

## **CYRIL BAŘINKA, Ph.D.**

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### EDUCATION AND RESEARCH

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- Institute of Biotechnology, Prague, Czech Rep.** 2010 - present
- Principal Investigator  
Tools and techniques targeting glutamate carboxypeptidases II and III  
Structure-function studies of histone deacetylases
- The National Cancer Institute, Frederick, USA** 2005 – 2010
- Postdoctoral fellow, Jacek Lubkowski lab  
Project 1: Structural characterization of glutamate carboxypeptidase II  
Project 2: Urokinase system – structural characterization  
Project 3: Structural and biological properties of mammalian defensins
- Institute of Organic Chem. & Biochem., Prague, Czech Rep.** 2003 - 2005
- Junior researcher, Jan Konvalinka lab  
Project 1: Glutamate carboxypeptidase II – biochemical characterization  
Project 2: Biological properties of mouse serine racemase
- Charles University, Prague, Czech Republic** 1998 - 2003
- Ph.D., Biochemistry, Nov 2003  
Thesis: Glutamate carboxypeptidase II – heterologous over-expression and biochemical characterization
- Institute of Organic Chem. & Biochem., Prague, Czech Rep.** 1996 - 1998
- Mandatory civil service  
Project: Combinatorial libraries targeting HIV protease
- Charles University, Prague, Czech Republic** 1990 - 1995
- MSc, Biochemistry & Molecular Biology, June 1995  
Thesis: Lipoprotein and hepatic lipase in triglyceride metabolism
  - BSc, Chemistry, March 1993

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## HONORS

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- EMBO Installation grantee, 2010 - 2015
- Exceptional Stipend Increase Award by the Director of the Centre for Cancer Research, The National Cancer Institute, 2009
- Fellows Award for Research Excellence, The National Institutes of Health, 2008
- Biochemical Journal Young Investigator's Award, 18<sup>th</sup> International Congress on Fibrinolysis and Proteolysis, 2006
- The best Ph.D. Thesis at the Institute of Organic Chem. & Biochem., 2004

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## GRANTS AND FELLOWSHIPS

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- EMBO short term fellowship, ASTF56/2012, Development of Anticalin-based biologics targeting prostate-specific membrane antigen (PSMA), prof. Skerra lab, Technische Universität München, Germany, Sept 2012 – Feb 2013
- Czech Science Foundation, P303/11/2164, 2012 – 2016; principal investigator
- The Education for Competitiveness Operational Programme, CZ.1.07/2.3.00/30.0045, 2012 – 2015, principal co-investigator
- IRG Reintegration Grant #249220, 2011 – 2014; principal investigator
- Grant by the Ministry of Education, Youth, and Sports, ME10031, 2010 – 2012; principal investigator
- The fellowship of J.E. Purkyne, The Czech Academy of Sciences, 2010 - 2014
- EMBO Installation Grant #1978, 2010 – 2015; principal investigator
- FEBS Fellowship, Structure-solving of human GCPII complexes, R. Hilgenfeld lab, University of Luebeck, Germany, Nov 2003 – Feb 2004
- EC grant HPRI-CT-1999-00097, Structure of glutamate carboxypeptidase from human neurons, R. Hilgenfeld lab, Center for Design and Structure in Biology, Jena, Germany, Sep 2000, Dec 2001; co-recipient
- NATO Collaborative Linkage Grant, Recombinant overexpression of aspartic protease from blood-fluke *Schistosoma japonicum* in *Pichia pastoris*, J. McKerrow lab, Dept. of Pathology, UCSF, CA, Feb 2000 – March 2000; co-recipient

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## INVITED TALKS

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- PSMA – Targeting prostate cancer; Symposium at University clinic; Ulm, Germany, Sept 2013
- Institute of Parasitology, Ceske Budejovice, Czech Republic, Feb 2011

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## EXPERTISE

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- X-ray crystallography, enzymology, inhibition studies, assay development, structure-based drug design, biophysical techniques, general molecular biology techniques, protein expression and purification
- Metallopeptidases, proteases, deacetylases
- prostate cancer, neurologic disorders
- Reviewer for *J. Med Chem.*, *J. Biomol. Screening*, *Prostate*, *Bioorg. Med. Chem. Letters*, *Cancer Letts*, *J Neurochem*, *Chem Biol & Drug Design*, *FEBS Journal*, *Acta Cryst D*, *Acta Cryst F*, *Asian J of Andrology*.

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## PUBLICATIONS

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30. Pavlicek J, Ptacek J, Cerny J, Byun Y, Pavlíček J, Skultetyova L, Pomper MG, Lubkowsi J, and **Bařinka C\***.: Structural characterization of P1'-diversified urea-based inhibitors of glutamate carboxypeptidase II. *Bioorg Med Chem Lett* 2014, 24:2340-2345.
29. Navratil M, Ptacek J, Sacha P, Starkova J, Lubkowski J, **Barinka C**, Konvalinka J: Structural and biochemical characterization of the folyl-poly- $\gamma$ -l-glutamate hydrolyzing activity of human glutamate carboxypeptidase II. *FEBS J* 2014, doi: 10.1111/febs.12857
28. Alquicer G, Sedlák D, Byun Y, Pavlíček J, Stathis M, Rojas C, Slusher B, Pomper MG, Bartůněk P, and **Bařinka C\***.: Development of a high-throughput fluorescence polarization assay to identify novel ligands of glutamate carboxypeptidase II. *J Biomol Screening* 2012, 17:1030-1040.
27. Tykvart J, Sacha P, **Barinka C**, Knedlik T, Starkova J, Lubkowski J, Konvalinka J: Efficient and versatile one-step affinity purification of in vivo biotinylated proteins: expression, characterization and structure analysis of recombinant human glutamate carboxypeptidase II. *Protein Expr Purif* 2012, 82:106-115.

26. Pavlicek J, Ptacek J, **Barinka C\***: Glutamate Carboxypeptidase II: An Overview of Structural Studies and Their Importance for Structure-Based Drug Design and Deciphering the Reaction Mechanism of the Enzyme. *Curr Med Chem* 2012, 19:1300-1309.
25. **Barinka C\***, Rojas C, Slusher B, Pomper M: Glutamate Carboxypeptidase II in Diagnosis and Treatment of Neurologic Disorders and Prostate Cancer. *Curr Med Chem* 2012, 19:856-870.
24. Plechanovova A, Byun Y, Alquicer G, Skultetyova L, Mlcochova P, Nemcova A, Kim HJ, Navratil M, Mease R, Lubkowski J, Pomper MG, Konvalinka J, Rulisek L, **Barinka C\***: Novel substrate-based inhibitors of human glutamate carboxypeptidase II with enhanced lipophilicity. *J Med Chem* 2011, 54:7535-7546.
23. Zhang Y, Doherty T, Li J, Lu W, **Barinka C**, Lubkowski J, Hong M: Resonance assignment and three-dimensional structure determination of a human alpha-defensin, HNP-1, by solid-state NMR. *J Mol Biol* 2010, 397:408-422.
22. Zhang AX, Murelli RP, **Barinka C**, Michel J, Cocleaza A, Jorgensen WL, Lubkowski J, Spiegel DA: A remote arene-binding site on prostate specific membrane antigen revealed by antibody-recruiting small molecules. *J Am Chem Soc* 2010, 132:12711-12716.
21. Wang H, Byun Y, **Barinka C**, Pullambhatla M, Bhang HE, Fox JJ, Lubkowski J, Mease RC, Pomper MG: Bioisosterism of urea-based GCPII inhibitors: Synthesis and structure-activity relationship studies. *Bioorg Med Chem Lett* 2010, 20:392-397.
20. Mlcochova P, **Barinka C**, Tykvart J, Sacha P, Konvalinka J: Prostate-specific membrane antigen and its truncated form PSM'. *Prostate* 2009, 69:471-479.
19. Klusak V<sup>#</sup>, **Barinka C<sup>#</sup>**, Plechanovova A, Mlcochova P, Konvalinka J, Rulisek L, Lubkowski J: Reaction mechanism of glutamate carboxypeptidase II revealed by mutagenesis, X-ray crystallography, and computational methods. *Biochemistry* 2009, 48:4126-4138.
18. Hlouchova K, **Barinka C**, Konvalinka J, Lubkowski J: Structural insight into the evolutionary and pharmacologic homology of glutamate carboxypeptidases II and III. *FEBS J* 2009, 276:4448-4462.
17. Rovenska M, Hlouchova K, Sacha P, Mlcochova P, Horak V, Zamecnik J, **Barinka C**, Konvalinka J: Tissue expression and enzymologic characterization of human prostate specific membrane antigen and its rat and pig orthologs. *Prostate* 2008, 68:171-182.
16. **Barinka C**, Prahel A, Lubkowski J: Structure of human monocyte chemoattractant protein 4 (MCP-4/CCL13). *Acta Crystallogr D Biol Crystallogr* 2008, 64:273-278.
15. **Barinka C\***, Hlouchova K, Rovenska M, Majer P, Dauter M, Hin N, Ko YS, Tsukamoto T, Slusher BS, Konvalinka J, et al.: Structural basis of interactions

- between human glutamate carboxypeptidase II and its substrate analogs. *J Mol Biol* 2008, 376:1438-1450.
14. **Barinka C**, Byun Y, Dusich CL, Banerjee SR, Chen Y, Castanares M, Kozikowski AP, Mease RC, Pomper MG, Lubkowski J: Interactions between human glutamate carboxypeptidase II and urea-based inhibitors: structural characterization. *J Med Chem* 2008, 51:7737-7743.
  13. Sacha P, Zamecnik J, **Barinka C**, Hlouchova K, Vicha A, Mlcochova P, Hilgert I, Eckschlager T, Konvalinka J: Expression of glutamate carboxypeptidase II in human brain. *Neuroscience* 2007, 144:1361-1372.
  12. Mlcochova P, Plechanovova A, **Barinka C**, Mahadevan D, Saldanha JW, Rulisek L, Konvalinka J: Mapping of the active site of glutamate carboxypeptidase II by site-directed mutagenesis. *FEBS J* 2007, 274:4731-4741.
  11. Hlouchova K, **Barinka C**, Klusak V, Sacha P, Mlcochova P, Majer P, Rulisek L, Konvalinka J: Biochemical characterization of human glutamate carboxypeptidase III. *J Neurochem* 2007, 101:682-696.
  10. **Barinka C\***, Starkova J, Konvalinka J, Lubkowski J: A high-resolution structure of ligand-free human glutamate carboxypeptidase II. *Acta Crystallogr Sect F Struct Biol Cryst Commun* 2007, 63:150-153.
  9. **Barinka C**, Rovenska M, Mlcochova P, Hlouchova K, Plechanovova A, Majer P, Tsukamoto T, Slusher BS, Konvalinka J, Lubkowski J: Structural insight into the pharmacophore pocket of human glutamate carboxypeptidase II. *J Med Chem* 2007, 50:3267-3273.
  8. Mesters JR<sup>#</sup>, **Barinka C<sup>#</sup>**, Li W, Tsukamoto T, Majer P, Slusher BS, Konvalinka J, Hilgenfeld R: Structure of glutamate carboxypeptidase II, a drug target in neuronal damage and prostate cancer. *EMBO J* 2006, 25:1375-1384.
  7. **Barinka C**, Parry G, Callahan J, Shaw DE, Kuo A, Bdeir K, Cines DB, Mazar A, Lubkowski J: Structural basis of interaction between urokinase-type plasminogen activator and its receptor. *J Mol Biol* 2006, 363:482-495.
  6. Caffrey CR, Placha L, **Barinka C**, Hradilek M, Dostal J, Sajid M, McKerrow JH, Majer P, Konvalinka J, Vondrasek J: Homology modeling and SAR analysis of *Schistosoma japonicum* cathepsin D (SjCD) with statin inhibitors identify a unique active site steric barrier with potential for the design of specific inhibitors. *Biol Chem* 2005, 386:339-349.
  5. **Barinka C**, Sacha P, Sklenar J, Man P, Bezouska K, Slusher BS, Konvalinka J: Identification of the N-glycosylation sites on glutamate carboxypeptidase II necessary for proteolytic activity. *Protein Sci* 2004, 13:1627-1635.
  4. **Barinka C**, Mlcochova P, Sacha P, Hilgert I, Majer P, Slusher BS, Horejsi V, Konvalinka J: Amino acids at the N- and C-termini of human glutamate carboxypeptidase II are required for enzymatic activity and proper folding. *Eur J Biochem* 2004, 271:2782-2790.

3. Strisovsky K, Jiraskova J, **Barinka C**, Majer P, Rojas C, Slusher BS, Konvalinka J: Mouse brain serine racemase catalyzes specific elimination of L-serine to pyruvate. *FEBS Lett* 2003, 535:44-48.
2. **Barinka C**, Rinnova M, Sacha P, Rojas C, Majer P, Slusher BS, Konvalinka J: Substrate specificity, inhibition and enzymological analysis of recombinant human glutamate carboxypeptidase II. *J Neurochem* 2002, 80:477-487.
1. Rinnova M, Hradilek M, **Barinka C**, Weber J, Soucek M, Vondrasek J, Klimkait T, Konvalinka J: A picomolar inhibitor of resistant strains of human immunodeficiency virus protease identified by a combinatorial approach. *Arch Biochem Biophys* 2000, 382:22-30.

#shared first authorship

\*corresponding author

- 704 citations, H-index = 16
- 1 book chapter