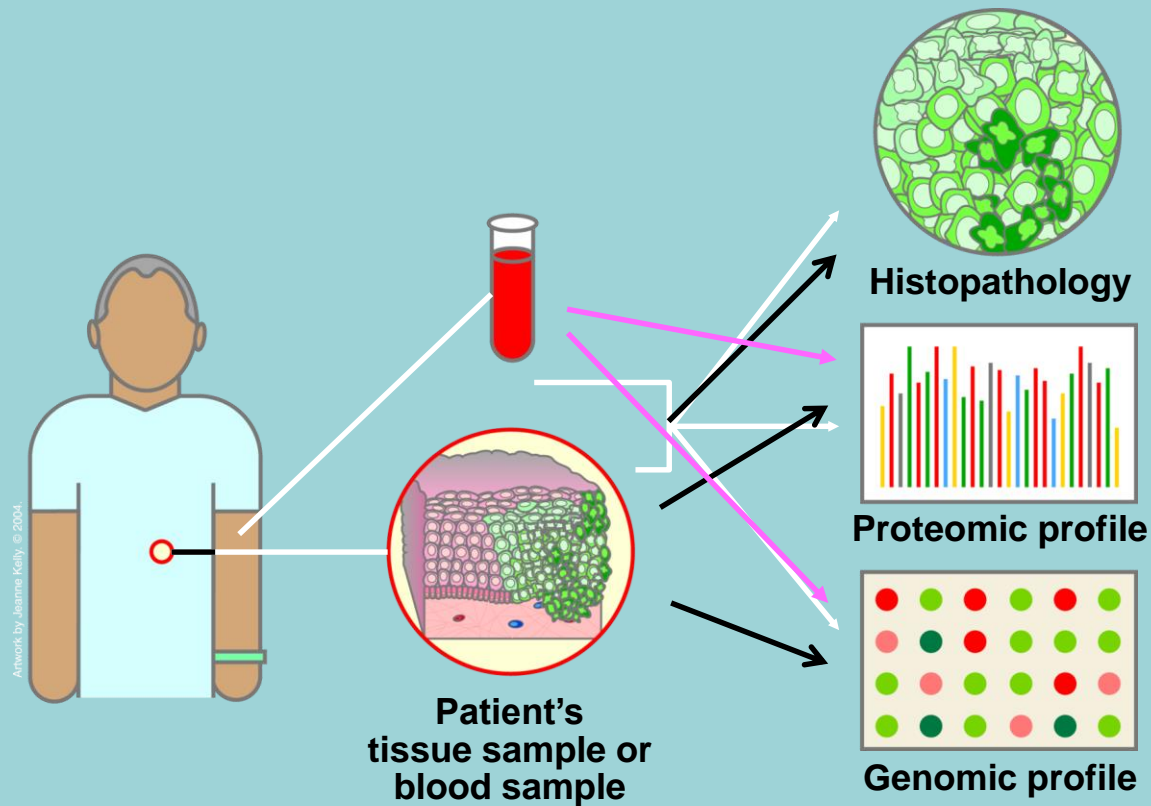
Cancer Screening for Early Detection

Diagnostics is instrumental for rational downstream actions



- **Reliable markers**
- **Costs**
- **Feasibility**
- **Invasiveness**

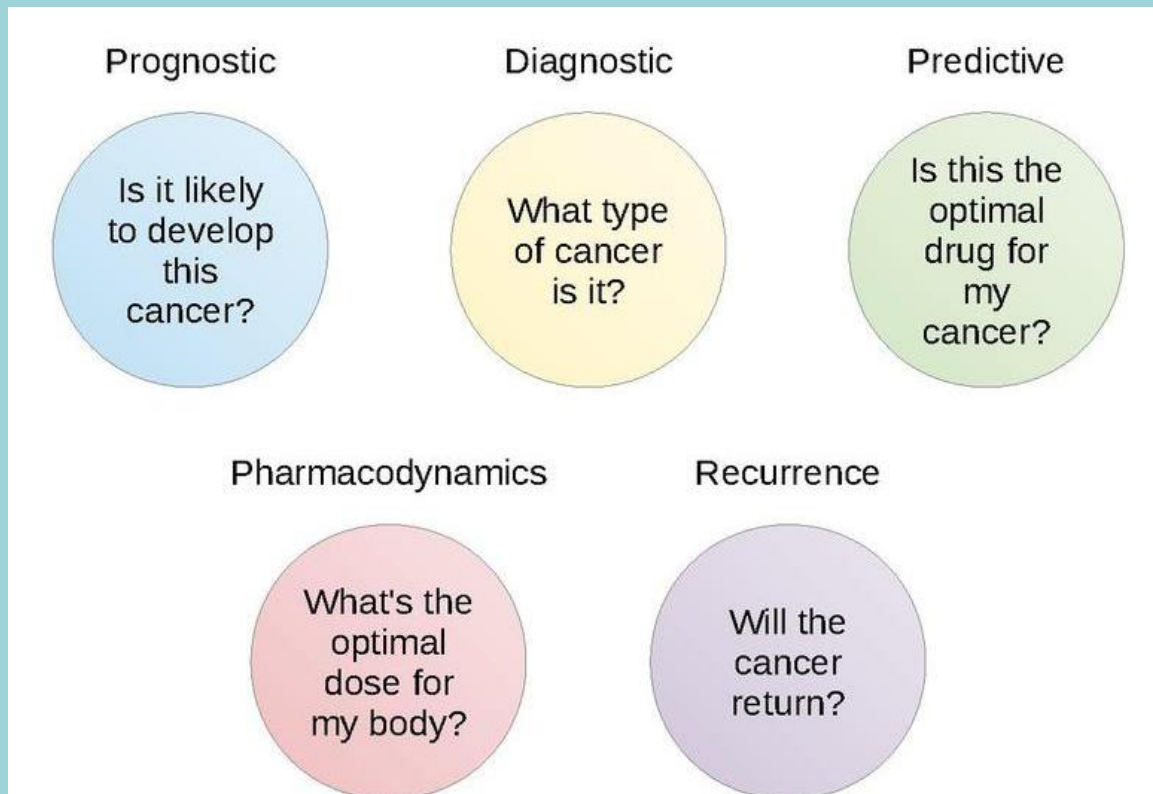
Biopsy (conventional & liquid)

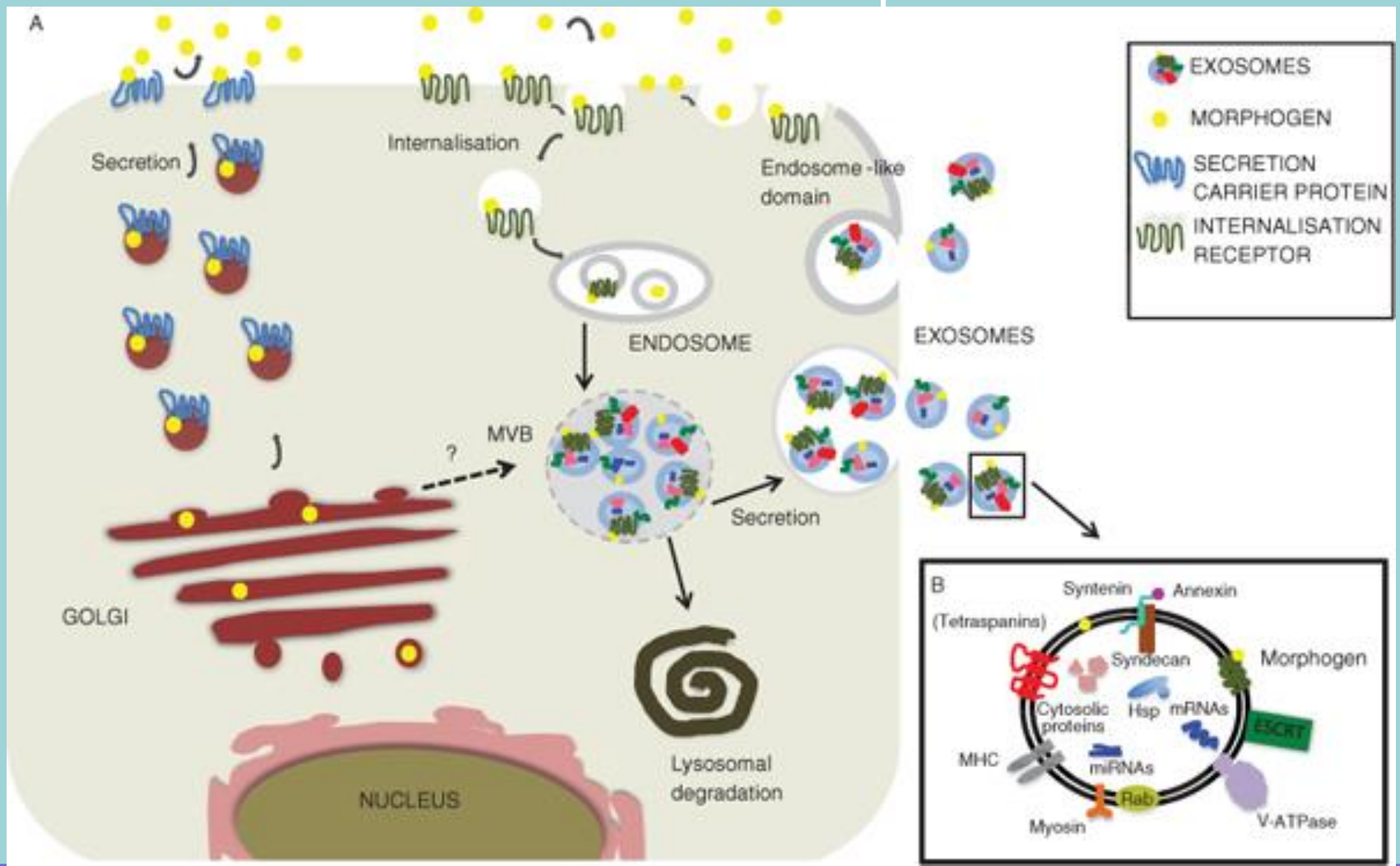


Liquid Biopsy

Looking for suitable circulating biomarkers:

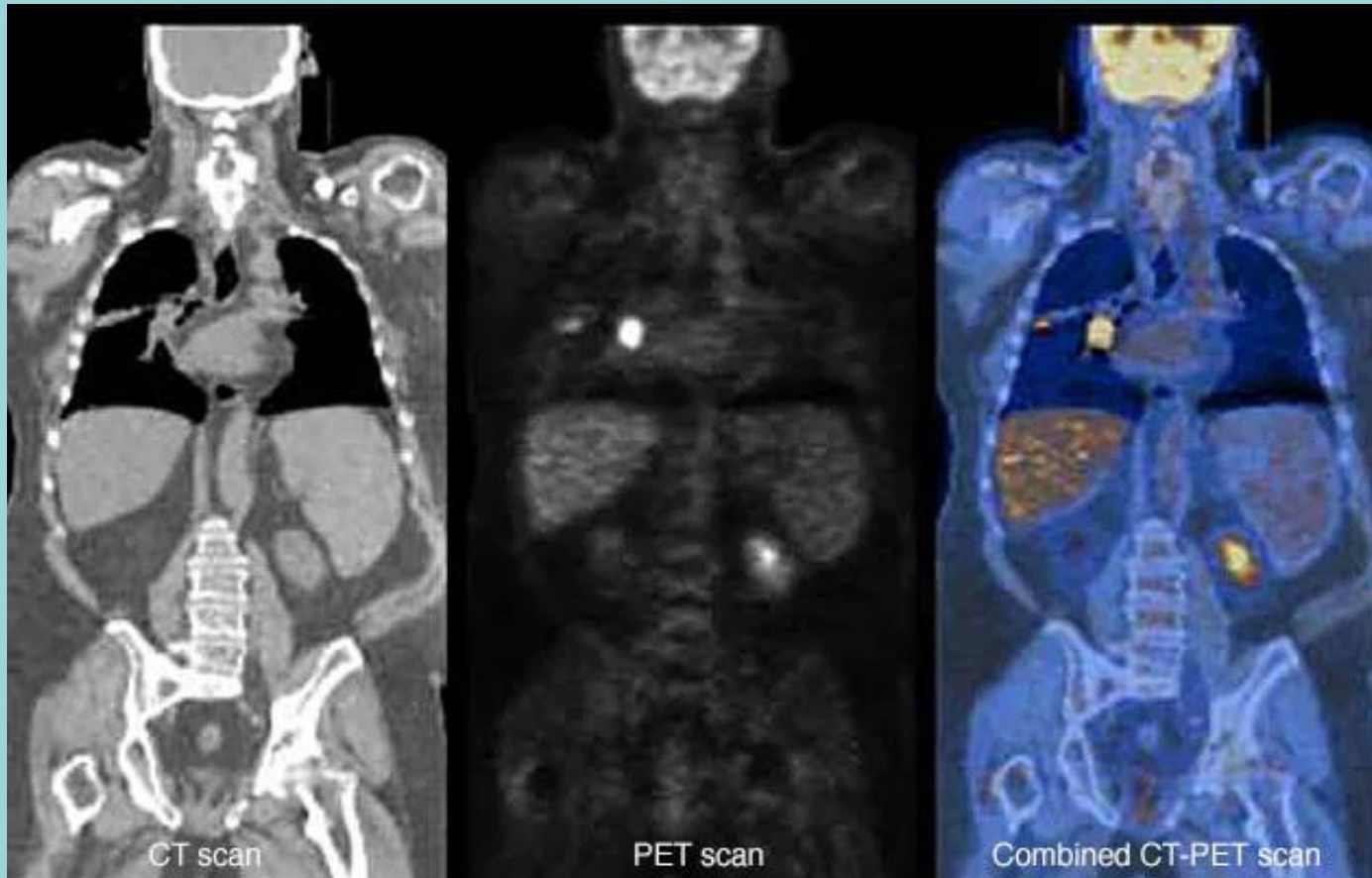
- Proteins
- Nucleic acids
- Lipids
- Metabolites





In vivo imaging

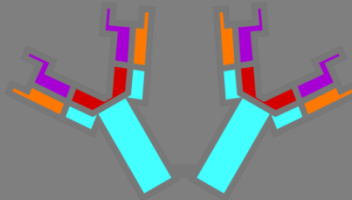
Conventional & Ab-dependent: signal-to-noise ratio



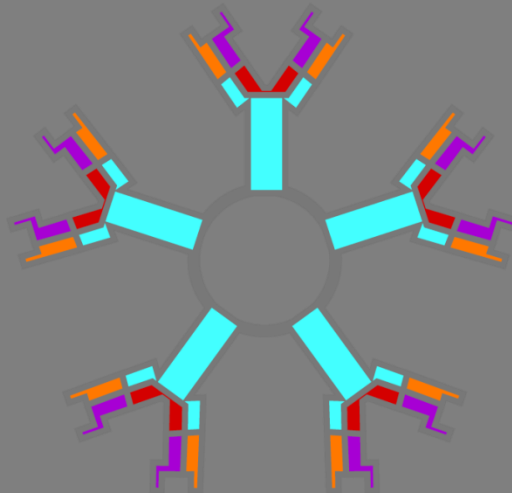
Immunoglobulins



IgG, IgD, IgE, and IgA



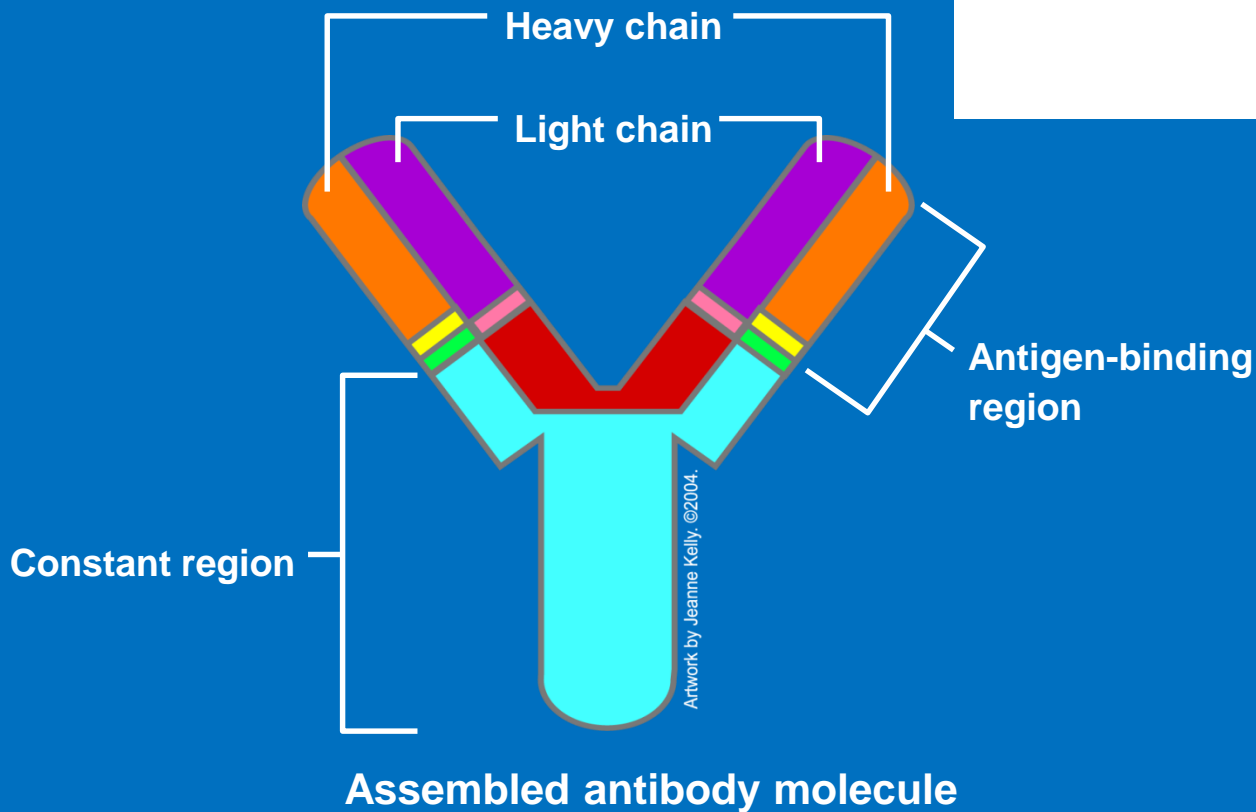
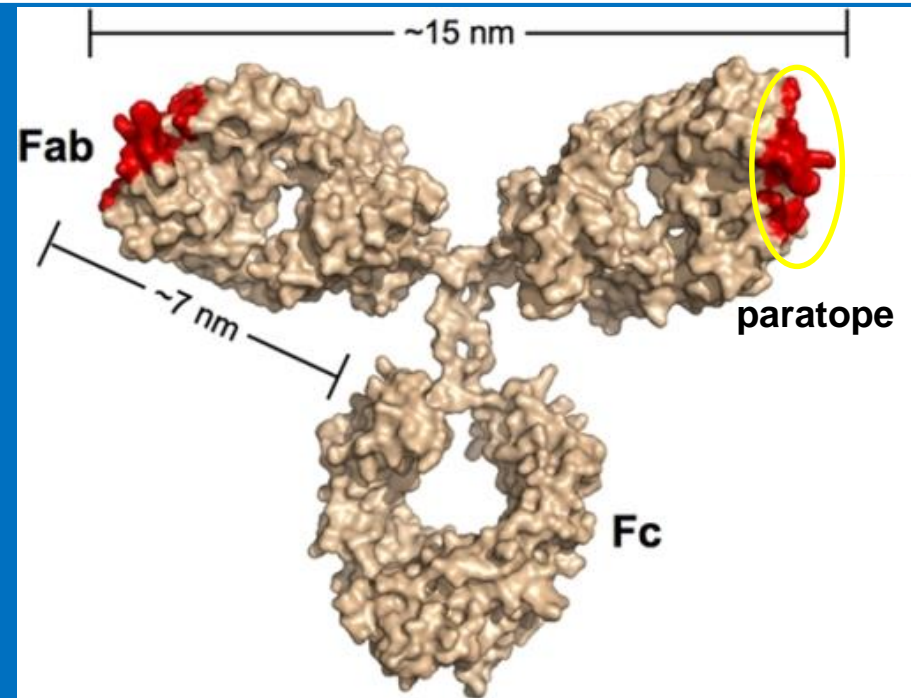
IgA



IgM

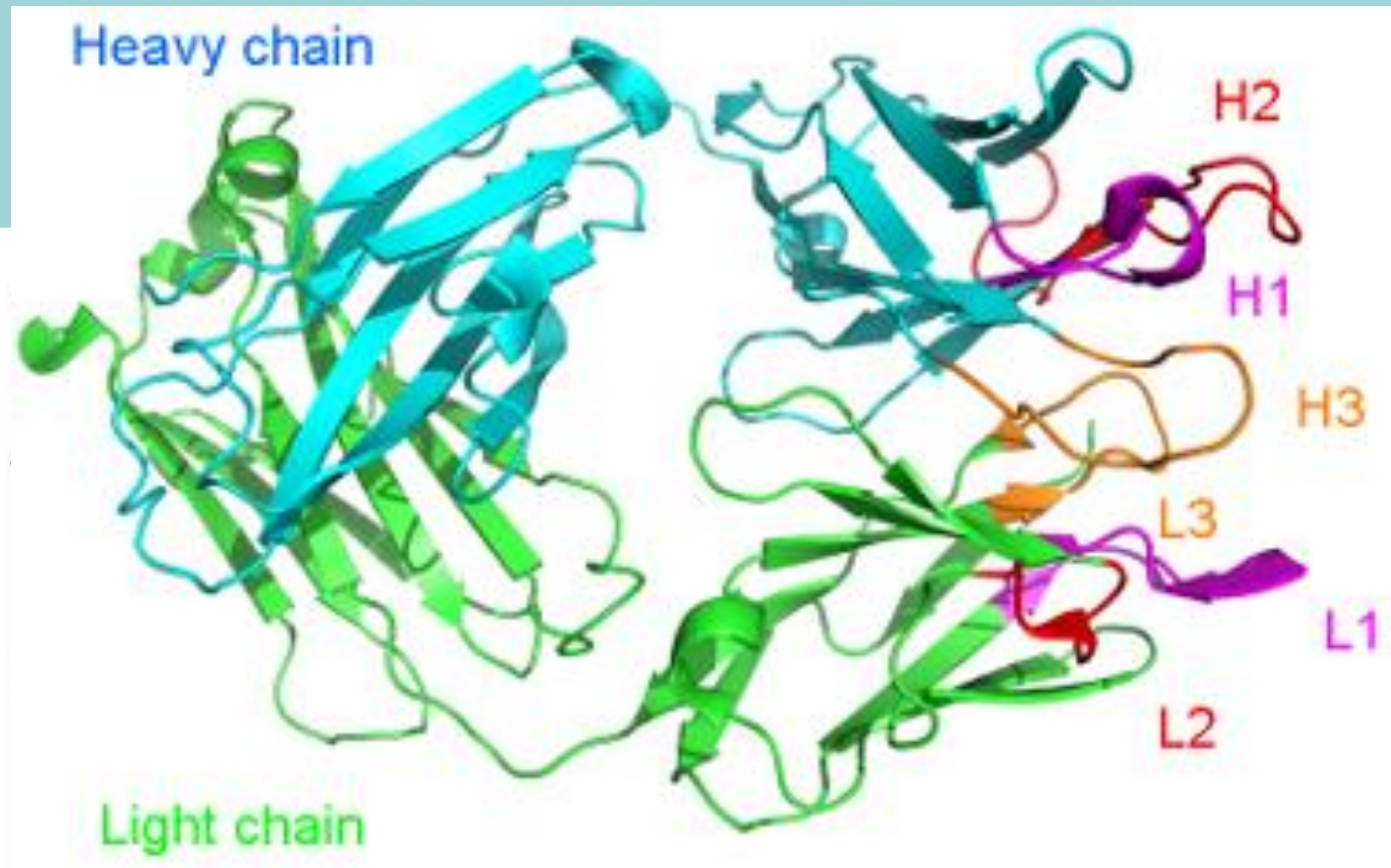
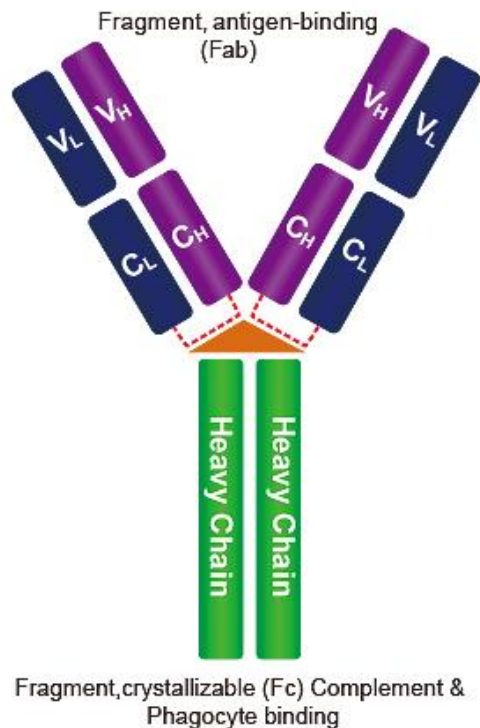
Artwork by Jeanne Kelly. ©2004.

IgG Antibodies



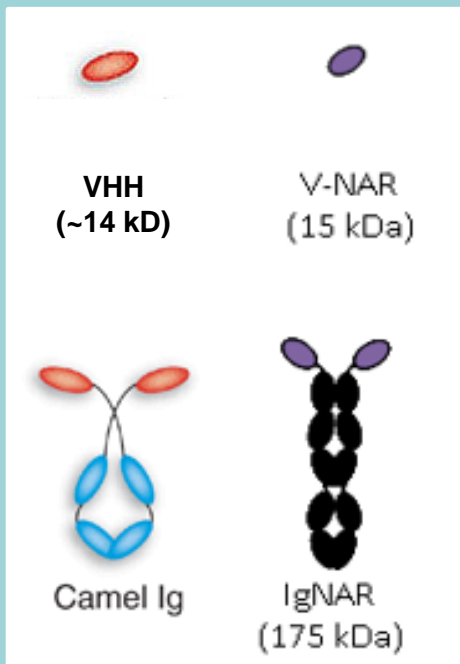
IgG antibodies

6 loops, corresponding to the 3 CDRs of each variable region, form the (flat) paratope of a conventional IgG antibody

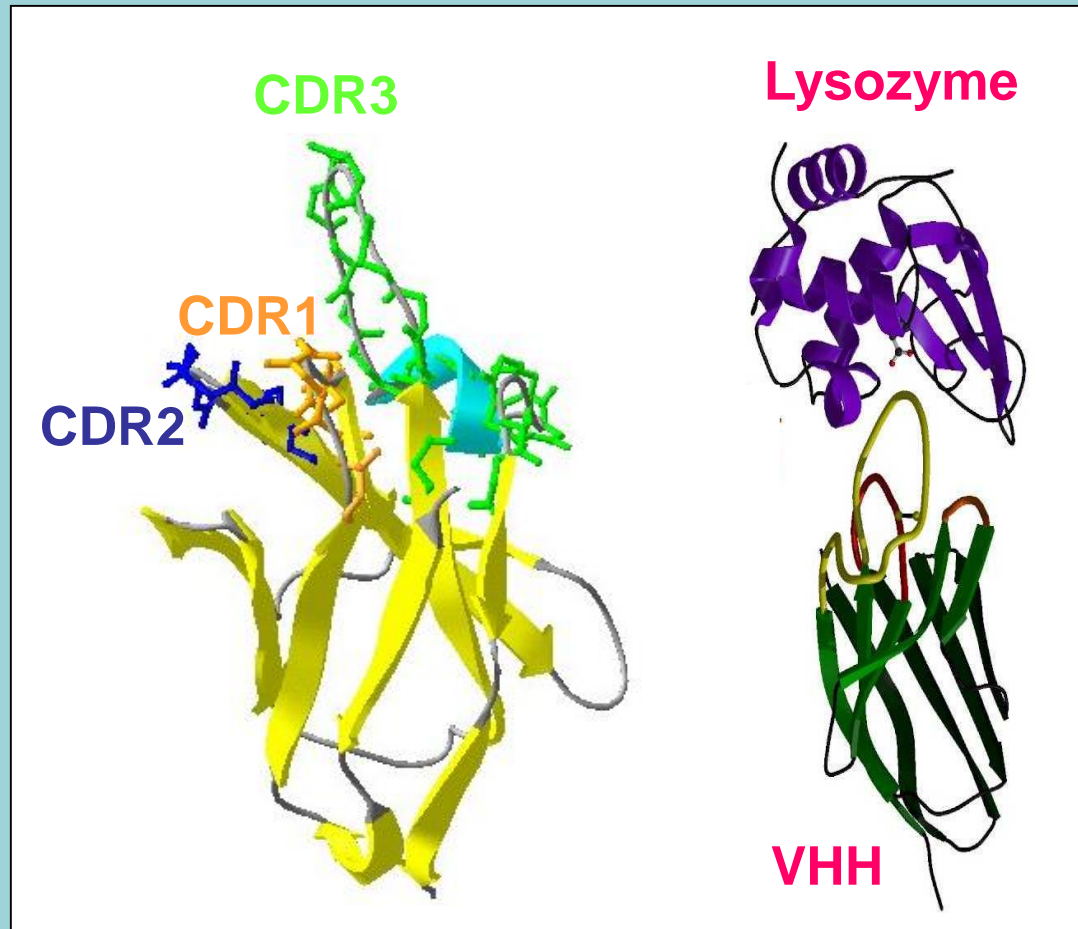


Antibody fragments

Camelidae & shark antibodies (but also alternative scaffolds) are suitable for molecular recognition and binding



Epitope characteristics & multiple binding



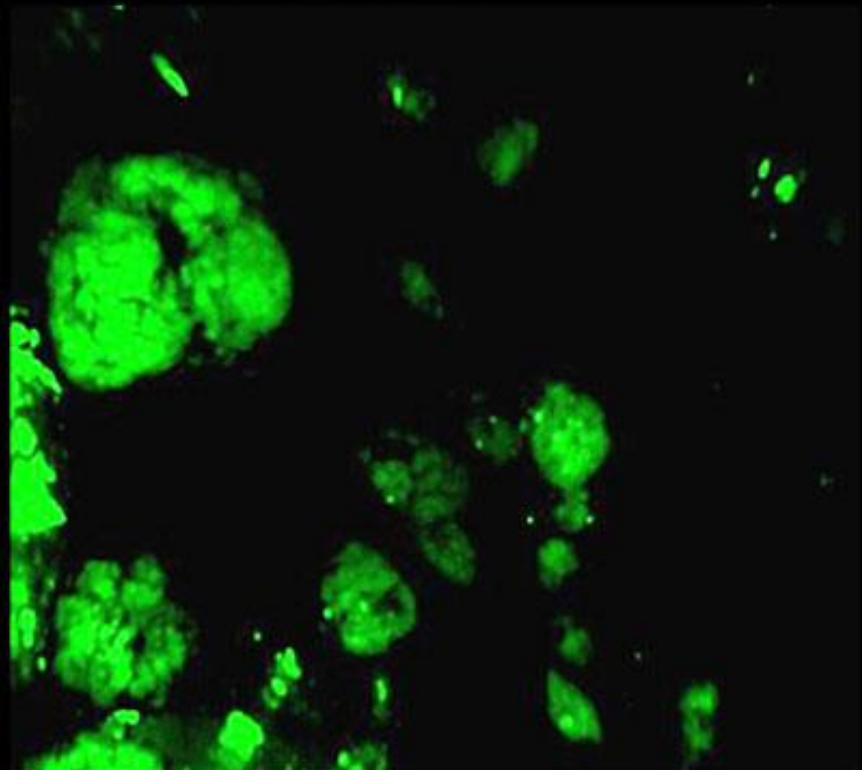
Fluorescence-assisted surgery

Why? To identify the tumor margins

Surgeon's former view


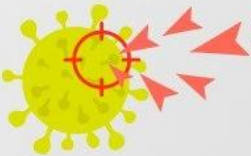
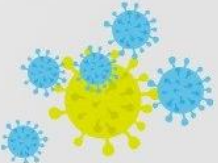


Surgeon's new view



Targeted therapy

Why? To reduce toxicity due to unspecific activity

	How does it work?	Side Effects	Limitations
 Chemotherapy	Targets rapidly dividing cells (mostly cancer cells)	Hair loss, intestinal damage, nausea	Cancer cells develop resistance to chemotherapy, not specific
 Targeted Therapy	Targets Proteins required for cancer growth	Liver problems, diarrhea, skin rash	Cancer cells develop resistance
 Immunotherapy	Uses our immune system against cancer	Autoimmune effects	Tailored and expensive

How to target tumors?

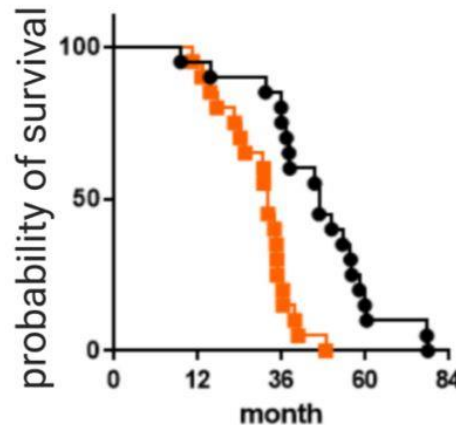
Exploiting the Biomarkers (molecules present only in the tumor cells) for selective delivery

Biomarker

diagnostic



prognostic



predictive



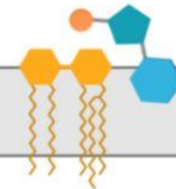
clinical and laboratory features



protein



DNA

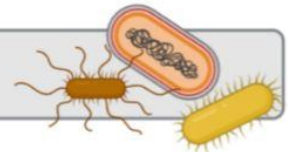


metabolome



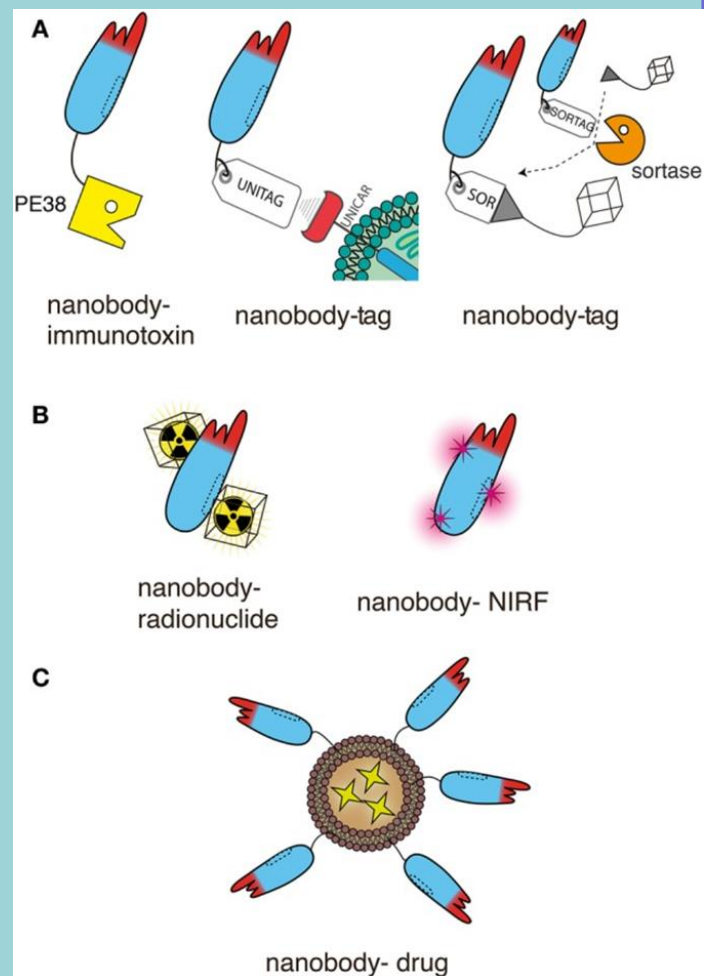
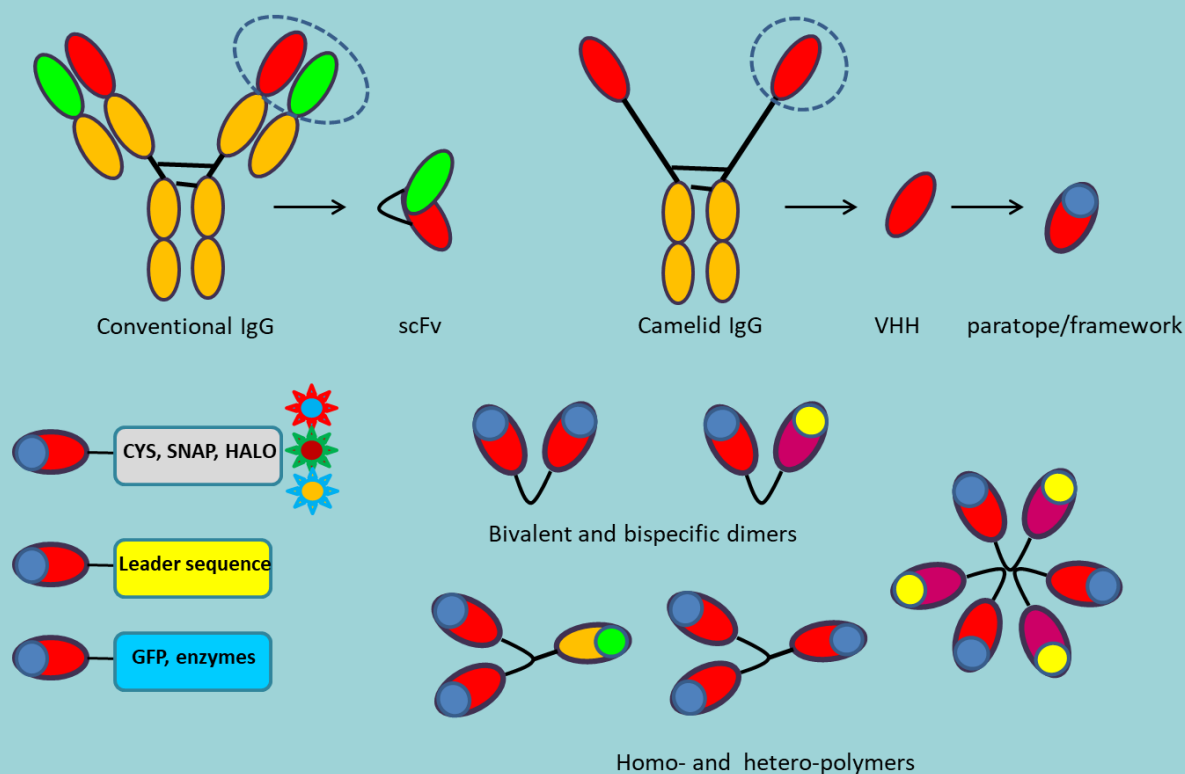
immune /stroma

microbiome



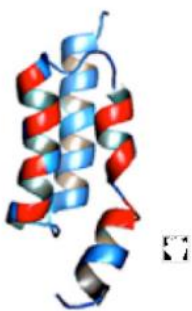
Our contribution

Binders and reagents – optimization and functionalization

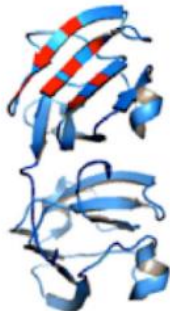


Our contribution

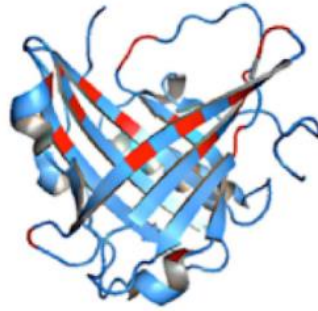
Alternative scaffolds



Affibodies
PDB: 2KZI



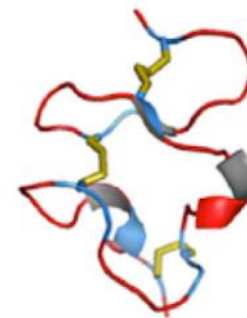
Affilins
(γ -B-crystallin)
PDB: 2JDF



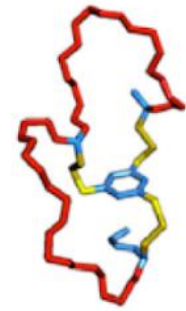
Anticalins
PDB: 4GH7



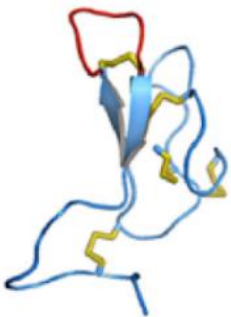
Atrimers
PDB: 3L9J



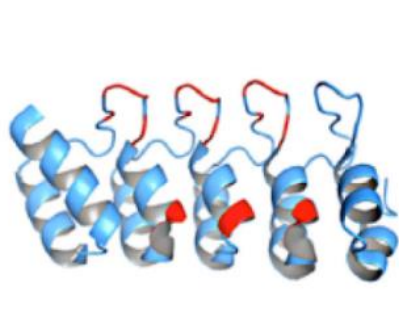
Avimers
PDB: 1AJJ



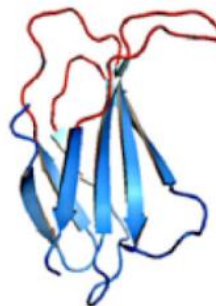
Bicyclic peptides
PDB: 3QN7



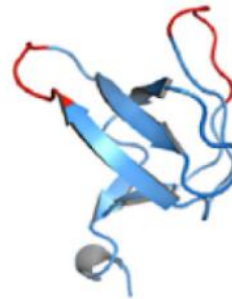
Cys-knots
PDB: 1HYK



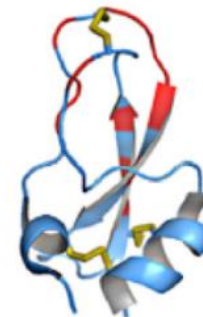
DARPins
PDB: 1SVX



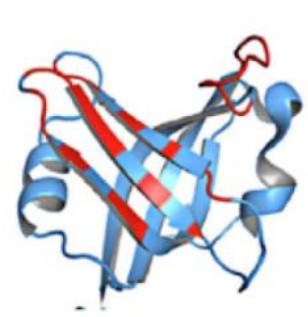
FN3
(Adnectin)
PDB: 1FNF



Fynomers
PDB: 4AFS



Kunitz domains
PDB: 4BQD



OBodies
PDB: 4GLV