



LABORATORY OF

STRUCTURAL BIOLOGY

Protein crystallography, human carbonic anhydrase IX, structure-assisted inhibitor design, antibody engineering

Pavlína Maloy Řezáčová

The main interests of our group are structural studies of various proteins of biological or medicinal interest using protein crystallography. We use the structural knowledge in understanding the protein function and in some projects also in modulating its function by design of specific inhibitors.

In our structure-based drug discovery project, we target enzymes from pathogenic organisms as well as human enzymes (e.g., human nucleotidases or cancer-specific carbonic anhydrase IX); the knowledge of protein structures provides a platform for the rational design of specific inhibitors.

Our group also focuses on engineering recombinant antibody fragments of potential diagnostic use. We employ several approaches aiming at practical use of recombinant antibody fragments.

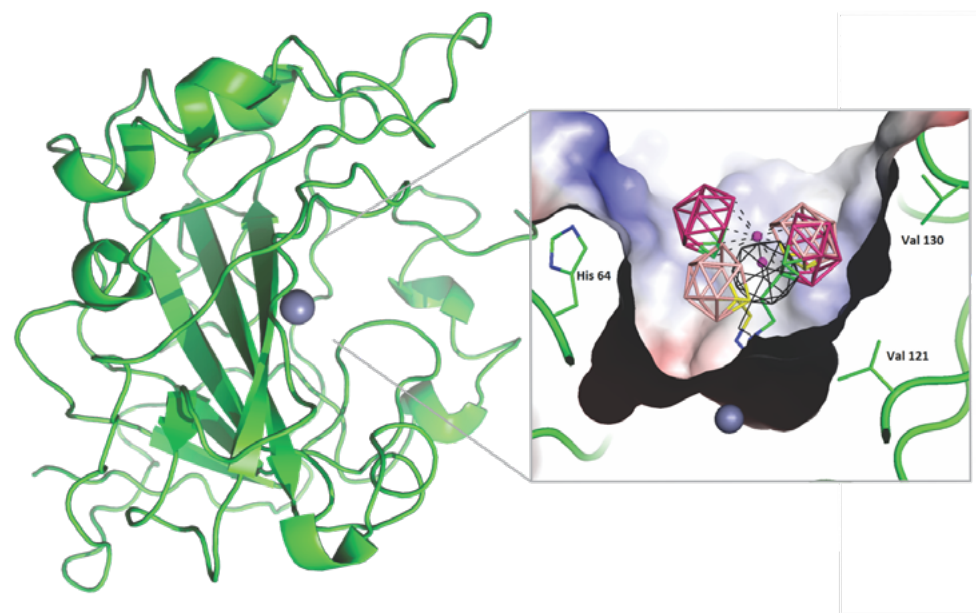


Figure 1. Binding of various carborane-based inhibitors into the active site of cancer-specific carbonic anhydrase IX. High-resolution crystal structures were used in structure-assisted inhibitor design.

Selected publications:

1. Grüner B*, Brynda J, Das V, Šicha V, Štěpánková J, Nektivinda J, Holub J, Pospíšilová K, Fábry M, Pachi P, Král V, Kugler M, Mašek V, Medvedíková M, Matějková S, Nová A, Lišková B, Gurská S, Džubák P, Hajdúch M*, Řezáčová P* (2019) Metallacarborane sulfamides: unconventional, specific, and highly selective inhibitors of carbonic anhydrase IX. *J Med Chem*, **62**:9560-9575.
2. Pola R, Král V, Filippov SK, Kaberov L, Etrych T, Sieglöva J, Sedláček J, Fábry M*, Pechar M* (2019) Polymer cancerostatics targeted by recombinant antibody fragments to GD2-positive tumor cells. *Biomacromolecules*, **20**:412-421.
3. Hnízda A*, Fábry M, Mariyama T, Pachi P, Kugler M, Brnsa V, Ascher DB, Carroll WL, Novák P, Žaliová M, Trka J, Řezáčová P, Yang JJ, Veverka V* (2018) Relapsed acute lymphoblastic leukemia-specific mutations in NT5C2 cluster into hotspots driving intersubunit stimulation. *Leukemia*, **32**:1393-1403.
4. Pachi P, Škerlová J, Šimčíková D, Kotik M, Křenková A, Mader P, Brynda J, Kapešová J, Křen V, Dłwinowski Z, Řezáčová P* (2018) Crystal structure of native α -L-rhamnosidase from *Aspergillus terreus*. *Acta Cryst D*, **74**:1078-1084.
5. Sharma S, Čermáková K, De Rijck J, Demeulemeester J, Fábry M, El Ashkar S, Van Belle S, Lepšík M, Tesina P, Duchoslav V, Novák P, Hubálek M, Srb P, Christ F, Řezáčová P, Hodges HC, Debyszer Z, Veverka V* (2018) Affinity switching of the LEDGF/p75 IBD interactome is governed by kinase-dependent phosphorylation. *Proc Natl Acad Sci USA*, **115**:E7053-E7062.



In the picture: 1. Brynda Jiří | 2. Kugler Michael | 3. Sedláček Juraj | 4. Fábry Milan | 5. Hořejší Magdalena | 6. Král Vlastimil | 7. Mrkvičková Věra | 8. Siegllová Irena | 9. Řezáčová [Maloy] Pavlína | 10. Krejčířková Veronika