



## Laboratory of Structural Biology

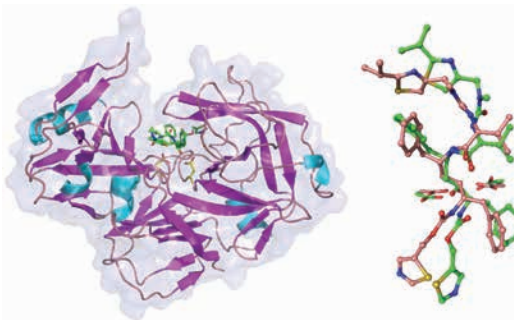
Protein crystallography, HIV protease, antibody engineering

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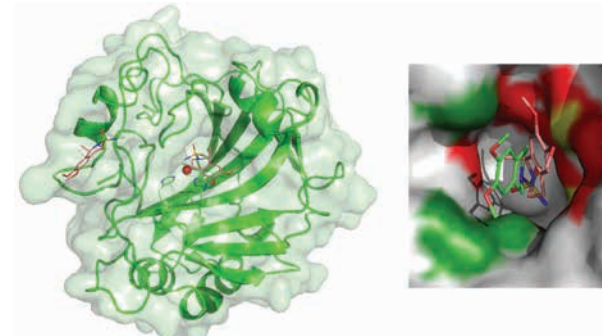
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The main interests of our group are structural studies of various proteins of biological or medicinal interest using protein crystallography. We use the structural knowledge in understanding the protein function and in some projects also in modulating its function by design of specific inhibitors. Among our targets, there are enzymes from pathogenic organisms [1], as well as human enzymes [4, 5].

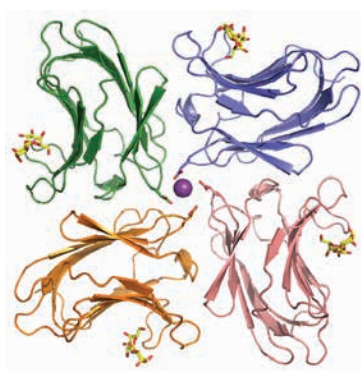
Our group also focuses on engineering recombinant antibody fragments of potential diagnostic use [e.g. against carbonic anhydrase IX, a cancer marker]. We employ several approaches aiming at practical use of recombinant antibody fragments. For instance, we recently constructed single-chain variable fragment, scFv, comprising an auxiliary polypeptide segment which is rich in tyrosine. This protein shows a higher capacity to bind iodine radionuclide, as compared to the parental scFv [2]. We also participated in design of targeted polymers carrying toxic payloads or fluorescence tags [3]. The contact of the scFv with the polymer is mediated by the interaction of two peptides forming coiled-coil interface. Such interaction is specific and does not require any other chemistry for antibody-polymer conjugation.



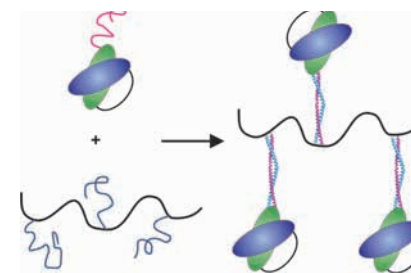
**Fig. 1.** Crystal structure of secreted aspartic protease 1 from *Candida parapsilosis* (Sapp1p) in complex with anti-HIV drug ritonavir [see reference 1 for details]. The protein in the ribbon representation is coloured by secondary structure, the drug molecule is represented by sticks. Right panel shows comparison of ritonavir binding modes in the active sites of *Candida* protease Sapp1p (sticks coloured green) and HIV protease (sticks coloured pink).



**Fig. 2.** Crystal structure of human carbonic anhydrase II in complex with isoquinoline inhibitor [see reference 4 for details]. The main chain of the protein is represented by a ribbon and a transparent solvent accessible surface. The zinc ion is shown as a red sphere with three coordinating histidine residues in sticks. Inhibitor is depicted in the stick model with carbon atoms coloured pink. Right panel shows unusual inhibitor binding mode [compare with similar compound in green in canonical binding mode] providing clues for the future design of selective inhibitors.



**Fig. 3.** Crystal structure of mouse galectin-4 in complex with lactose [see reference 5 for details]. Crystallographic tetramer is shown with individual monomers in cartoon representation and lactose bound to the carbohydrate binding site as sticks.



**Fig. 4.** Schematic representation of targeted polymers [see reference 3]. The contact of the antibody fragment with the polymer is mediated by the interaction of two peptides forming specific coiled-coil interface.



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- GA CR, GA203/09/0820 - Structure based drug design of specific nucleotidases inhibitors, potentially pharmacologically important compounds, 2009-2013, J. Brynda
- TA CR, TA02010797 - Labeling of recombinant antibody fragments with use of microfluidic systems, 2012-2014, J. Sedláček



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From the left:  
Věra Mrkvíčková / Technician · Jitka Kredbová / Technician · Juraj Sedláček, DSc / Research Fellow · Petr Páchl, MSc / PhD Student · Milan Fábry, PhD / Research Fellow · Pavlína Maloy Rezáčová, PhD / Head of Laboratory · Jana Písačková, MSc / PhD Student · Vlastimil Král, PhD / Research Associate · Irena Siegllová, MSc / Research Assistant

Not in the picture:  
Jiří Brynda, Assoc. Prof, PhD / Research Fellow · Pavel Mader, PhD / Postdoctoral Fellow · Veronika Krejčířiková, PhD / Postdoctoral Fellow [maternity leave] · Magdalena Hořejší, MSc / Research Assistant · Petr Těšina, MSc / PhD Student