Tutorial 1 to the lecture „Modern Methods in Drug Discovery“ WS22/23

1. Compile a list of as many as possible ACE inhibitors. Start looking up captopril in wikipedia.

a) In the captopril entry of wikipedia: retrieve further Angiotension-Converting Enzyme Inhibitors.

b) Navigate to ChEMBL: https://www.ebi.ac.uk/chembl/
and search for captopril. In the corresponding compound entry scroll down to “Activity Charts”. Move the mouse over the according slice in the "Bioactivity Summary" pie chart.
How many IC50 values are available for captopril?

c) Navigate to UniProt https://www.uniprot.org/ in a new browser tab.
Search for “Angiotensin converting enzyme”.
What is the UniProt accession code for the human ACE (not the ACE2)?
In this UniProt entry scroll down to the section “Chemistry”.
What is the ChEMBL entry number for this target?

2. Follow the link to the ChEMBL entry of this target.
Scroll down to “Drugs and Clinical Candidates” and look for moexipril.
What is the IC50 value (in nM) of moexipril for the inhibition of the human Angiotensin-converting enzyme? (there are several target organisms given).
What is this concentration in mol/litre?
For comparison: Captopril has an IC50 value of 23 nM. Which of both ligands binds stronger to ACE?
For which other ACE-inhibitors were IC50 values reported in the same publication (and same CHEMBL assay ID as moexipril?
(Klick on the IC50 slice in "Bioactivity chart" and then follow the corresponding link in the column "Assay ChEMBL ID". Next click on the "Bioactivity" chart)
List only those which end on “pril” or “prilat”.

3. Try searching for captopril and other inhibitor names in conjunction with the keywords (sue several at once):
„International nonproprietary names“, „WHO“, „Drug Information“, „use of stems“ in Google to get even more ACE-Inhibitors

4. Draw a common substructure for the majority of these inhibitors (exclude captopril). This substructure is similar to a class of natural compounds. Which one?

5. What is the difference between those inhibitors ending with the suffix „pril“ and those terminating with „prilat“ ?