Tailoring Chemistry to promote new tools for biology, diagnostic and therapy

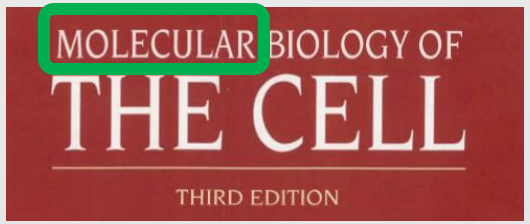
Molecular Synthetic Chemistry

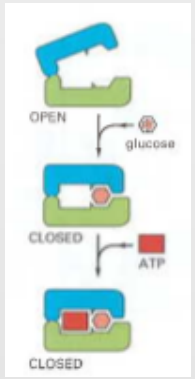
designing molecules to leverage atomic investigations

Chosen exemples.

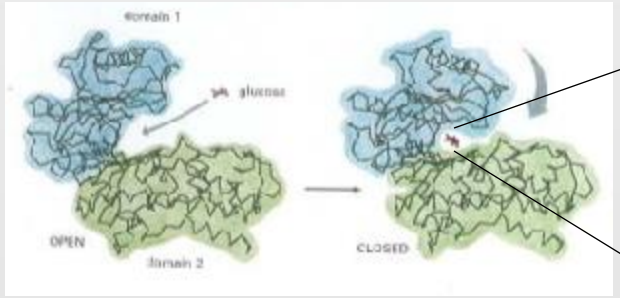
Emmanuel GRAS, Ph.D.
CNRS Researcher & Directeur du Laboratoire Commun Trans-NMDA
Laboratoire Hétérochimie Fondamentale et Appliquée
Université de Toulouse – CNRS UMR 5069

Beyond words - The reality of molecular design

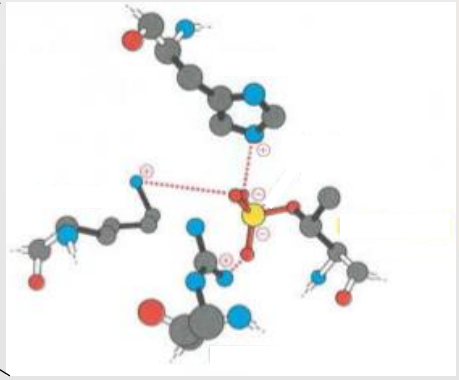




« For simplicity, the actual structure of the protein has been replaced by a schematic diagram »



Conformational change in hexokinase caused by glucose binding



One word – Many views…

Our work:

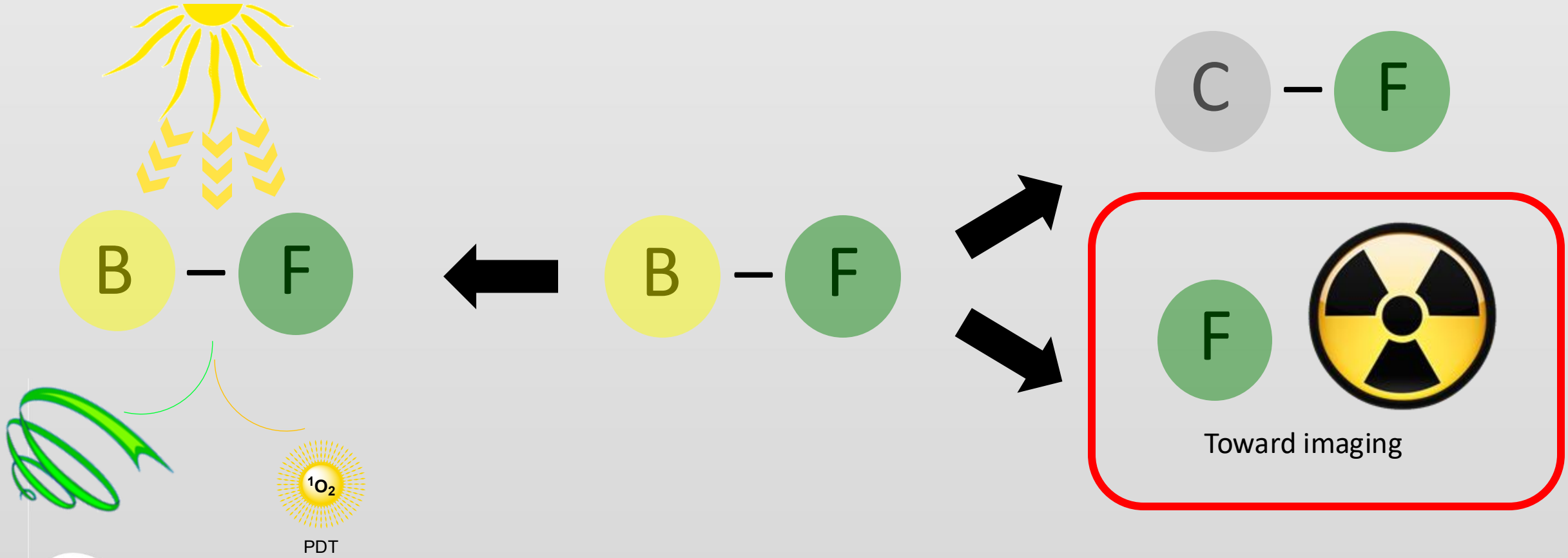
Designing / Synthesizing Small Molecules interacting with biomacromolecules.
Decorating the best ones with probes (Fluorescent, Radiofluorinated) and Preparing radiofluorination precursors

Decorating relevant biomacromolecules (proteins, antibodies…) to develop innovative targeting tools

^{18}F Radiochemistry

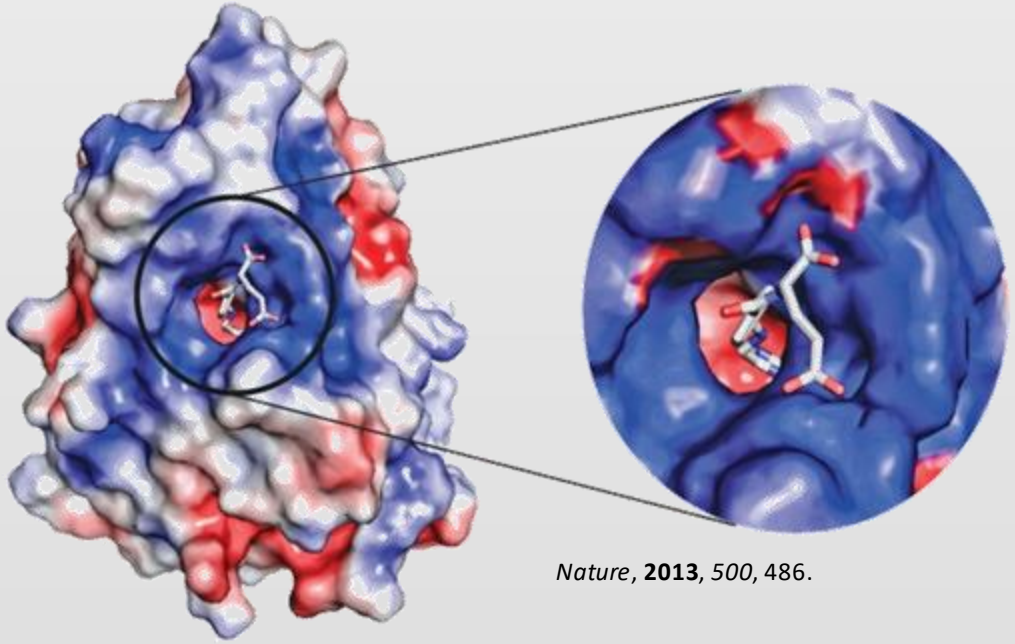
Playing with Boron

Boron and Fluoride: A perfect fit?
From fluorination to radiofluorination, or the other way round… …

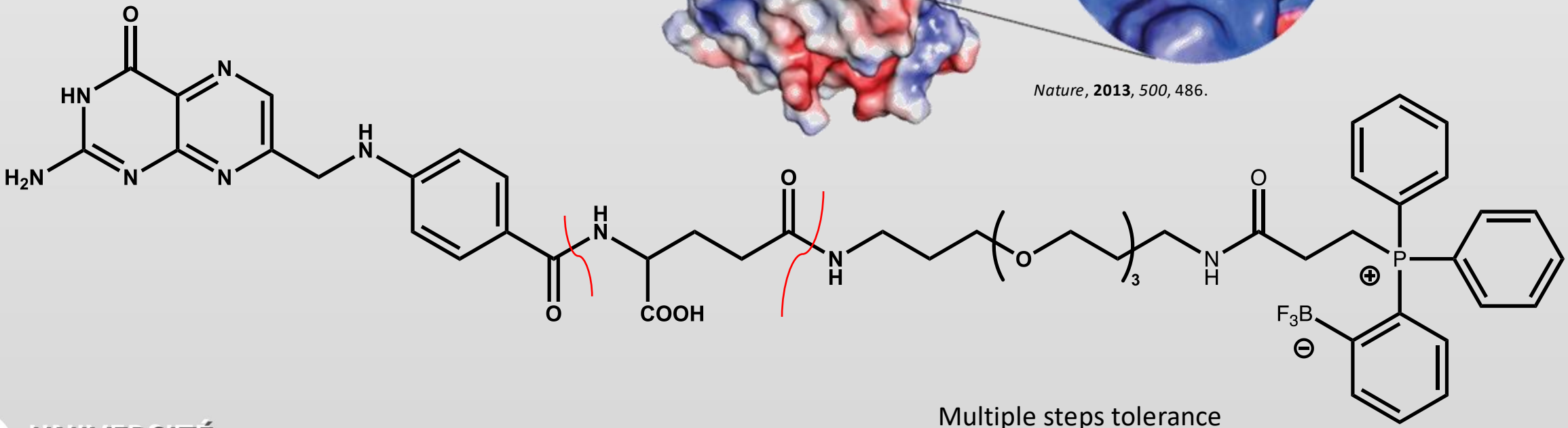


Toward Radiofluorination in water: more practical examples

Selective g-linkage to folic acid.

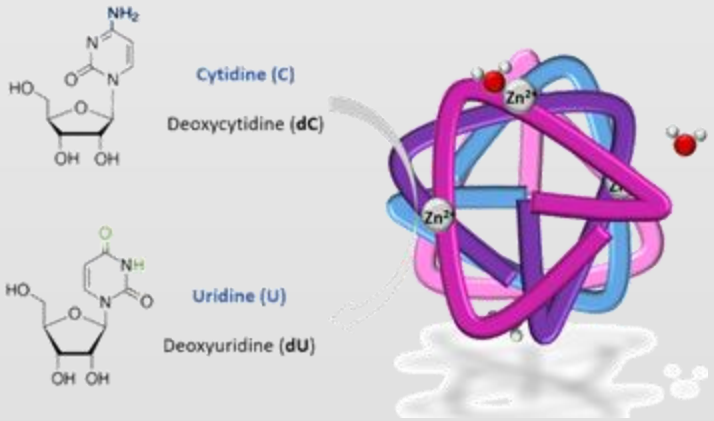


Nature, **2013**, *500*, 486.



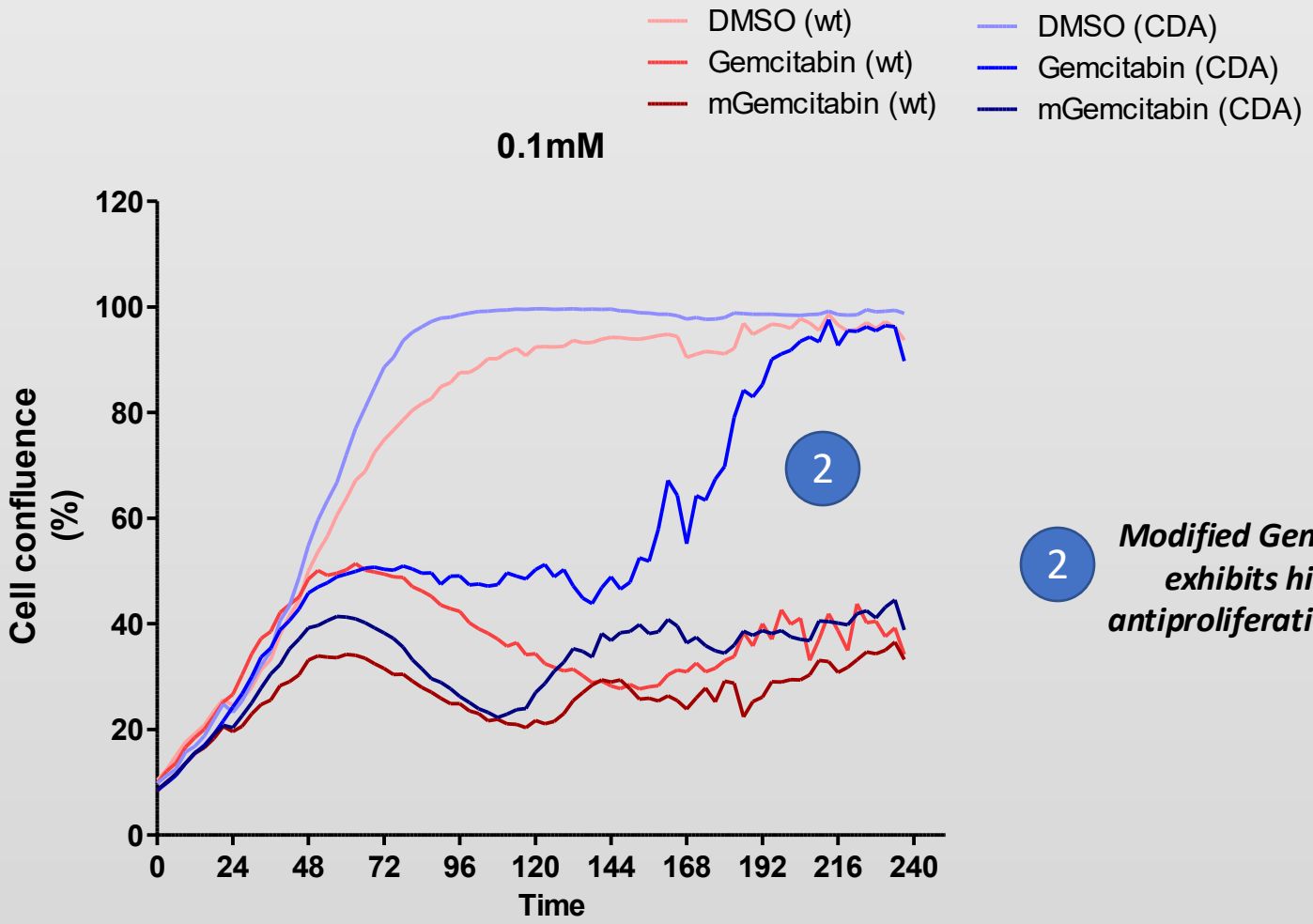
Multiple steps tolerance
Full g-selectivity

Toward pancreatic cancer imaging and may be more…



Cytidine désaminase (CDA)

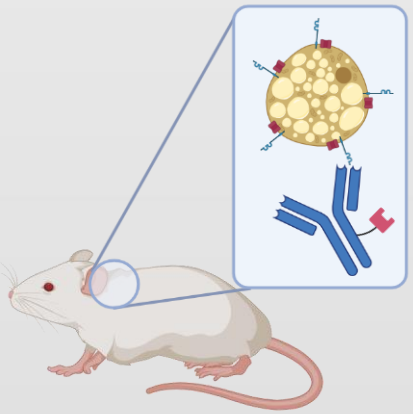
Main resistance factor to chemotherapy with Gemcitabin

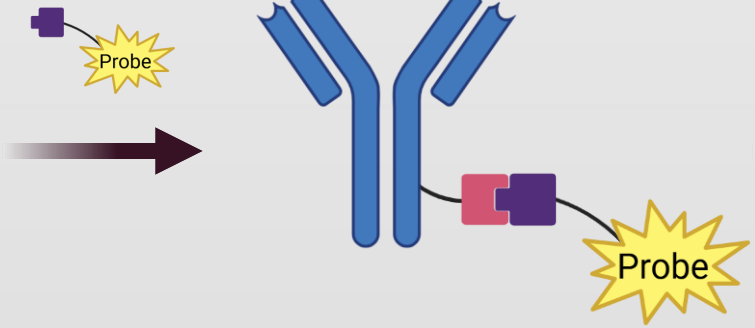


2 ***Modified Gemcitabin exhibits higher antiproliferative effect***

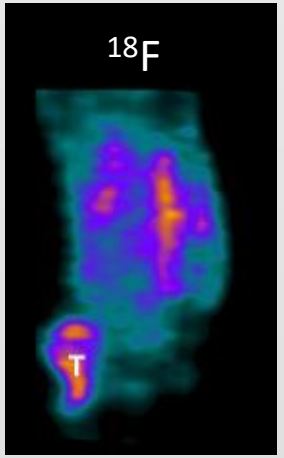
In coll. with Dr P. Cordelier @ CRCT

Using antibodies from diagnostic to targeted drug delivery.



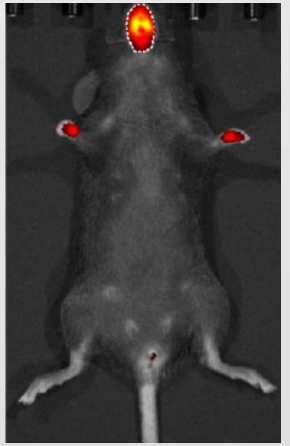


Radio labeling



1

Near-infrared dyes



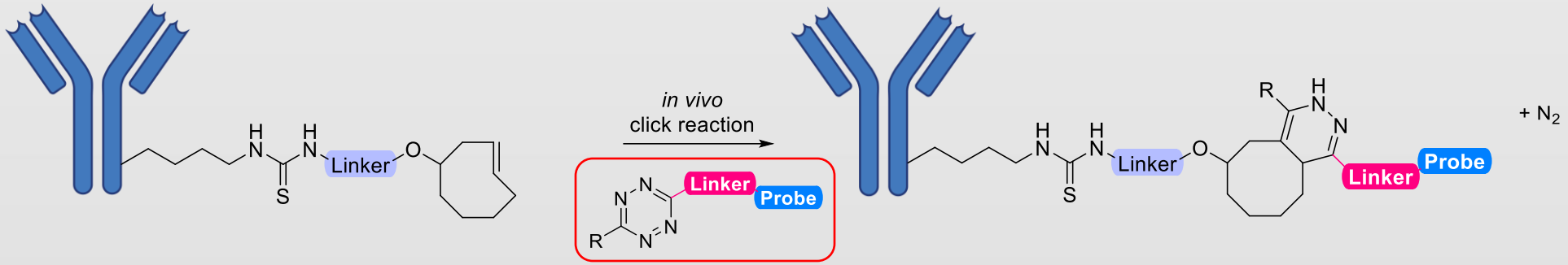
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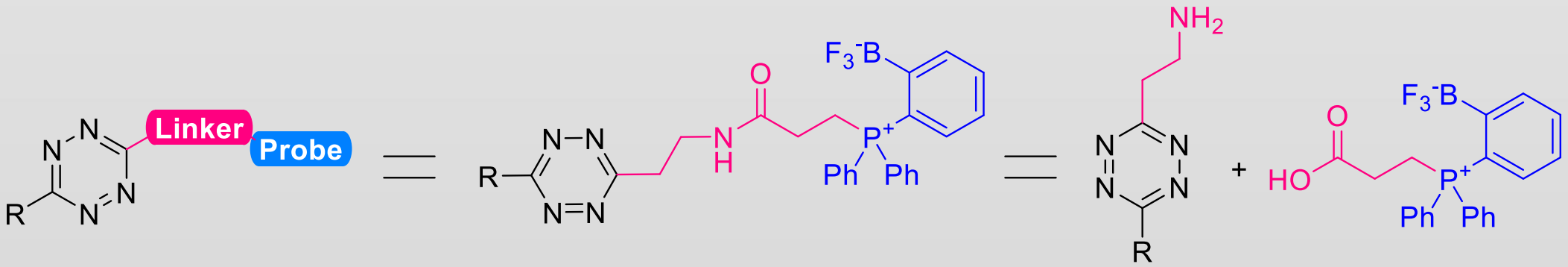
Select an antibody with extracellular epitope
+
Pretargeting

Bioconjugate antibody with imaging probes

Aplication in multiple *in-vivo* imaging methods

Using antibodies from diagnostic to targeted drug delivery.



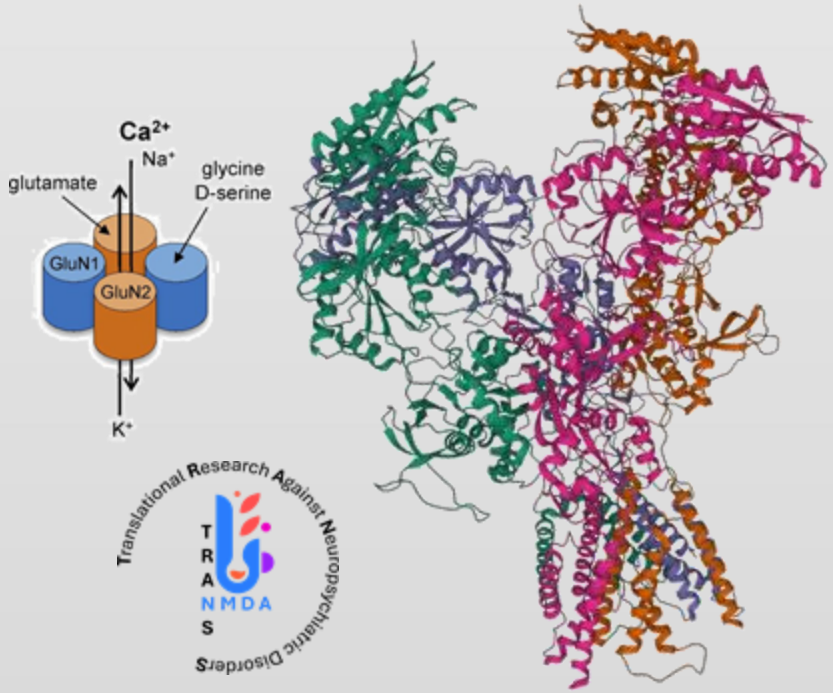


Organic Synthesis toward fluorinated molecules for PET imaging (and further applications).

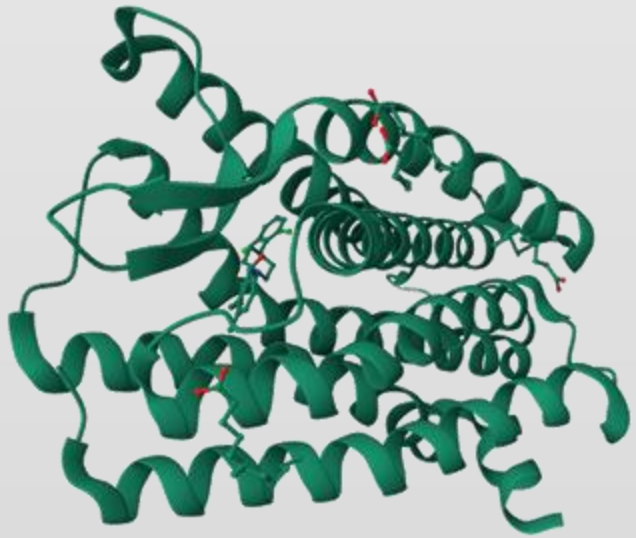
Medicinal chemistry followed by organic synthesis oriented by ^{18}F properties

Our current targets

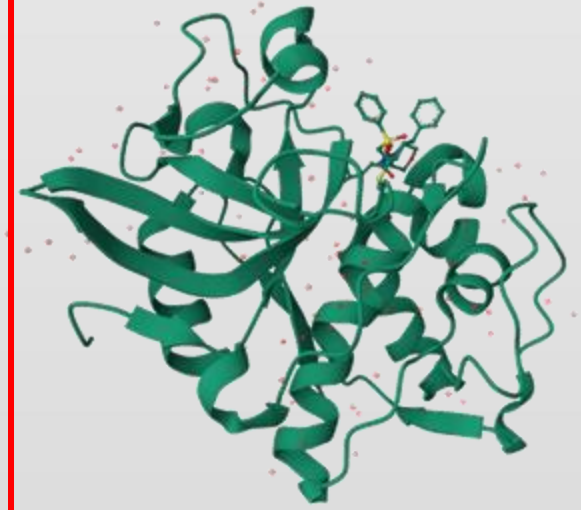
NMDA (N-Methyl-D-Aspartic) receptors



NOP (Nociceptin Opioid Peptide) Receptor

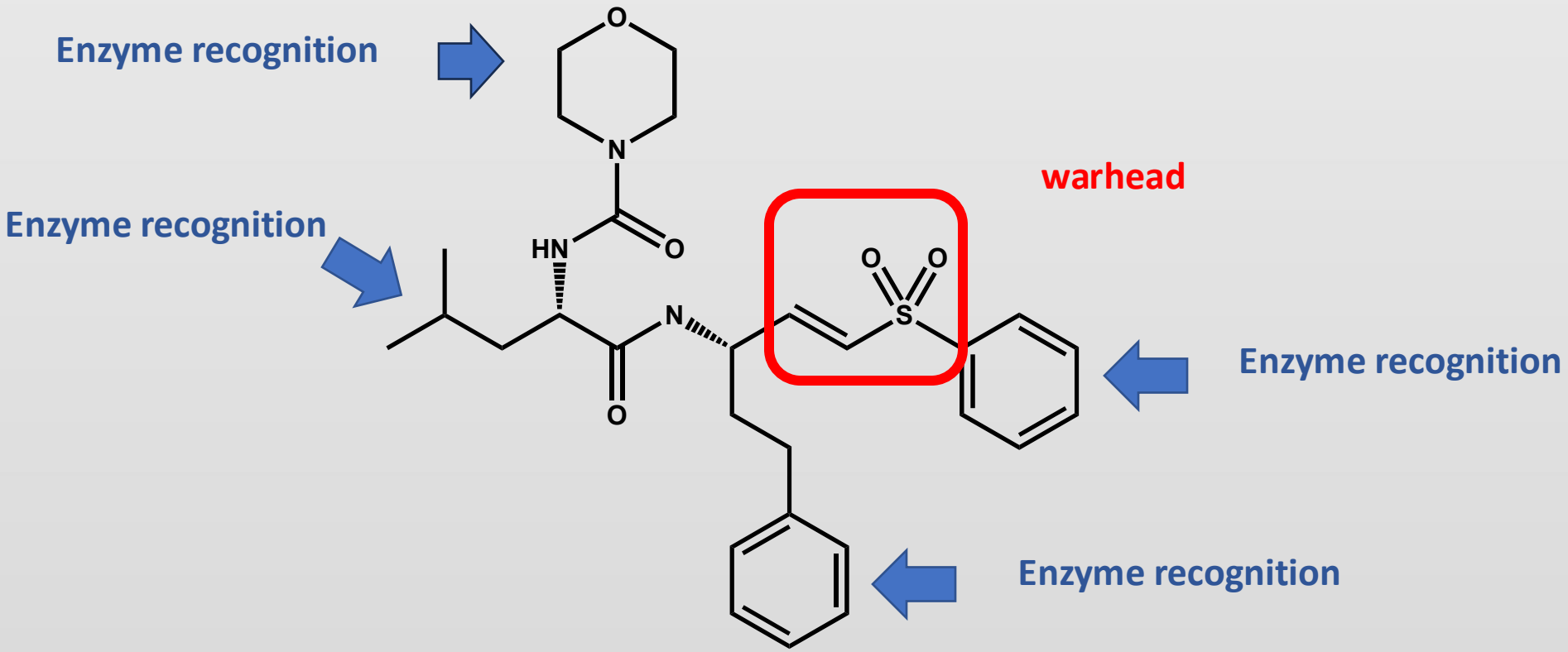


Cysteine proteases



Generating new routes to promote innovative applications

Organic Synthesis – New routes for chemical libraries and further applications.



LHVS: Cysteine protease inhibitor (Cathepsin S) Ki= 5 nM



