METAXIA I. VLASSI

Address: Protein Structure & Molecular Modeling Laboratory

Institute of Biosciences & Applications, National Centre for Scientific Research "DEMOKRITOS", 15310 Ag. Paraskevi-Attikis, Athens/Greece

<u>Tel: +</u>30-210-6503575,

E-mail: meta@bio.demokritos.gr

Education:

1984: BSc in Physics, Physics Dept., University of Patras, Greece.

1985-1989: Graduate student towards a PhD degree, Dept de Chimie Quantique, Université Catholique de Louvain-la-Neuve, Belgium /Chemistry Dept., University of Patras, Greece 1989: PhD in X-ray Crystallography, Chemistry Dept., University of Patras, Greece.

Positions held:

- 2007-today: Senior Researcher (Grade A'), Institute of Biosciences & Applications (IB-A, former Institute of Biology), National Center for Scientific Research (NCSR) "Demokritos", Athens, Greece. Head of the Protein Structure & Molecular Modeling laboratory
- 1995-2007: Researcher (Grades C' and B'), Institute of Biology (I.B.), NCSR "Demokritos", Athens, Greece
- 1994-1995: Collaborating Research Scientist in the field of Protein Crystallography, Institute of Molecular Biology & Biotechnology, Division of Macromolecular Structures, Herakleion, Crete, Greece.

1989-1993: Postdoctoral Fellow in the field of Protein Crystallography, Institute of Molecular Biology & Biotechnology and Univ. of Crete, Herakleion, Crete, Greece.

1993: Short term post-doctoral fellow in the field of Protein Crystallography, EMBL/DESY Hamburg, Germany

Research interests:

- Protein folding
- Sequence/structure/function relationships
- Conformational preferences of amino-acid sequence repeats
- Conformational changes and protein stability
- Phosphorylation and conformational changes
- Molecular dynamics of proteins
- Protein interactions
- Disordered proteins

Current research activities:

Current research activities focus on structural studies of proteins with emphasis on repeatcontaining proteins (e.g. arginine/serine repeats and other repeats found in disordered protein regions / protein interaction modulators) and on enzymes mainly related to diseases aiming at elucidating sequence/structure relationships and fundamental aspects of repeat-mediated protein interactions and at unraveling the atomic details of the function of enzymes as potential therapeutic targets. The approach includes mainly *in silico* techniques (3D-modeling, molecular dynamics simulations, molecular docking) combined with biochemical and biophysical data (mainly Circular Dichroism (CD))

Other activities related to Structural Molecular Biology

- Co-responsible for the operation of the Circular Dichroism (CD) service unit of IB_A
- Member of INSTRUCT and of the INSTRUCT-EL network (linked to the European INSTRUCT: An Integrated Structural Biology Infrastructure for Europe), an initiative of Greek scientists for a national RI on Integrated Structural Biology (proposal submitted to the Greek General Secretariat for Research & Technology (GSRT) in the framework of the National Roadmap for Research Infrastructures program, 2013 (pending evaluation).
- Member of the national network BE/OPT-XFEL (Network to Optimize use of the European X-FEL by the Greek Research Community) linked to the European XFEL Infrastructure (funded by the GSRT/ESFRI: BE/OPT-XFEL (2010-2011))
- Organizer of the International workshop entitled: "XFEL Radiation & its Applications" at NCSR "Demokritos", 18-19 June 2010 (see also <u>www.xfel.gr</u>), aiming at adequately preparing the Greek scientific community for the research opportunities created by the European X-FEL facility. The workshop was organized in the framework of the BE/OPT-XFEL program and was financed by the GSRT. The speakers (13) were invited scientists, experts in X-Ray Free Electron Lasers (XFELs), including members of the European X-FEL scientific advisory board and users of similar infrastructures (CFEL/Germany, SLAC/Stanford/USA, Spring-8 Center/Japan). The presentations covered basic principles of XFEL operations and scientific applications in a wide range of fields that were inaccessible prior to XFEL.
- Presentation of research activities related to Bioinformatics & Computational Biology at NCSR "Demokritos"» in the Joint Meeting of the Hellenic Society of Computational Biology & Bioinformatics (HSCBB) – the GSRT – Coordinators of the European ELIXIR project, 30-31 March, 2009, Athens, Greece.
- Member (2002-2007) of the Scientific Advisory Committee (for topics related to Structural Molecular Biology) of the international research center, SESAME (<u>Synchrotron-light source for Experimental Science and Applications in the Middle East</u>).
- Participation as member of the SESAME SAC, in the: 1st (20-21 December 2002, CCLRC Daresbury Laboratory, UK), 2nd (15-16 April, 2004, UNESCO, Paris, France), 3rd (5-6 May 2005, UNESCO, Paris, France) and 4th (November 2006, Cairo, Egypt) Joint Meetings of the SESAME Beamlines & Science Committees.
- Ad-hoc reviewer for international peer-reviewed journals (Acta Crystallographica D, Nucleic Acid Research, Neurochemical Research etc)
- Founding member and member of the administrative board (2001-2003) of the Hellenic Crystallographic Association.
- Co-organizer of the 1st Hellenic workshop on Bioinformatics, University of Athens, May 2002.
- Co-organizer of the 1st Congress of the Hellenic Crystallographic Association, Agricultural University of Athens, May 2002
- Co-organizer of the 1st Hellenic workshop on Bioinformatics, May 2002, University of Athens,

Athens, Greece

- Co-organizer of the International workshop entitled: "Bioinformatics and Structural Modeling", Sabanci University, Istanbul, Turkey, September 2001 (see errata, Synchrotron Radiation News, 15:1, 22-22, doi:10.1080/08940880208602928) of SRN, 14:6, 24-25)
- Member (2000-2002) of the Structural Molecular Biology (SMB) sub-committee of the SESAME project
- Presentation (April 2000), as member of the SESAME SMB sub-committee, on the current status of SMB related research activities in Greece in the Inaugural Meeting of the SMB Science Sub-committee of SESAME in the framework of the 1st Workshop on Structural Molecular Biology at SESAME 6-7 April, 2000, Athens, Greece (see SRN Vol 13, No 4, pp 25-27)
- Presentation (December 2000), as member of the SESAME SMB sub-committee, on the current status of SMB related research activities in Greece and of a proposal for an SMB Institute at SESAME (in collaboration with Pierre Rizkallah) in the framework of the 2nd Workshop on Structural Molecular Biology at SESAME, 6-7 December, 2000, Nicosia, Cyprus
- Organizer of the 1st Hellenic workshop on "Crystallographic Data Collection and Processing" (IB, NCSR "Demokritos", 1999). The workshop took place at the CCM (see below), was financed by the Greek GSRT through a "Career development program for Greek speaking scientists" (coordinator: M. Vlassi), and was attended by students and scientists from various Greek universities and research institutions.
- Co-responsible Scientist for the establishment (1998) of the Centre for Crystallographic Studies of Macromolecules (CCM) at NCSR "Demokritos", financed by the Greek GSRT/EPETII-Research Infrastructures (Nov. 1996) as a network of three Institutes of NCSR "Demokritos" (the former: Biology, Physical Chemistry and Radioisotopes & Radiodiagnostic Products) and other Greek academic Institutions.

Educational activities/Teaching

- Supervisor (until today) of various graduate- (PHD- and MSc-), undergraduate- and rotationstudents
- Co-Instructor (2003-today) of the course: "Current Biochemical & Biophysical Methods" in the framework of the graduate (Master's) program: "Clinical Biochemistry Molecular Diagnosis" of the Biology-Chemistry Depts, University of Athens.
- Co-Instructor (2003-2010) of the course: "Introduction to Research Methodology" in the framework of the graduate (Master's) program: "Molecular Medicine" of the Medical School, University of Athens.
- Instructor (2003-2006) in the framework of the graduate (Master's) program: "Bioinformatics", Biology Dept, University of Athens
- Co-Instructor (1998-2007) of the course "Structural & Computational Biology" in the framework of the graduate program of the IB-A (former IB), NCSR "D".
- Tutor (lectures & preparation of practical exercises) of the 1st Hellenic workshop on Bioinformatics, May 2002, University of Athens, Athens, Greece
- Tutor (lectures and preparation of practical exercises) of the 1st Workshop in Bioinformatics & Structural Modeling, 3-9 Sept 2001, Istanbul, Turkey

- Instructor in the framework of the "Intensive Course on Plant Biotechnology and Applications 1999-2000", Mediterranean Agronomic Institute of Chania (MAICH), Crete, May 2000.
- Presentations in the framework of NCSR "D" Summer Schools (1998, 1999, 2001, 2002, 2005)
- Tutor (lectures and preparation of practical exercises) of the practical course "Computer Applications in Structural Biology and Sequence Analysis" organized at the University of Crete, Dept. of Biology, 2-6 Sept 1996, Heraklion-Crete, Greece
- Tutor of the 2nd European practical course in "Protein Design" organized under the support of Directorate-General for Science, Research and Development of the EU, at the IMBB Institute, Heraklion-Crete, Greece (Sept.-Oct. 1990).
- Tutor of the 1st European practical course in "Protein Design" organized under the support of Directorate-General for Science, Research and Development of the EU at the IMBB Institute, Heraklion-Crete, Greece (Sept.-Oct. 1990).

Other activities (Administrative)

- Member (2000-2008 and 2010-2012) and President (2002-2004) of the Scientific Advisory Board the Institute of Biology (IB; currently:IB-A) of NCSR "Demokritos"
- Deputy Director (Nov 2010- Dec 2011) of the Institute of Biology (currently: Institute of Biosciences & Applications)
- Member (2008) and surrogate member (2010- 9/2013) of the Research Committee of NCSR "D"
- Member (2012) of the evaluation committee of the University of Thessaly (School of Health Sciences, Dept. of Biochemistry & Biotechnology) for the appointment of an Associate Professor in the field of Biophysics with emphasis on structure/function studies of proteins
- Member (2012) of the evaluation committee of IB-A/NCSR "D" for the appointment of an Associate Research Scientist in the field of the "Design, Synthesis and Evaluation of Chemicals with Biological and Pharmaceutical Activity"
- Member of ad hoc evaluation committees of grant applications in the framework of bilateral research programs (General Secretariat for Research & Technology, Greece).
- Member of the committee responsible for the graduate (PhD) education program of the I.B/NCSR "D" (2001-2003)
- Responsible for the establishment of the computer local area network of IB (1996)
- Responsible for the design and maintenance of the Institute's web site (1998-2002)

<u>SELECTED PUBLICATIONS</u> (out of a total of 41) (in peer-reviewed journals)

Vlassi M*, Brauns, K, Andrade-Navarro MA (2013) Short tandem repeats in the inhibitory domain of the mineralocoricoid receptor: prediction of a beta-solenoid structure. <u>BMC Struct Biol</u> <u>13:17</u> (doi:10.1186/1472-6807-13-17) (*co-Corresponding author)

Sellis D, Drosou V, Vlachakis D, Voukkalis N, Giannakouros T, **Vlassi M**. (2012) Phosphorylation of the arginine/serine repeats of lamin B receptor by SRPK1-Insights from molecular dynamics simulations. <u>*Biochim Biophys Acta (General Subjects)* 1820(1):44-55</u>.

Balatsos N, Vlachakis D, Chatzigeorgiou V, Manta S, Komiotis D, **Vlassi M**, Stathopoulos C (2012) Kinetic and in silico analysis of the slow-binding inhibition of human poly(A)-specific ribonuclease (PARN) by novel nucleoside analogues. <u>*Biochimie*</u>. 94(1):214-21

Sellis, D., Vlachakis, D., **Vlassi, M**. (2009) Gromita: A fully integrated graphical user interface to Gromacs 4. *Bioinformatics & Biology Insights* 2009:3, 99-102.

Balatsos, N., Vlachakis, D., Maragozidis, P., Anastasakis, D., Kyritsis, A., **Vlassi, M**., Koumiotis, D., Stathopoulos, C (2009) Competitive Inhibition of Human Poly(A)-Specific Ribonuclease (PARN) by Synthetic Fluoro-Pyranosyl Nucleosides. <u>*Biochemistry* 48(26):6044-6051</u>

Palaiomylitou, M., Tartas, A, Vlachakis, D., Tzamarias, D., **Vlassi, M**. (2008) Investigating the structural stability of the Tup1 interaction domain of Ssn6: Evidence for a conformational change in the complex. <u>*Proteins* 1;70 (1):72-82</u>

Grigoroudis, AI, Panagiotidis, CA, Lioliou, EE, **Vlassi, M***, Kyriakidis, D. (2007) Molecular modeling and functional analysis of the AtoS-AtoC two-component signal transduction system of Escherichia coli. *Biochim Biophys Acta-General Subjects* 1770(8):1248-58. (* *Corresponding author*)

Nikolopoulos, G., Pyrpassopoulos, S., Thanassoulas, A., Klimentzou, P.,Zikos,C., **Vlassi, M.**, Vorgias, C, Yannoukakos, D., Nounesis, G. (2007) Thermal Unfolding of Human BRCA1 BRCT-Domain Variants. *Biochim Biophys Acta - Proteins & Proteomics* 1774(6):772-80.

Benaki, D., Zikos, C., Evangelou, A., Livaniou, E., **Vlassi, M.**, Mikros, E., Pelecanou, M (2006) Solution structure of Ser14Gly-humanin, a potent rescue factor against neuronal cell death in Alzheimer's disease. *Biochem Biophys Res Comm* 349, 634-42

Kosmopoulou, A., **Vlassi, M**, Stavrakoudis, A., Sakarellos, C., Sakarellos-Daitsiotis, M. (2006) T-cell epitopes of the La/SSB autoantigen:prediction based on the homology modelling of HLA-DQ2/DQ7 with the insulin-B peptide/HLA-DQ8 complex. *J. Comp. Chem.* 27(9):1033-44

Glykos NM*, Papanikolau Y*, **Vlassi M***, Kotsifaki D, Cesareni G, Kokkinidis M. (2006) Loopless Rop: structure and dynamics of an engineered homotetrameric variant of the repressor of primer protein. <u>*Biochemistry*</u>. 45(36):10905-19</u>. (**Authors with equal contribution*)

Pyrpassopoulos, S, Ladopoulou, A., **Vlassi, M**., Papanikolau, Y., Vorgias, C.E., Yannoukakos, D., Nounesis, G (2005). Thermal denaturation of the BRCT tandem repeat region of human tumour suppressor gene product BRCA1. *Biophys Chem* 114, 1-12.

Benaki, D., Zikos, C., Livaniou, E., **Vlassi, M**., Mikros, E., Pelecanou, M. (2005) Solution structure of humanin, a peptide against Alzheime's disease-related neurotoxicity. <u>*Biochem Biophys Res</u>* <u>*Comm* 329, 152-160.</u></u>

Leonidas D, Chavali G, Oikonomakos N, Chrysina E, Kosmopoulou M, **Vlassi M**, Frankling C, Acharya KR (2003). High-resolution crystal structures of ribonuclease A complexed with adenylic and uridylic nucleotide inhibitors. Implications for structure-based design of ribonucleolytic inhibitors. <u>Protein Sci. 12(11), 2559-2574</u>. (*Note: This work was used as cover illustration of Protein Sci. vol. 12(11)*)

Gounalaki N, Tzamarias D, **Vlassi M.** (2000). Identification of residues in the TPR domain of Ssn6 responsible for interaction with the Tup1 protein. <u>FEBS Lett. 473(1):37-41</u>. (*Note: This work was used a cover illustration of FEBS Lett vol.* 473)

Vlassi, M., G. Cesareni, M. Kokkinidis (1999) A correlation between the loss of hydrophobic core packing interactions and protein stability. *J. Mol. Biol.* 285, 817-27.

Lassalle, M.W., H-J. Hinz, H. Wenzel, **M. Vlassi**, M. Kokkinidis, G. Cesareni (1998). Dimer-totetramer transformation: loop excision dramatically alters structure and stability of the ROP $4-\alpha$ helix bundle protein. *J. Mol. Biol.* 279, 987-1000.

Vlassi, M., Z. Dauter, K.S.Wilson and M. Kokkinidis (1998). Structural parameters for proteins derived from the atomic-resolution (1.09Å) structure of a designed variant of the *ColE1* ROP protein. <u>Acta Crystallogr</u>, D54, 1245-1260.

Athanasiadis, A., **M. Vlassi**, D. Kotsifaki, P.A. Tucker, K.S. Wilson, M. Kokkinidis (1994). Crystal structure of PVUII endonuclease reveals extensive structural homologies to EcoRV. <u>Nature</u> <u>Struct. Biol</u>, 1 (No 7), 469-475. (Note: An editorial referring to this work was published in Nature see: Riddihough G.(1994) Nature 370 (6484): 78-78)

Vlassi, M., C. Steif, P. Weber, D. Tsernoglou, K.S.Wilson, H.J.Hinz, M. Kokkinidis (1994). Restored heptad pattern continuity does not alter the folding of a 4- α -helical bundle. <u>*Nat. Struct.*</u> *Biol.*, 1 (No 10), 706-716.

Selected Recent Presentations at International Conferences

D. Sellis, T. Giannakouros, M. Vlassi (2012) Recognition of arginine/serine repeats by SR protein kinase 1: Insights from molecular dynamics simulations. Abstracts of the 22nd IUBMB & 37th Congress of the Federation of European Biochemical Societies (FEBS), Sept 4-9, 2012, Seville, Spain, *FEBS .J* 279 (Suppl. 1) pp: 553-554.

D. Sellis, T. Giannakouros, **M. Vlassi*** (2012) Molecular dynamics simulations of arginine/serine repeats: Implications for their role in molecular recognition. Book of abstracts of **6**th **International Conference of the Hellenic Crystallographic Association, Sept 28-29, 2012, Univ. of Athens, Athens, Greece** (*oral presentation) p O6

Vlachakis D, **Vlassi M** (2009) Molecular modelling of a novel series of Dengue virus (typeII) helicase potential inhibitors, by a de novo structure-based drug design **34th FEBS Congress**, July 4-8, **2009**, **Prague**, **Czech Republic**. Abstract in *FEBS J*. 276 (Suppl S1) p 171

Benaki, D., Zikos, C, Evangelou, A., Slaninova, J., **Vlassi, M**., Livaniou, E., Mikros, E., Pelecanou, M. (2008). Comparative structural studies of potent neuroprotective peptides of the Humanin family. **30th European Peptide Symposium (30EPS)**, 31 August – 5 September, **2008. Helsinki**, **Finland**, Abstract in *J. Peptide Science* 14(S1) p108

Nikolopoulos, G, Vlachakis, D., Waltenspiel, B., Warren, W.D., **Vlassi**, **M** (2008) Preliminary structural characterization of DEFL, a good candidate for anticancer research. **33rd FEBS Congress & 11th IUBMB Conference**, 28 June – 3 July, **2008. Athens, Greece.** Abstract in *FEBS J*. 275 (Suppl S1) p 232

Benaki, D., Zikos, C, Evangelou, A., Elbert, T., Slaninova, J., **Vlassi, M**., Mikros, M., Bouziotis, P., Paravatou-Petsotas, M., Papadopoulos, M., Pirmettis, I., Pelecanou, M., Livaniou, E. (2008). Investigation of the neuroprotective action of the humanin family of peptides with in vitro, in vivo, and structural studies. **33rd FEBS Congress & 11th IUBMB Conference**, 28 June – 3 July, **2008.** Athens, Greece, Abstract in *FEBS J*. 275 (Suppl S1) OP3A-1, p75

Vlachakis, D., Tartas, A, M. Vlassi (2007) Using molecular dynamics simulations to investigate

the structural stability of a repeat containing proteins. **32nd FEBS Congress, Molecular Machines**, July 7-12, **2007, Vienna, Austria**, Abstract in *FEBS J* 274 (Suppl S1): p377

Nikolopoulos, G., Pyrpassopoulos, S, Ladopoulou, A., Klimentzou, P., Zikos, C., **Vlassi, M**., Vorgias, C., Nounesis, G., Yannoukakos, D (2005) BRCA1 missense mutations destabilize its structure and alter the binding of the helicase BACH1 **30th FEBS Congress -9th IUBMB**, 2-7 July, **2005, Budapest, Hungary**, Abstract in *FEBS J* 272 (Suppl S1) p383

Selected Recent Presentations at National Conferences

D. Sellis, V. Drosou, D. Vlachakis, N. Voukkalis, T. Giannakouros, **M. Vlassi* (2011)** Phosphorylation of the Arginine/Serine Repeats of Lamin B Receptor by SRPK1 - Insights from Molecular Dynamics Simulations. Proceedings of the **62nd Congress of the Hellenic Society for Biochemistry and Molecular Biology (HSBMB)**, Dec 9-11, **2011**, **Athens**, **Greece**, p79

M. Vlassi*, D. Sellis, T. Giannakouros (**2011**) Using Molecular Dynamics simulations to study the conformation of Arg/Ser repeat-containing peptides. Proceedings of the **6th Conference of the Hellenic Society for Computational Biology and Bioinformatics (HSCBB)**, Oct 7-9, **2011**, **Patras**, **Greece**, p 12

Sellis, D., Vlachakis, D., Tartas, A., **Vlassi, M.*** (2010) Molecular dynamics simulations of proteins in aqueous solution: I. Development of the Gromita software. II. The example of a repeatcontaining protein of known structural dynamics. Book of abstracts of the **61**st **Conference of the Hellenic Society for Biochemistry & Molecular Biology**, 15-17 October, **2010**, **Alexandroupolis**, **Greece**, A45, p34

Chatzigeorgiou, V., Vlachakis, D., Zervakaki, V., Manta, S., Komiotis, D, Vlassi, M., Stathopoulos, K. and Balatsos, N. (2010) Inhibition mechanism of poly(A)-specific ribonuclease (PARN) by nucleoside analogues. Book of abstracts of the 61st Conference of the Hellenic Society for Biochemistry & Molecular Biology, 15-17 October, 2010, Alexandroupolis, Greece, P105, p90

M. Vlassi (2009) "Research activities related to Bioinformatics and Computational Biology at NCSR "Demokritos", **Meeting of the Hellenic Society of Computational Biology & Bioinformatics – General Secretariat for Research & Technology - Coordinators of the ELIXIR project**, 30-31 March **2009**, National Hellenic Research Foundation, **Athens, Greece**

Vlachakis, D., Sellis, D., Tartas, A., Nikolopoulos, G., Economou, I., **M. Vlassi (2008)** Evaluation of molecular dynamics simulations using the known structural behavior of a repeat containing protein **Proceedings of 30th Scientific Conference of the Hellenic Society for Biological Sciences**, 22-24 May, **2008**, Thessaloniki, Greece, p55

Vlachakis, D., Nikolopoulos, G, Waltenspiel, B., Warren, W.D., **Vlassi, M** (2008) Structure Predictions and Circular Dichroism Studies of DEFL, the Product of a Drosophila Uncharacterized Gene. Proceedings of the 4th **Conference of the Hellenic Crystallographic Association**, September 2008, Athens, Greece, p72

Nikolopoulos, G., Vlachakis, D., Waltenspiel, B., Warren, W., **M. Vla**ssi (2007) Structure predictions, cloning and overexpression of DEFL, the product of a drosophila uncharacterized gene. Book of abstracts of the **59th Meeting of the Hellenic Society of Biochemistry & Molecular Biology**, December 2007, Athens, Greece. p210

Benaki, D., Zikos, C., Evangelou, A., **Vlassi, M**., Slaninova, J., Livaniou, E., Mikros, E., Pelecanou, M (**2007**) Structural studies of humanin and its derivatives in the investigation of their neuroprotective role against Alzheimer's disease. **9th Annual Meeting of the Hellenic Research Club for Connective Tissue & Matrix Biology**, 10-12 May, **2007**, **Athens, Greece**, p22

Vlachakis, D., A. Tartas, M. Palaiomylitou, **M. Vlassi (2006)** Using molecular dynamics simulations to investigate the structural stability of the Tup1 interaction domain of the transcriptional regulator Ssn6. Book of abstracts of the **3nd Conference of the Hellenic Crystallographic Association**, September 22-24, 2006, Patras, Greece, p O27

Dragoumani, K., D. Vlachakis, **M. Vlassi (2006)** Structure-based design of potential inhibitors of the non-phosphorylating glyceraldehyde 3-phosphate dehydrogenase from streptococcus pyogenes. Book of abstracts of the **3nd Conference of the Hellenic Crystallographic Association**, September 22-24, 2006, Patras, Greece, p P5

Benaki, D., Zikos, Ch., Evangelou, A., Livaniou, E, **Vlassi, M**, Mikros, E., Pelecanou, M. (2005) Solution Stucture of Humanin, a Peptide against Alzheimer's Disease-Related Neurotoxicity, and Humanin Analogues. Proceedings of the 27° Scientific Conference of the Hellenic Society for Biological Sciences, May 2005, Nafplio, Greece. p 250