

Željko M. Svedružić

Curriculum Vitæ

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Research

- 1 Development of mechanism-based inhibitors of mammalian/human DNA methyltransferases with IC50 values below 50 nM. The most successful inhibitors can be used for control of functional organization of mammalian genome in research laboratories, biotechnology and, ultimately, in clinics for treatment of pathogenic mechanisms related to epigenetic processes (i.e. tissue regeneration, oncogenesis, psychiatric and neurological disorders, viral infections, immunological disorders).
- 2 Development of novel bivalent mechanism-based inhibitors of membrane -embedded protease γ -secretase. The most successful compounds can be used for treatment and early-diagnosis of Alzheimer's disease or for control of different physiological processes that depend on cell-to-cell communication. Paid consultant for pharmaceutical industry, γ -secretase modulators and assays.

Area of Expertise

Specialty	Enzymology: <i>In vivo</i> , <i>in vitro</i> and <i>in silico</i> approaches for studies of structure and function of biomolecules
Training	Biochemistry, physical biochemistry (i.e. biophysics), medicinal chemistry, bioinorganic chemistry, molecular genetics, biological membranes, medical biochemistry, cell biology
Expertise	Molecular mechanism in epigenetics and chromatin organization; molecular mechanisms in Alzheimer's disease; protein-protein and protein-ligand interactions; assay-development and drug-design based on enzyme structure-function principles; substrate channeling

Teaching

Currently	Molecular modeling and numerical methods in biomedical sciences, i.e. structure and function of biomolecules, enzyme kinetics and protein-ligand interactions. Courses taught: "Chemoinformatics" (<i>undergraduate level</i> and "Design of Biologically Active Molecules by Computational Methods" (<i>graduate level</i>))
Invited lectures	Molecular mechanisms in Alzheimer's disease or molecular mechanisms in epigenetics
Various	Mentoring individual students in research and thesis preparation

Work Experience

- 2013 – Present **Assistant professor**, *Department of Biotechnology, University of Rijeka, Rijeka.*
- 2010 – Present **Adjunct Senior Research and Teaching Assistant**, *Faculty of Medicine, University of Rijeka, Rijeka.*
- 2010 – 2013 **Supervisor of Laboratory for Medical Biochemistry**, *Psychiatry Hospital Rab, Rijeka.*

Senior Scientist Appointments

- 2007 – 2010 **Project leaders: Professor Bart de Strooper (KU Leuven) and Eric Karran, Ph.D. (Eli Lilly)**, *Faculty of Medicine KU Leuven and Eli Lilly and Company Neurodegenerative Diseases Drug Hunting Team, Leuven, Belgium.*
Molecular pathophysiology of Alzheimer's disease and inhibitors of intermembrane protease γ -secretase
- 2003 – 2006 **Project leader: Regents Professor Michael J. Smerdon**, *School of Molecular Biosciences, Washington State University, Pullman, USA.*
DNA damage induced changes in DNA flexibility and DNA-nucleosome interaction. DNA repair in nuclear extracts.

Postdoctoral Research

- 2001 – 2001 **Project leader: Assistant professor Johannes Rudolph**, *Department of Biochemistry, Duke University Medical Center, Durham, USA.*
Enzymology of protein phosphatase CDC25B with Cdk2/CycA protein complex as the substrate (Cdk2 = cyclin dependent kinase 2; CycA = cyclin A)
- 1998 – 2000; 2002 **Project leader: Professor Norbert O. Reich**, *Department of Chemistry and Epigenx Pharmaceuticals, Inc., University of California, Santa Barbara, USA.*
Enzymology and inhibitors of mammalian and bacterial cytosine DNA methyltransferases

Education

- 1993 – 1998 **Ph.D. degree**, *Department of Biochemistry and Molecular Biology, Oklahoma State University, Stillwater, USA.*
- 1992 – 1993 **Master degree in biochemistry**, *Max Plank Institute of Biochemistry, Munich, Germany.*
- 1988 – 1992 **Bachelor degree in molecular biology**, *Faculty of Science, University of Zagreb, Zagreb, Croatia.*

Ph.D. Thesis

- Title Substrate channeling between NAD(H) dehydrogenases: enzyme kinetics, protein-protein interaction and molecular modeling studies
- Supervisor Professor H. Olin Spivey (deceased)

Master Thesis

- Title Purification of p17 protein; a component of Actin-Myosin complex from *Dictostelium discoideum*
- Supervisor Emeritus Gunther Gerisch

Publications

Journal Papers

- 9 Svedružić Ž. M., Popović K., and Šendula-Jengiđ V. Modulators of γ -secretase activity can facilitate the toxic side-effects and pathogenesis of Alzheimer's disease. *PLoS ONE* **8**(1), January 7th (2013).
- 8 Svedružić Ž. M. Popović K., Smoljan I., and Šendula-Jengiđ V. Modulation of γ -secretase activity by multiple enzyme-substrate interactions: Implications in pathogenesis of Alzheimer's disease. *PLoS One* **7**(3), March 30th (2012).
- 7 Svedružić Ž. M. Mammalian Cytosine DNA methyltransferase Dnmt1: Enzymatic Mechanism, Novel Mechanism-Based Inhibitors, and RNA-directed DNA methylation. *Current Medicinal Chemistry* **15**(1), 92–106 (2008)
- 6 Svedružić Ž. M. and H. O. Spivey. Interaction between Mammalian Glyceraldehyde-3-phosphate Dehydrogenase and L-Lactate Dehydrogenase from Heart and Muscle. *Proteins, Structure, Function and Bioinformatics* **63**(3), 501–511 (2006).
- 5 Svedružić Ž. M., Wang C., Kosmoski J.V., and Smerdon M.J. Accommodation and Repair of a UV Photoproduct in DNA at Different Rotational Settings on the Nucleosome Surface. *Journal of Biological Chemistry* **280**(48), 40051–40057 (2005).
- 4 Svedružić Ž. M. and N.O. Reich. The Mechanism of Allosteric Regulation of Dnmt1's Processivity. *Biochemistry* **44**(45), 14972–14988 (2005).
- 3 Svedružić Ž. M. and N.O. Reich. DNA Cytosine C5 Methyltransferase Dnmt1: Catalysis Dependent Release of Allosteric Inhibition. *Biochemistry* **44**(27), 9472–9485 (2005).
- 2 Svedružić Ž. M. and N.O. Reich. The Mechanism of Target Base Attack in DNA Cytosine C5 Methylation. *Biochemistry* **43**(36), 11460–11473 (2004).
- 1 Lehoux E. A., Svedružić Ž., and Spivey, H. O. Determination of Specific Radioactivity of [¹⁴C] Lactate by Enzymatic Decarboxylation and CO₂ Collection. *Analytical Biochemistry* **253**(2), 190–195 (1997).

Book Chapters

- 1 Svedružić Ž. M. Mammalian DNA methyltransferase Dnmt1: Structure and Function. In: Modification of Mammalian DNA: Mechanism, Management, Missions, and Medical Implications. *Progress in Molecular Biology and Translational Science* **101**, 221–254 (Elsevier, 2011).