



1952 - 2022

## **Institute of Biochemistry**

advancing the frontiers of knowledge in modern biology

http://www.biochim.ro

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#### Overview

Mission statement. The Institute of Biochemistry of the Romanian Academy, IBAR, aims:

- to lead cutting edge research in molecular life sciences to the advantage of the society;
- to educate MSc & PhD students and post-docs in biochemistry and applied biosciences.
- to promote protein science by undertaking projects related to protein function, synthesis and transport with high practical impact in biomedicine, nano- & bio-technologies.

**Brief History**. The Institute of Biochemistry was founded in 1952 by Prof. Eugen Macovschi, member of the Romanian Academy as part of the Romanian Academy Institutes Network. In 1972 the Institute was integrated into the Central Institute of Biology and then re-established as an independent public unit by Dr. Cecilia Motaș in 1990, to activate ever since under the aegis of the Romanian Academy as a *Centre of Research and Advanced Education in Molecular Life Sciences and Protein Biosynthesis & Function*.

#### the founders





Eugen Macovschi

Cecilia Motas

In 1998 IBAR was the first Romanian research institution to set off an international peer reviewing program granted by the NATO Scientific Division, under the auspices of the Romanian Academy, with a recall in 2000.

This led to a significant restructuring and refocus reflected in the quality of research which has set new standards to the Romanian biological and medical research. Confirmation came in 2008, when IBAR ranked first at national level in relation to primary criteria /high impact publications/, and overall second behind the "*Octav Mayer*" Institute of Mathematics, in the Accreditations process of the Romanian Research Institutions conducted by ANCS, as stated in the ANCS Decision 9634 from 14.04.2008. In recognition, IBAR was awarded the Award for Excellence in Romanian Research in 2008.

**Current Activity**. IBAR currently carries the research program:

"Molecular Recognition, Signaling and Control Mechanisms in Biological Systems" structured on the following directions:

- Cellular pathways of protein biosynthesis and transport
- Cellular pathways of viral infections and molecular strategies for prevention
- Cellular signaling cascades and the structure and role of signaling enzymes;
- In silico structural biology correlated with experiment
- Protein interactions and bionanotechnologies



IBAR carried and carries also advanced educational programs in the molecular cell biology of protein biosynthesis and traffic such as: -a) the MSc Program in *Biological Chemistry* of the Superior Normal School, SNS Bucharest, -b) the PhD programs in *Biochemistry* and *Molecular Cell Biology* of the School of Advanced Studies of the Romanian Academy, SCOSAAR; -c) the international advanced courses in the *Recombinant DNA Technology* granted by FEBS. These programs seem quite attractive, if judged by the number of attendees and their evaluation. In recognition, in 2010, IBAR was granted from the European Social Fund 4M € for coordinating an Educational Consortium that carries the Post Doctoral Program "*Cellular and Molecular Biotechnologies for Medical Application*", 2010-2013. This Program produced so far 96 research articles in journals with an overall impact factor IF > 180.

Due to the influx of young researchers, IBAR has an average age of the research staff around 40. The fine balance of youth and experience reflected on the results, and made this Centre internationally recognized. For instance, since 1993 IBAR has a unique, special relation with the University of Oxford, and collaborates with many other advanced research centers in US and EU such as the Universities of Yale, Berkeley, Davis, Illinois IT, Lausanne, Wageningen or Gőteborg and Institutes such as Max Plank, NIH Bethesda or INRA.

Along the past three decades many members of IBAR understood to take responsibilities in serving the Romanian biochemists research and education community at national and European level by organizing the Romanian Biochemistry and Molecular Biology Society, its meetings, advanced and permanent education courses, and by representing Romania in FEBS or other international scientific or evaluation bodies. In addition, over the past two difficult years, 2020-2021, many members of IBAR took action in fighting Covid-19 by working or training pro bono personnel in hospital virus testing units, or by undertaking research for rapid Covid-19 test development and antibody generation.

#### **IBAR Structure**

**Board** 

Director:Stefana M.PetrescuStefana.Petrescu@biochim.roDeputy Director:Norica Branza-NichitaNorica.Nichita@biochim.ro

**Departments:** Molecular Cell Biology; Molecular Virology; Bioinformatics &

Biocomputing; Enzymology; Applied bio-nano-technologies.

Personnel

| Positions          |    |
|--------------------|----|
| Researchers        | 27 |
| Research Assitants | 15 |
| Administration     | 6  |
| Total              | 48 |
| PhD Students       | 28 |



#### PostDoc Program "Cellular and Molecular Biotechnologies for Medical Applications":

Co-ordinator Stefana M.Petrescu

#### **SCOSAAR PhD Programs:**

Molecular Cell Biology Molecular Virology Enzymology & Molecular Biology Bioinformatics & Biocomputing Stefana M.Petrescu Norica Nichita Stefan E.Szedlacseck Andrei-J. Petrescu

#### **Members in International Organizations**

ERC: European Research Council

Development Cell Biology Panel 2008 - 2014 Stefana M.Petrescu

ESFRI: European Strategy Forum on Research Infrastructures

Life Science Pannel 2006 - 2009 Stefana M.Petrescu

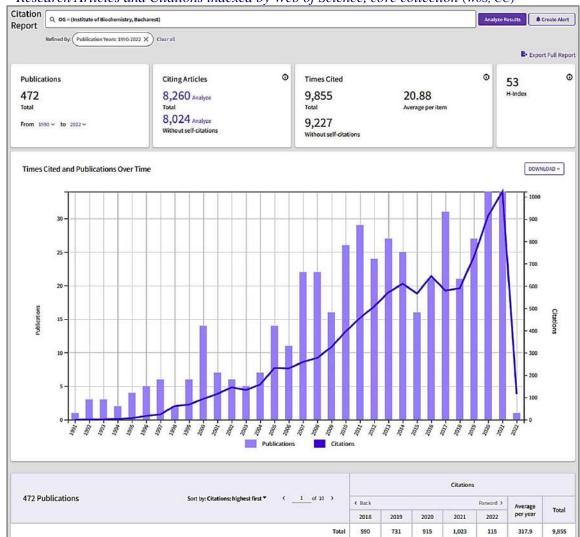
ELIXIR: European Bioinformatics Infrastructure

Bioinformatics Communities Committee 2007 - 2009 Andrei-J Petrescu

#### **IBAR** Activities in a nut shell

#### Research at a Glance

Research Articles and Citations indexed by Web of Science, core collection (WoS, CC)





|              |                              | 2017 | 2018 | 2019 | 2020 | 2021 | Tot              |
|--------------|------------------------------|------|------|------|------|------|------------------|
| Publications | ISI-Publications             | 31   | 21   | 27   | 34   | 34   | >145             |
|              | Overall Impact Factor (ISI)  | >70  | >60  | >120 | >107 | >120 | >475             |
| Visibility   | Overall IBAR Citations (ISI) | 585  | 590  | 731  | 915  | 1023 | >3800            |
| Grants       | International                | 11   | 10   | 9    | 9    | 11   | <sup>av</sup> 10 |
|              | Domestic                     | 14   | 25   | 24   | 22   | 19   | <sup>av</sup> 21 |
| Education*   | PhD Students                 | 17   | 24   | 20   | 23   | 25   | <sup>av</sup> 22 |

#### IBAR researchers with international visibility

researchers that fulfill also the habilitation criteria for PhD coordination

|     |                       | ISI Papers | Citations* | H-Index* | Status |
|-----|-----------------------|------------|------------|----------|--------|
| 1.  | Stefana M. Petrescu   | 75         | > 2500     | 26       | CP1    |
| 2.  | Norica Branza-Nichita | 57         | > 1600     | 23       | CP1    |
| 3.  | Andrei-J Petrescu     | 60         | > 2800     | 27       | CP1    |
| 4.  | Anca Roseanu          | 50         | > 1000     | 15       | CP1    |
| 5.  | Gabriela Negroiu      | 40         | > 850      | 15       | CP1    |
| 6.  | Stefan E.Szedlacsek   | 55         | > 800      | 14       | CP1    |
| 7.  | Trif Mihaela          | 20         | > 700      | 12       | CP1    |
| 8.  | Robi Tacutu           | 30         | > 1300     | 17       | CP2    |
| 9.  | Livia E. Sima         | 60         | > 900      | 18       | CP2    |
| 10. | Lazar Catalin         | 30         | > 450      | 13       | CP2    |
| 11. | Ionut-Costin Popescu  | 20         | > 500      | 9        | CP2    |
| 12. | Sorin Tunaru          | 25         | >1900      | 17       | CP3    |
| 13. | Laurentiu Spiridon    | 25         | > 750      | 13       | CP3    |
| 14. | Cristian V.Munteanu   | 27         | > 200      | 7        | CP3    |

<sup>\*</sup> according to Web of Science, all databases: WoS all DB

#### **IBAR research articles with over 100 citations** (WoS, all DB)

Petrescu AJ; Milac AL; Petrescu SM; Dwek RA; Wormald MR, "Statistical analysis of the 356 protein environment of N-gly sites: implications for occupancy, structure & folding" *Glycobiology* **14** 103-114 (2004) Wormald MR; Petrescu AJ; Pao YL; Glithero A; Elliott T; Dwek RA, "Conformational 337 studies of oligosaccharides and glycopeptides: Complementarity of NMR, X-ray crystallography, and molecular modelling" Chem.Rev. 102 371-386 (2002) Saldova R; Royle L; Radcliffe CM; Hamid UMA; Evans R; Arnold JN; Banks RE; Hutson R; 306 Harvey DJ; Antrobus R; Petrescu SM; Dwek RA; Rudd PM, "Ovarian cancer is associated with changes in glycosylation in both acute-phase proteins and IgG", Glycobiology 17 1344-1356 (2007) Haversen L; Ohlsson BG; Hahn-Zoric M; Hanson LA; Mattsby-Baltzer I, "Lactoferrin down-242 regulates the LPS-induced cytokine production in monocytic cells via NF-kappa B", Cell.Immunol. 220 83-95 (2002) Maekawa T; Cheng W; Spiridon LN; Toeller A; Lukasik E; Saijo Y; Micluta M A; Somssich I 199 E; Takken FLW; Petrescu A-J; Chai J; Schulze-Lefert P, "Coiled-Coil Domain-Dependent Homodimerization of Intracellular Barley Immune Receptors Defines a Minimal Functional Module for Triggering Cell Death" Cell Host & Microbe 9 187-199 (2011)



| 6  | Hinsen K; <u>Petrescu AJ</u> ; Dellerue S; Bellissent-Funel MC; Kneller GR, " <i>Harmonicity in slow protein dynamics</i> ", <i>Chemical Phys.</i> <b>261</b> 25-37 (2000)  | 180  |      |
|----|---|------|------|
| 7  | Zapun A; <u>Petrescu SM</u> ; Rudd PM; Dwek RA; Thomas DY; Bergeron JJM, " <i>Conformation-independent binding of monoglucosylated ribonuclease B to calnexin</i> ", <i>Cell</i> 88 29-38 (1997)  | 174  |      |
| 8  | Plati J; <u>Bucur O</u> ; Khosravi-Far R, " <i>Apoptotic cell signaling in cancer progression and therapy</i> ", <i>Integrative Biology</i> <b>3</b> 279-296 (2011)   | 171  |      |
| 9  | <u>Tacutu R</u> ; Thornton Dl; Johnson E; Budovsky A; Barardo D; Craig T; Diana E; Lehmann G; Toren D; Wang J; Fraifeld V; deMagalhaes J, " <i>Human Ageing Genomic Resources: new and updated databases</i> ", <i>Nucl.Acid.Res.</i> <b>46</b> D1083-1090 (2018)   | 166  |      |
| 10 | Helle F; Vieyres G; Elkrief L; <u>Popescu C-I</u> ; Wychowski C; Descamps V; Castelain S; Roingeard P; Duverlie G; Dubuisson J, "Role of N-Linked Glycans in the Functions of Hepatitis C Virus Envelope Proteins Incorporated into Infectious Virions", <b>J. Virology 84</b> 11905-11915 (2010)   | 154  |      |
| 11 | Neeft M; Wieffer M; de Jong AS; Negroiu G; Metz CHG; van Loon A; Griffith J; Krijgsveld J; Wulffraat N; Koch H; Heckt AJR; Brose N; Kleijmeer M; van der Sluijs P, "Munc13-4 is an effector of Rab27a and controls secretion of lysosomes in hematopoietic cells", Mol. Biol.Cell 16 731-741 (2005)   | 153  |      |
| 12 | Ganea E; Harding JJ, "Glutathione-related enzymes and the eye", Current Eye Res. 31 1-11 (2006)   | 143  |      |
| 13 | MattsbyBaltzer I; Roseanu A; Motas C; Elverfors J; Engberg I; Hanson LA, "Lactoferrin or a fragment thereof inhibits the endotoxin-induced interleukin-6 response in human monocytic cells", <b>Pediatric Res. 40</b> 257-262 (1996)  | 135  |      |
| 14 | Durantel D; <u>Branza-Nichita N</u> ; Carrouee-Durantel S; Butters TD; Dwek RA; Zitzmann N, "Study of the mechanism of antiviral action of iminosugar derivatives against bovine viral diarrhea virus", <b>J. Virology 75</b> 8987-8998 (2001)  | 134  |      |
| 15 | Popescu CI; Callens N; Trinel D; Roingeard P; Moradpour D; Descamps V; Duverlie G; Penin F; Heliot L; Rouille Y; Dubuisson J, "NS2 Protein of Hepatitis C Virus Interacts with Structural and Non-Structural Proteins towards Virus Assembly", PLoS Pathogens 7 e1001278 (2011)   | 122  |      |
| 16 | Slootweg E; Roosien J; Spiridon LN; Petrescu A-J; Tameling W; Joosten M; Pomp R; van Schaik C; Dees Robert; B JW; Smant G; Schots A; Bakker J; Goverse A, "Nucleocytoplasmic Distribution Is Required for Activation of Resistance by the Potato NB-LRR Receptor Rx1 and Is Balanced by Its Functional Domains", Plant Cell 22 4195-4215 (2010) | 122  |      |
| 17 | Plati J; <u>Bucur O</u> ; Khosravi-Far R, " <i>Dysregulation of apoptotic signaling in cancer: Molecular mechanisms and therapeutic opportunities</i> ", <b>J.Cell. Biochem. 104</b> 1124-1149 (2008)   | 120  |      |
| 18 | Tabernero L; Aricescu AR; Jones EY; <u>Szedlacsek SE</u> , " <i>Protein tyrosine phosphatases: structure-function relationships</i> ", <i>Febs Journal</i> 275 867-882 (2008)   | 110  |      |
| 19 | Szedlacsek SE; Duggleby Rg, "Kinetics Of Slow And Tight-Binding Inhibitors", Enzyme Kin.& Mech, 249 144-180 (1995)  | 110  |      |
| 20 | <u>Petrescu AJ; Petrescu SM;</u> Dwek RA; Wormald MR, "A statistical analysis of N- and O-glycan linkage conformations from crystallographic data", <b>Glycobiology 9</b> 343-352 (1999)  | 106  |      |
|    | IBAR research articles in high profile journals ( ${ m IF} > 10$ or ${ m AI} > 5$   | )    |      |
|    |   | AIS  | FI   |
|    | Zhang Y, Cheng TC, Huang G, Lu Q, <u>Surleac MD</u> , Mandell JD, Pontarotti P, <u>Petrescu AJ</u> , Xu A, Xiong Y, Schatz DG. " <i>Transposon molecular domestication and the evolution of the RAG recombinase.</i> ", <i>Nature</i> . <b>569</b> :79-84 (2019).   | 22.0 | 41.0 |
|    | Zapun A, <u>Petrescu SM</u> , Rudd PM, Dwek RA,,Bergeron JJ. "Conformation-independent binding of monoglucosylated ribonuclease B to calnexin." Cell. 88(1):29-38 (1997)  | 26.0 | 38.0 |
|    | Wormald M, <u>Petrescu AJ</u> , PaoYL, Glythero A, Elliot T, Dwek RA "Conformational Studies of Oligosacharides and Glycopeptides", Chem.Rev., 102: 371-387 (2002)  | 13.0 | 21.0 |
|    | Branza-Nichita N, Petrescu A-J, Negroiu G, Dwek RA, Petrescu SM, "N-glycosylation Processing and GP Folding", Chem Rev, 100, 4697-4711 (2000)   | 12.0 | 20.0 |



| Maekawa T, Cheng W, <u>Spiridon LN</u> , Töller A,, <u>Micluta MA</u> , Somssich IE, Takken FLW, <u>Petrescu A-J</u> , Chai J, Schulze-Lefert P, " <i>Coiled-coil domain-dependent homodimerization of intracellular MLA</i> ", <i>Cell Host-Microbe</i> , <b>9(3)</b> , 187-199 (2011)     | 7.0 | 13.0 |
|---|-----|------|
| Avelar RA, Ortega JG, <u>Tacutu R</u> , Tyler EJ,, Fraifeld VE, Bishop CL, de Magalhães JP " <i>A multidimensional systems biology analysis of cellular senescence in aging and disease.</i> ", <i>Genome Biol.</i> <b>21(1)</b> :91 (2020)   | 6.8 | 13.0 |
| Kammenga JE, Doroszuk A, Riksen JA, Hazendonk E, <u>Spiridon L</u> , <u>Petrescu A-J</u> ,, Bakker J "A Caenorhabditis elegans wild type defies the temperature-size rule owing to a single nucleotide polymorphism in tra-3.", <b>PLoS Genet. 3(3)</b> , e34 (2007)                        | 6.0 | 9.0  |
| Wróblewski T, <u>Spiridon L</u> , <u>Martin EC</u> , <u>Petrescu AJ</u> , Cavanaugh K, J, Michelmore RW, Takken FL " <i>Genome-wide functional analyses of plant CC-NLR-type pathogen receptors</i> ." <i>PLOS Biology</i> <b>16(12)</b> : e2005821 (2018)                                  | 5.5 | 9.0  |
| <u>Petrescu A-J</u> , Wormald MR, Dwek RA., "Structural aspects of glycomes with a focus on N-glycosylation and glycoprotein folding.", <b>Curr Op Str Biol</b> , <b>16</b> , 600-607 (2006)  | 5.0 | 9.5  |
| Vlad MO, Morán F, Popa VT, <u>Szedlacsek SE</u> , Ross J. "Functional, fractal nonlinear response with application to rate processes with memory, allometry, and population genetics." <b>Proc</b> Natl Acad Sci U S A. 104(12):4798-803. (2007)  | 5.0 | 9.5  |
| Vlad MO, <u>Szedlacsek SE</u> , Pourmand N, Cavalli-Sforza LL, Oefner P, Ross J. "Fisher's theorems for multivariable, time- and space-dependent systems, with applications in population genetics and chemical kinetics." <i>Proc Natl Acad Sci U S A</i> . <b>102(28)</b> :9848-53 (2005) | 5.0 | 9.5  |
| Slootweg E, Roosien J, <u>Spiridon LN</u> , <u>Petrescu A-J</u> , Tameling W,, Bakker J, Goverse A. "Nucleocytoplasmic Distribution is Required for Activation of NB-LRR Receptor Rx1 and is Balanced by its Functional Domains.", <b>Plant Cell</b> , <b>22(12)</b> : 4195-4215 (2010)     | 4.0 | 10.0 |
| <u>Tacutu R</u> , Thornton D, Johnson E, Budovsky A,, Fraifeld VE, de Magalhães JP. " <i>Human Ageing Genomic Resources</i> ." <i>Nucl.Acid.Res.</i> <b>46(D1)</b> :D1083-D1090 (2018)  | 3.6 | 11.0 |
| Kozuki T, Chikamori K, <u>Surleac MD</u> , <u>Micluta MA</u> , <u>Petrescu AJ</u> , Norris EJ,, Ganapathi MK "Roles of the C-ter domains of topoisomerase IIα and IIβ in regulation of the decatenation checkpoint. <i>Nucl. Acid Res.</i> <b>45(10)</b> :5995-6010 (2017)                  | 3.6 | 11.0 |
|   |     |      |

#### **IBAR Main International Grants (2000-2022)**

#### 2000 - 2010

- UK Wellcome Trust (1998-2001): "N-glycosylation and folding of human and mouse tyrosinases", Dr. Petrescu S-M
- UK Wellcome Trust (2001-2004): "Morphogenesis of BVDV Virus", Dr. Branza-Nichita N
- EU FP5 Integrated Project (2002-2004): "NONEMA", Dr. Petrescu A.-J.
- EU FP6 Marie Currie (2006-2010) "PTPNET", Dr. Szedlacseck SE

#### 2010 - 2022

- CH-Ro Collaborative Grant (2012-2015) "*ERAD Pathway*", Dr. Petrescu S-M
- EEA/2013 RO-NO-5 (2014-2017) "GREENVAC", Dr. Norica Nichita
- ERANET-2014 (2014-2017) "*HCVASSEMBLY*", Dr. Popescu C. I

- UK Wellcome Trust (2001-2004):
  "Chaperone mediated folding of tyrosinase",
  Dr. Petrescu S-M
- UK Wellcome Trust (2002-2005):"A database with structural information of glycoproteins", Dr. Petrescu A.-J.
- EU FP6 Integrated Project (2005-2011): "BIOEXPLOIT", Dr. Petrescu A.-J.
- EU FP6 Marie Currie (2005-2007) "*HDPTP*", Dr. Tanase C
- EU FP7 COST (2013-2016) "EFFECTOME", Dr. Petrescu A-J
- EEA/2013 RO-NO-47 (2014-2017) "YePlaHeMe", Dr. Petrescu A-J
- ERANET-2014 (2016-2019) "*HCVAsmImage*", Dr. Popescu I



- ERANET-2016 53 (2016-2019) "INinRAGI", Dr. Petrescu A-J
- EUK-2017-02-0030 (2018-2021) "*XploitAD* ", Dr. Milac A
- EEA/2019 RO-NO-1 (2019-2021) "SmartVac", Dr. Norica Nichita
- H2020 MSCA-RISE-2016 (2017-2022) "LysoMod", Dr. Petrescu S-M
- ERA-NET NEURON III (2019-2022) "EMBED", Dr. Tacutu R
- EEA/2021 RO-NO-34 (2021-2023) "NEXTDRUG", Dr. Tunaru Sorin

#### **IBAR** organised international events:

- 2000 FEBS Workshop "Biochemical research in Eastern Europe"
- 2001 FEBS Course "DNA Recombinant Technology"
- 2001 The 12th Meeting "Balkan Biochemical Biophysical Days"
- 2003 FEBS Course " DNA Recombinant Technology and Protein Expression"
- 2004 The Conference "Glycosylation and Disease"
- 2005 The FEBS-IUBMB Satellite Meeting "Protein Folding in Health and Disease"
- 2005 FEBS Course "DNA Recombinant Technology and Protein Expression"
- 2008 FEBS Course "DNA Recombinant Technology and Protein Expression"
- 2010 The Conference "Life and Chemistry" honorring Barry Blumberg, Nobel Price
- 2010 The Diaspora Conference "Trends in medical genomics and proteomics"
- 2000-2018 The Annual International Meetings of RSBMB (the Romanian Society of Biochemistry and Molecular Biology)

#### **IBAR Alumni**

#### **Exquisite PhD Graduates of IBAR, since 2000**

Nichita-Branza Norica, 2000, suma cum laude: "The Study of tyrosinase folding mechanisms by",

Costin Emilia, 2001, cum laude: "The uptake and transport of N-glycosylation modulators",

Constantinescu Alexandru, 2002, magna cum laude: "Structural and functional studies on the small Ypt7p",

Fulga Tudor, 2002, cum laude: "Functional characterisation of the mamalian SRP receptor",

Cismasiu Valeriu, 2003, cum laude: "Structure and activity of receptor PTPases",

*Milac Adina-Luminita*, 2004, cum laude: "Knowledge-based analysis of protein structures and complexes",

**Paduraru Crina**, 2007, magna cum laude: "The role of N-linked glycans in intracellular processing of CD1d protein"

Catalin Lazar, 2008, magna cum laude: "Characterisation of BVD Virus system as in vitro model to study HepC Virus"

Alina Macovei, 2009, magna cum laude: "Host Cell Factors Involved in Enveloped Viruses Entry and Morphogenesis"

Livia Sima, 2011, cu distinctia foarte bine: "Molecular Mechanisms of Melanoma Antigen Presentation"

**Laurențiu Spiridon**, 2011, suma cum laude: "Investigation of Protein Structure and their PTM using Bioinformatics"

**Bucur Octavian**, 2014, suma cum laude: "Novel Regulatory Mechanisms of FOXO3/1 Tumor Suppresor"



Chiritoiu Marioara, 2014, magna cum laude: "Role of EDEM3 in ERAD"

Munteanu Cristian, 2016, suma cum laude: "Insights into functional Interaction Proteomics of ERAD"

*Chiritoiu Gabriela*, 2016, magna cum laude: "Role of N-glycosylation and functional ERAD in modulation of tyrosinase immunogenicity"

Surleac Marius, 2017, magna cum laude: "Metode de Calcul cu Utilizări în Modelarea și Simularea Moleculară"

**Dobrică Olivia**, 2018, suma cum laude: "Obținerea de Noi Antigene Virale pentru Producerea de Vaccinuri pentru Hepatitele B & C"

#### Exquisite MSc and Undergraduate students trained in IBAR, since 2000

Aricescu Radu, PhD University Colledge London, PostDoc Univ of Oxford, UK

Creangă Adrian, PhD student at John Hopkins University, Maryland, US

Denes Alexandru, PhD student at EMBL Heidelberg, D

Giambasu Madalin, PhD at Minessotta Univ, USA; Post Doc Rutgers Univ USA

Moldovan Lucian, PhD at MPI Munchen, D, Post Doc, Harvard US

Pena Vlad, PhD at EMBL Heidelberg, D; Group Leader at MPI Gottingen, D

Tăcutu Robi, PhD at Ben Gurion Univ. Is; Post Doc Liverpool Univ. UK

Dorobantu (Radulescu) Cristina, PhD at Radboud Univ. Nijmegen, NI;

Căldăraru Octav, PhD at Lund Univ. Sw; Res. Zealand Pharma



## **IBAR Departments**

https://www.biochim.ro/research-groups/



#### DEPARTMENT OF MOLECULAR CELL BIOLOGY.

#### **Members:**

Stefana M. Petrescu, PhD – Head Gabriela Negroiu, PhD – Senior Res. Simona Ghenea, PhD – Senior Res. Marioara Chiritoiu, PhD – Senior Res. Livia Sima, PhD – Senior Res. Ioana Popa, PhD – Senior Res. Florentina Pena PhD - Senior Res. Gabriela Chiritoiu, PhD- Senior Res. Petruta Alexandru, PhD Anca Filimon, PhD Ioana Militaru, PhD student Alina Rus, PhD student Andreea Anghel, PhD student



#### **Main Focus:**

"Cellular pathways of protein biosynthesis and transport"

#### **Current Work**

Protein homeostasis is fundamental for cell function and survival because proteins are critical facilitators of all cellular processes. Our goal is to better understand the processes that maintain the fine balance between newly synthesized and old or misfolded proteins, preserving the protein homeostasis and preventing various diseases. Current projects in the laboratory are focused therefore on processes regulating protein lifetime: protein folding and maturation, trafficking, subcellular localization and degradation. Our research explores new ways of investigating the quality control process occurring in the endoplasmic reticulum that facilitates protein secretion towards the Golgi apparatus whilst regulating degradation of misfolded proteins by ERAD pathways.

Protein processing with focus on antigen processing and presentation is currently investigated and aims at determining the exact role of ERAD components in the generation of tyrosinase-derived tumour antigens. Understanding of basic mechanisms of antigen processing and presentation to T cells will provide valuable clues to enhance the efficacy of peptide-based cancer vaccines. Deciphering the pathways mediated by the tyrosinase-related antigen, TRP-2 is another focus of our group aiming at uncovering the potential implications of this antigen in the prognostic and therapy of malignant melanoma.

We develop new tools to extend our knowledge on the role of ERAD in the endoplasmic reticulum of secretory cells. Proinsulin matures in the endoplasmic reticulum of pancreatic  $\beta$ -cells and depending on the ER folding capacity is either secreted or destroyed. Our hypothesis is that up-regulation of ERAD enhancers may alleviate the ER burden in pancreatic  $\beta$ -cells by recruiting misfolded proteins for degradation. To verify this hypothesis



we use model  $\beta$ -cells, intact primary islets and animal models with modified ERAD and test the insulin secretion upon glucose-stimulation.

#### **Future Projects**

In the next years our research will focus on the molecular mechanisms of the folding and intracellular transport of soluble and membrane bound glycoproteins. In particular, melanoma proteins will be investigated in terms of maturation, degradation and antigen presentation.

#### **Selected Publications**

- 1. Sima LE, et al. "Loss of host tissue transglutaminase boosts antitumor T cell immunity by altering STAT1/STAT3 phosphorylation in ovarian cancer" *J.Imm.Ther.Cancer*, *9*:e002682 (2021) IF= 13.7
- Anghel SA et al. "Promising Epigenetic Biomarkers for the Early Detection of Colorectal Cancer: A Systematic Review". *Cancers*, 13(19):4965, (2021).
- 3. Munteanu CVA, Chiriţoiu GN, Chiriţoiu M, Ghenea S, Petrescu AJ, Petrescu ŞM. "Affinity proteomics and deglycoproteomics uncover novel EDEM2 endogenous substrates and an integrative ERAD network." *Molecular & Cellular Proteomics e100125*. (2021) IF=5.91
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#### DEPARTMENT OF MOLECULAR VIROLOGY

#### **Members:**

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#### **Main Focus**

Cellular pathways of viral infections and molecular strategies for prevention. Development of novel antiviral strategies against Hepatitis B and C viruses. HBV infection and morphogenesis

#### **Current Work**

The Viral Glycoproteins group was founded in 2002 with the aim to apply the methods developed in the Institute for the study of glycoprotein folding, to a more specific but highly challenging field of molecular biology, the viral envelope packing.

Human hepatitis B and C viruses cause infections of the liver. Worldwide about 300 million people are chronically infected with either HBV or HCV. Of these patients, more than 500.000 die annually from complications of liver disease. Most of these cases occur in developing countries resulting in widespread social and economic problems, especially among the poor people. Sadly, Romania has the highest prevalence of HBV/HCV infections among the EU countries (up to 7% of the population).

Current therapies against HBV, based on replication inhibitors and immune system activators, are associated with severe side effects, resulting frequently in early discontinuation of treatment, while the HCV direct acting antivirals of novel generations are very costly and their use is limited to advanced liver disease. In addition, both viruses are prone to development of resistance to antiviral inhibitors, which reduces significantly the efficiency of treatment. Efficient anti- HBV vaccines are available on market; however, up to 10% individuals fail to develop a protective immune response and remain exposed to infection. In the case of HCV, although intensive research is undergoing, no vaccine has been developed yet and 3-4 million of new infections are expected to occur every year.

Our group is focused on i) studying the interaction between HBV/HCV and their host, the human hepatocyte and identifying novel cellular factors and pathways involved in viral assembly and trafficking that could be targeted by antiviral therapies; ii) designing new viral antigens with improved immunogenic properties; iii) producing these antigens at low costs, using complementary expression systems such as plants and insect cells; iV) developing



improved assays adapted for highthroughput screening of chemical compounds with antiviral properties; v) educating and training young researchers in the molecular virology field.

#### **Future Projects**

Future projects wiill continue to address production of novel HBV/HCV antigens with improved immunogenic properties, in a cost-effective manner and the role of inositides in the HBV/HCV life cycles.

#### **Selected Publications:**

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#### DEPARTMENT OF ENZYMOLOGY.

#### **Members**

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Ionescu Aura, PhD
Alexandra Bănică, PhD Student
Cosmin Trif, PhD Student
Andrei Vasilescu, PhD Student
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#### **Main Focuss:**

Cătălin Bică, Tech.

"Cellular signalling cascades and the structure and role of signalling enzymes".

#### **Current Work**

The central research topic of the group is the study of the structure-function relationships of signaling enzymes, with emphasis on tyrosine phosphatase proteins. We aim to contribute to the understanding of how their structural characteristics are correlated with specific signaling functions. To this end, we analyze each signaling enzyme that we investigate from several directions:

- as a classical enzyme, trying to evaluate its stability under different conditions, pH dependence of activity, specific activity, kinetic parameters at steady state, substrate specificity and also the identification of specific inhibitors as well as the corresponding inhibition constants;
- as a protein, trying to crystallize the purified enzyme preparation and then determine its 3D structure
- as a signaling entity, trying to find its subcellular location, physiological substrate (s), regulatory interactions, the role played in signaling pathways, etc.

The combination of results thus obtained in this way is further used to shed light on the signaling mechanism and the overall functional role of the given enzyme.

The group has good experience and is currently involved in the production, isolation and purification of recombinant proteins, expressed in both prokaryotic and eukaryotic systems. The research activity of the group is performed by molecular biology instruments (recombinant DNA. site-directed mutagenesis, (RT) -PCR, Western blot. immunoprecipitation, spectroscopic analysis (UV-VIS fluorescence etc.). and spectrophotometry), cell biology, protein crystallization and enzyme kinetic analysis.

Our team is involved in numerous national research projects and international collaborations. Thus, the specific research projects in progress are:

• Identification of signaling mechanisms involved in tumorigenesis, as a result of dephosphorylation by EYA3 of the specific substrate WDR1;



- Study of the mechanism of action of some interference peptides involved in inhibiting the internalization of AMPA neuronal receptors;
- Identification of new tumor markers in acute myeloid leukemia, thyroid cancer, lung cancer, colorectal cancer. Potential ways of targeted diagnosis;
- Design and laboratory experimentation of a molecular vector based on Holmium166 for targeted radiodiagnosis and radiotherapy.

#### **Selected Publications**

- Patras L, Ionescu AE, Munteanu C, Hajdu R, Kosa A, Porfire A, Licarete E, Rauca VF, Sesarman A, Luput L, Bulzu P, Chiroi P, Tranca RA, Meszaros MS, Negrea G, Barbu-Tudoran L, Potara M, Szedlacsek S, Banciu M." Trojan horse treatment based on PEG-coated extracellular vesicles to deliver doxorubicin to melanoma in vitro and in vivo.", Cancer Biol Ther. 2021 Dec 29:1-16. doi: 10.1080/15384047.2021.2003656. Online ahead of print. PMID: 34964693
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#### **Main Focuss**

"In silico structural biology correlated with experiment"

#### **Mission Statement**

The Department of Bioinformatics & Structural Biochemistry (DBSB) was set in 1999 as the first research unit in Romania aiming by mission to consistently implement computational biology techniques - bioinformatics, modeling, simulation - and use them to guide experimental research in molecular biology and biochemistry.

#### Overview

The Department of Bioinformatics & Structural Biology was funded in 1999 by Andrei-J. Petrescu and have function ever since aiming to consistently implement biocomputing techniques in the realm of bioinformatics, modeling & simulation - and use them to guide experimental research in molecular biology and biochemistry. Since then, the Department deliver structural bioinformatics and molecular modeling results in investigating glycoprotein folding and degradation, the relation between glycosylation and glycoprotein's structure, and more generally studying the biophysical aspects of protein folding, structure and interactions. Currently, the group develops techniques computational techniques in this field and applies them to a variety of problems in structural biology, immunobiology, molecular medicine and in silico pharmacology.

In 2012, Adina Milac († 2019), with her PhD in DBSB, returned from the National Institute of Health, NIH Bethesda, USA, where she carried out two PostDoc stages in Lawrence Tabak's and Robert Guy's lab. Adina brought in fresh molecular modeling and simulation techniques and new research topics related to structure-function relation in ion-channel systems and drug-design.

In 2016, Laurentiu Spiridon, with his PhD in DBSB, also returned from a PostDoc at the Illinois Institute of Thechnology in David Minh Lab. Laur has brought in new Free-Energy computational methods that we are currently using in ligand screening and drug design. Since his return Laur has actively worked to develop a new generation of Gibbs sampling techniques based on robotic algorithms that have been implemented in the Robosample simulation platform.



Another research direction we pursue is led by Cristian Munteanu who focused on coupling computational techniques with Mass Spectrometry, Surface Plasmon Resonance and data derived from the high-throughput Drug Screening Platform of the Institute, aiming to step up the scale of biological system investigation to the global proteome and interactome level.

Since 2016, the department greatly increased its size, with the addition of the Computational and Systems Biology of Ageing Group led by Robi Tacutu, also a DBSB alumni who recently returning to the Institute from the University of Liverpool, UK. Robi's group is developing and using bioinformatics tools and omics data to better understand the ageing process and agerelated diseases. The group has a strong multidisciplinary background, mixing gerontology, bioinformatics and machine learning techniques in order to analyze large amounts of data from heterogenous high-throughput technologies and from a wide variety of OMICS.

The department is supported by the computational infrastructure provided by the High Performance Computing Centre, one of the central facilities of the Institute, which is smoothly run by Dr. Marius Micluta, and is vital to our molecular simulations and bioinformatics analyses.

#### **Present work and future prospects**

We have ongoing projects to developing new statistical and machine learning techniques useful in biocomputing and bioinformatics. Another priority of DBSB in the near future will be to coupling computational techniques with Mass Spectrometry, Surface Plasmon Resonance and data derived from the Highthroughput Drug Screening Platform of IBAR, aiming to step up the scale of biological system investigation to global proteome and interactome level.

#### **Selected Publications**

- 1. <u>Munteanu CVA, Chirițoiu GN, Chirițoiu M, Ghenea S, Petrescu AJ, Petrescu ȘM</u>. "Affinity Proteomics and Deglycoproteomics Uncover Novel EDEM2 Endogenous Substrates and an Integrative ERAD Network", **Mol Cell Proteomics**. **20**:100125 (2021).
- 2. <u>Matei IV, Samukange VNC, Bunu G, Toren D, Ghenea S, Tacutu R</u>. "*Knock-down of odr-3 and ife-2 additively extends lifespan and healthspan in C. elegans.*" *Aging*, **13(17)**, 21040-21065 (2021)
- 3. <u>Constantinescu V</u>, Chiru C, Boloni T, Florea A, <u>Tacutu R</u>. "*Learning flat representations with artificial neural networks*." *Applied Intelligence*, 2456–2470. (2021)
- 4. <u>Kulaga AY</u>, <u>Ursu E</u>, <u>Toren D</u>, Tyshchenko V, Guinea R, Fraifeld VE, <u>Tacutu R</u>, "*Machine Learning Analysis of Longevity-Associated Gene Expression Landscapes in Mammals.*" *Int.J.Mol.Sci*, **22(3)** (2021).
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- 7. <u>Toren D, Kulaga A</u>, Jethva M, Rubin E, Snezhkina AV, <u>Tacutu R</u>, Moskalev AA, Fraifeld VE. "*Gray whale transcriptome reveals longevity adaptations associated with DNA repair and ubiquitination.*" *Aging cell*, **19(7)**:e13158. (2020)
- 8. Baudin M, Martin EC, Sass C, Hassan JA, Bendix C, Petrescu AJ, Lewis JD. "A natural diversity screen in Arabidopsis thaliana reveals determinants for HopZ1a recognition in the ZAR1-ZED1 immune complex." Plant Cell Environ.;44(2):629-644 (2021)



- 9. <u>Bunu G, Toren D, Ion CF</u>, Barardo D, <u>Sârghie L</u>, Grigore LG, de Magalhães JP, Fraifeld VE, <u>Tacutu R</u>. "SynergyAge, a curated database for synergistic and antagonistic interactions of longevity-associated genes." *Scientific data*, **7(1)**:366. (2020)
- 10. <u>Martin EC</u>, Vicari C, Tsakou-Ngouafo L, Pontarotti P, <u>Petrescu AJ</u>, Schatz DG. "*Identification of RAG-like transposons in protostomes suggests their ancient bilaterian origin.*" *Mob DNA*. 11, 17 (2020).
- 11. <u>Spiridon L</u>, <u>Sulea TA</u>, Minh DDL, <u>Petrescu AJ</u>. "Robosample: A rigid-body molecular simulation program based on robot mechanics." **Biochim Biophys Acta Gen Subj. 1864(8)**, 129616. (2020)
- 12. <u>Martin EC</u>, Sukarta OCA, <u>Spiridon L</u>, Grigore LG, <u>Constantinescu V</u>, <u>Tacutu R</u>, Goverse A, <u>Petrescu A-J</u>, "*LRRpredictor A New LRR Motif Detection Method for Irregular Motifs of Plant NLR Proteins Using an Ensemble of Classifiers*", *Genes* 11(3), 286-300 (2020)
- 13. Avelar RA, Ortega JG, <u>Tacutu R</u>, Tyler EJ, Bennett D, Binetti P, Johnson E, Thornton D, Fraifeld VE, Bishop CL, de Magalhães JP . "A multidimensional systems biology analysis of cellular senescence in aging and disease." *Genome biology*, **21(1)**: 91 (2020)
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- 16. <u>Munteanu CVA</u>, Chiriţoiu GN, <u>Petrescu AJ</u>, Petrescu ŞM. "*Profiling Optimal Conditions for Capturing EDEM Complexes in Melanoma Using Mass Spectrometry*." *Adv Exp Med Biol.*, **1140**, 155-167 (2019)
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#### DEPARTMENT OF PROTEIN INTERACTIONS & BIONANOTECHNOLOGIES.

#### **Members:**

Anca Roseanu, PhD. – Head Mihaela Trif, PhD. – Senior Res. Paula Florian, PhD. – Senior Res. Madalina Icriverzi, PhD – Res.



#### **Main Focus:**

Protein interactions and bionanotechnologies. Anti-inflammatory and immunomodulatory activities of Lactoferrin

#### **Current Work**

Lactoferrin (Lf) is an iron binding glycoprotein of transferrin family, present in almost all mammalian secretions and neutrophils. A variety of biological functions have been ascribed to Lf, including anti-inflammatory and immunomodulatory effects. The protective action of Lf during inflammation is related to its influence on cytokine production and capacity to bind potentially toxic iron at inflammation foci. In our previous studies performed in collaboration with the Department of Clinical Bacteriology, University of Goteborg, we found that LPS (lipopolysaccharide) -induced cytokine production, in particular TNF-a, IL-1 $\beta$ , IL-6, are inhibited by Lf. The binding of protein to LPS could partly explain its inhibitory activity since the effect could be seen when Lf was added before as well after cell stimulation. This suggests that other mechanism(s) than simple LPS scavenging property of Lf is (are) responsible for the inhibitory activity.

In this respect, our group approaches two aspects:

The mode of action of Lf on intracellular signal transduction pathways.

Our preliminary results showed that Lf is taken up by monocytic cells. Therefore it is possible that Lf, following the binding to the cells, might affect some intracellular pathways involved in the cell response to external stimuli such as bacterial endotoxins. LPS stimulation of monocytes has been shown to induce the activation of three subgroups of MAPKinase familly-p38, ERK1/2 and JNK. These enzymes play an important role in the control of proinflammatory cytokine production mediated by LPS. We propose to study the effect of Lf on the phosphorylation and activation of MAPKinases in the presence/absence of LPS. The results will be related to the effect of Lf on the LPS-induced cytokine production in monocytic THP-1 cells. This aspect involves collaboration with Dr. Inger Mattsby-Baltzer group from the Department of Clinical Bacteriology, University of Gothenburg, Sweden.

The anti-inflammatory properties of Lf in vivo: use of liposomes as possible carriers for Lf in the treatment of Rheumatoid Arthritis.

Exhibiting antimicrobial and anti-inflammatory activities Lf could have therapeutic potential in arthritic disease. We are investigating the ability of free and liposome-entrapped Lf to reduce inflammation when administrated to the joint. Current studies aim to establish the



suitable liposomal formulation able to deliver Lf efficiently into the joint of mice with collagen-induced rheumatoid arthritis. Liposomes-entrapped Lf is expected to serve as a better tool and therapeutic agent against inflammation. This part is developed in collaboration with Dr. James Brewer group from the Department of Clinical Immunology, Glasgow University, UK, coordinated by Prof. F. Y. Liew.

The project should provide important information for understanding the anti-inflammatory activity of Lf in vivo.

#### **Future projects**

In the next years our research will focus on the cellular and molecular mechanisms involved in the anti-inflammatory and immunomodulatory activities of Lf.

#### **Selected Publications**

- 1. Bonciu AF, <u>Orobeti S, Sima LE, Icriverzi M</u>, Filipescu M, Moldovan A, Popescu A, Dinca V, Dinescu M, "Pyramidal shaped ceria nano-biointerfaces for studying the early bone cell response." **Appl.Surf.Sci.**, **533(10)**. (2020)
- 2. <u>Icriverzi M</u>, Dinca V, <u>Moisei M</u>, Evans RW, <u>Trif M</u>, <u>Roseanu A</u>. "*Lactoferrin in Bone Tissue Regeneration*." Curr.Med.Chem, 12(16). (2019)
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- 11. <u>Florian PE</u>, Rouillé Y, Ruta S, <u>Nichita N</u>, <u>Roseanu A</u>, "*Recent advances in human viruses imaging studies*." *J.Basic.Microbiology*, **56(6)**:591-607. (2016)
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## **IBAR Core Facilities**







#### The PROCERA Project 2010 - 2012

"Development of IBAR research infrastructure for increasing research capacity in biomedical proteomics" - 28.400.000 Lei

The PROCERA Project was aimed to upgrade the facility core of IBAR in order to increase its research capacity in biochemistry and molecular biology. The project created the stage for high quality results and inovation with increased economical potential, in line with the aims of European Knowledge-Based Bio-Economy – KBBE. Procera set up the following openaccess laboratories:

Molecular Biomarkers; Proteomics; Structural Biochemistry; Medical Glycobiology; Bioinformatics & Biocomputing; Nanotech & Biocompatibility; Antiviral drugs equipped with cutting-edge equipment for analysis of the structure, function, biosynthesis and systems biology of proteins and for the development of easily transferable applications in clinical and pharmaceutical industry.



#### General, Analytical & Structural Biochemistry





Facilities for recombinant DNA technology; FPLCs, HPLCs, Ultra & Bench Centrifuges, Scanner Difractometer; Spectrophotometers; Nanodrop spectrofluprimeters; Dark room etc.

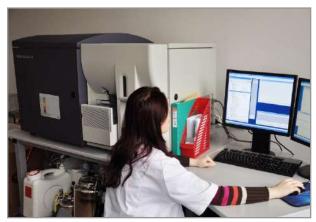


#### Molecular Biomarkers & Bionanotechnologies









Mamalian cell culture facilities; Confocal, Fluorescence & Stereo Microscopes; Flow and Sorting Cytometres; Ultracentrifuges; Radioactivity Facilities for Pulse Chase & IPP; Liposome Preparation Facility; HPLC; Laser Nefelometer for Colloid Characterization System for Quantitative Histo-microsopy

#### **Proteomics**





2D Electrophoresis; Mass Spectrometry; Surface Plasmon Resonance



## **Medical Glycobiology**





HP Anion. Exch. Cromatograph; Integrated ELISA-FRET system; Phosphoimmager

### **Bioinformatics & Modelling Laboratory**





High Perf. Computing Center; Graphic Stations; Biocomputing Softwares; Data Bases

#### **Antiviral drugs**





P2 Facility for viral investigation; Automated Highthroughput Drug Screening Facility; Preparative Ultracentrifuge



## **Advanced Research Training Programs** coordinated by IBAR









2007-2013





#### **Example: The Postdoctoral Program** "Cellular and Molecular Biotechnologies for Medical Application" 2010 - 2013

The Postdoctoral fellowship Program: "Celluar and Molecular Biotechnologies for Medical Application" carried out by a Consortium formed by: IBAR; USAMV Cluj; Clinical Institute Fundeni; INFLRP Magurela; the UMF Timisoara; and the Faculty of Chemistry, University of Bucharest aimed at training of young PhDs in biology, chemistry, physics medical & pharmaceutical sciences for careers in research on the following research topics:

- Genomics, Proteomics, Metabolomics and Bioinformatics;
- -b) Molecular Cell Biology;
- Cellular Therapies; -c)
- Biomaterials, nanostructures and pharmacophores. -d)

#### Post Doc Researchers and their Topics



**Simona Ghenea** - IBAR, former: Post.Doc. at Queens University, Canada Research Topics: "Protein celluar homeostasy in normal and pathological states"



**Ioan-Costin Popescu** - IBAR former: PhD at University of Oxford, UK Research Topics: "The morfology and intracellular trafic of Hep B & C viruses"



former: PhD at University of Utrecht, thr Netherlands Florentina Pena - IBAR Research Topics: "Hipoxy and unfolded protein accumulation in cancer"



**Ioana Popa -** IBAR former: PhD at University of Utrecht, thr Netherlands Research Topics: "Modulation of the receptor expression for advanced glycosylation products in diabetes and inflamatory diseaes"



**Laurentiu Spiridon** - IBAR former: PhD at IBAR Research Topics: "Development of bioinformatics methods for proteomics"



Adina Milac - IBAR, former: Post.Doc. at NIH Bethesda, USA

Research Topics: "Computational models of structure and function of biomedically relevant proteins and their interaction with potential drugs"



**Diana David-Rus** - IBAR, former: PhD at Rutgers University, USA

Research Topics: "Bioinformatics and mathematical modeling of epigenetic and aging processes"



Catalin Lazar - IBAR former: PhD at IBAR

Research Topics: "The morfology and intracellular trafic of Hep B & C viruses"



**Alina Macovei -** IBAR *former*: PhD at IBAR

Research Topics: "The morfology and intracellular trafic of Hep B & C viruses"



**Corina Flangea** - IBAR, *former*: PhD at UMF Timisoara

Research Topics: "Mass Spectrometry of Endoplasmic Reticulum-Associated Protein Degradation (ERAD) products"



**Lisandru Daniela** - IBAR, *former*: PhD Institute of Virology, Romanian Acad.

Research Topics: "Molecular mechanisms of endoplasmic reticulum stress and pancreatic beta cells"



Vargolici Bogdana - IBAR, former: PhD UMF Bucuresti.

Research Topics: "Pancreatic beta-Cells in Diabetes and Regenerative Medicine."



**Zurac Sabina** - IBAR, former: PhD UMF Bucuresti.

Research Topics: "Mechanisms involved in tumor regression in malignant melanoma and corroboration with prognostic factors and disease progression."



Georgiana Petrareanu - IBAR, former: PhD IBAR.

Research Topics: "The structure and function of cellular signaling enzymes."



**Mihaela Menzel** - IBAR, *former*: PhD IBAR.

Research Topics: "The structure and function of cellular signaling enzymes."



**Vulpe Silviu** - IBAR, *former*: PhD University of Bucharest.

Research Topics: "Biopolymer fibers with magnetic mineral nanoparticles insertion for controlled release of drugs."



**Oana Craciunescu** - IBAR, *former*: PhD University Polytehnica Bucharest.

Research Topics: "Lipid nanostructures as controlled delivery systems for antiinflammatory bioactive molecules."





**Daniela Cucu** - Fundeni Clinics, *former*: PhD Catholic University Leuven, Belgium. Research Topics: "The desmoplastic reaction and pancreatic cancer progression."



**Tudor-Rasvan Grigorie** - Fundeni Clinics, *former*: PhD UMF Bucharest. Research Topics: "Applied genomics for organ and cellular transplant."



Catalina Luca - Fundeni Clinics, former: PhD University of Bucharest. Research Topics: "Hematopoietic stem cell therapies in Hepatic Disease."



Laura Buburuzan - Fundeni Clinics. former: PhD Iasi University. Research Topics: "Applied genomics for organ and cellular transplant."



**Luminita Ivan** - Fundeni Clinics, former: PhD "N Simionescu" Institute, Rom.Acad. Research Topics: "Pancreatic beta-Cells in Diabetes and Regenerative Medicine."



Bleotu Coralia - Fundeni Clinics, former: PhD Inst. of Virology, Romanian Acad. Research Topics: "Cellular therapy in pancreatic disorders."



Anca Botezatu - Fundeni Clinics, former: PhD Inst. of Virology, Romanian Acad. Research Topics: "Epigenetics of pancreatic oncogenesis for biomarker identification."



**Valentin Ordodi** - UMF Timisoara, *former*: PhD UMF Timisoara. Research Topics: "Mesenchymal stem cell diferentiation toward adipocytes."



**Maria Bojin** - UMF Timisoara, *former*: PhD UMF Timisoara. Research Topics: "Comparative studies on Mesenchymal stem cell and tumoral fibroblasts."



**Alexandra Boleman-Ivan** - UMF Timisoara, *former*: PhD UMF Timisoara. Research Topics: "Mesenchymal stem cell therapies for re-epithelisation."



**Dumitrita-Olivia Rugina** - USAMV Cluj, *former*: PhD USAMV Cluj. Research Topics: "Metabolomics - molecular markers for taxonomical recognition."



Simona-Ioana Vicas - USAMV Cluj, former: PhD USAMV Cluj. Research Topics: "Glucosinolates, molecular markers of Brassica vegetables."





Sonia-Ancuta Socaci - USAMV Cluj, former: PhD USAMV Cluj.

Research Topics: "Applied chemometry for food authentification."



**Cristian D Ene** - University of Bucharest, former: PhD University of Bucharest. Research Topics: "Controled sythesis and screening of streso-protector compounds."



Augustin M Ofiteru - University of Bucharest, former: PhD University of Bucharest

Research Topics: "Investigation of cellular response to abiotic stress conditions in S.cerevisiae."



Magdalena Ulmeanu - INFPLR (Lasers), former: PhD University of Bucharest

Research Topics: "Biomaterials Laser Nanostructuring for Pharmaceutical Application, Treatment and Organ Cell Reconstruction."



Catalin R Luculescu - INFPLR (Lasers), former: PhD Tohoku University, Japan

Research Topics: "Nanostructures for controlled drug release."



Carmen C Surdu-Bob - INFPLR (Lasers), former: PhD Aston University, UK

Research Topics: "The biocompatibility and activity of implant nanostructures."



Gabriel Socol - INFPLR (Lasers), former: PhD University of Bucharest

Research Topics: "Compound laser transfer for nanostructurate coverings applied in controled drug release, cell reconstruction & implants."



Nicolae-Felix Sima - INFPLR (Lasers), former: PhD University Haute-Alsace, Fr

Research Topics: "Thin coatings of biodegradable polymers and proteins/drugs obtained by pulsed lasers for pharmaceutical and regenerative medicine."



Livia E Sima - INFPLR (Lasers), former: PhD IBAR

Research Topics: "Analysis of the differentiation programme of hMSCs grown in interaction with implant-type nanostructures."



Mihaela Mindroiu - INFPLR (Lasers), former: PhD University Politehnica Bucharest

Research Topics: "Laser living cells transfer for applications in tissue engineering and organ reconstruction."

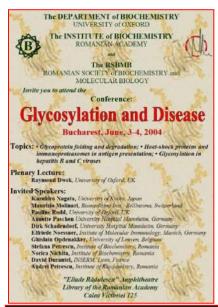


Aurelian Marcu - INFPLR (Lasers), former: Post.Doc Nagaoka University Japan

Research Topics: "Nanostructures for controlled drug release."

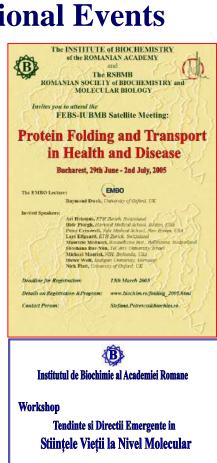


## **IBAR International Events**











Conférința Diaspora în Cercetarea Științifică Românească



## 1952 - 2022

# IBAR A history in images



# 21 March 1952



#### Inaugurarea Institutului de Biochimie al Academiei R. P. R.

In cadrul sesiunii generale stiințifice a Academiei R.P.R. să facut Vinerl la amiaA. Academiei R.P.R. să facut Vinerl la amiaA. futr'un cadru festiv. Inaugurarea înstitutului de Biochimie al Academiei R.P.R. Au fost de față acad. prof. dr.
C. I. Parhon, acad prof. Traian Săvulescu a arătat că cercetarile în dome dical și administrativ al institutului. In cuvăntarea sa, acad, prof. Traian Săvulescu a arătat că cercetarile în dome niul blochimiei trebue să se orienteze după exemplui știnței biochimice sovietice; ele trebue să ala la bază învătătura marrist-leninistă, principille materialismul dielecit. Vă trebui dată e mare împortanță cercetărilor experimentale, pelante și animale.

În inchefere, acad. prof. Traian Săvulescu a indemnat pe toți colaboratorii Institutului să pună toată răvina ca cercetările în fumenului blochimiei să siujească poporul.

A vorbit apoi directorul Institutului de

porul.

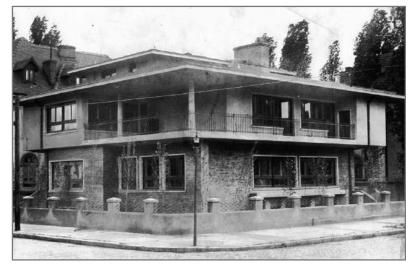
A vorbit apoi directorul Institutulul de Blochimie, acad. prof. Eugen Macovschi, care a arătat că prin crearea acestul institut se pun pentru Intâis oară în țara noastră temelille unei școli științifice de blochimie. Inaugurarea Institutulul de

lor.

In Inchelere, acad. E. Macovschi a multumit particului și guvernului pentru ajulorul și pentru condițiile optime de lucru puse la dispoziția celor care lucrează în acest institut.

La sfârșit, acad. prof. dr. C. I. Parhon a urat celor ce muncesc în Institutul de Blochimie o muncă rodnică pentru progresul știnței biologiee în tara noastră.

Asistența a vizitat apoi Institutul. (A-gerpres).



The Institute of Biochemistry of the Romanian Academy Str. Docentilor, Bucharest

No. 4356 April 25, 1953 NATURE 737

#### MOLECULAR STRUCTURE OF NUCLEIC ACIDS

#### A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

J. D. WATSON F. H. C. CRICK

F. F.
Medical Research Council Unit for the
Study of the Molecular Structure of
Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.





Cecilia Motaş, Sanda Rădulescu, *Acad.* Eugen Macovschi, Lucia Buzila, Horst Schell, Doina Popov



Horst Schell, Florin Mihăilescu, Traian Benţia, *Acad.* Eugen Macovschi, Natalia Moldoveanu, Ştefan Hulea, Mihai Şerban, Sorin Vassu



Upper: Central: Lower: Doina Onica, Corina Dragomirescu, Cecilia Motaş, Cornel Medeşan, Mihai Şerban Doina Popov, **Acad. Eugen Macovschi**, Sanda Rădulescu, Lili Botoşeneanu Viorica Frunzeti, Ioana Hagima, Mioara Cârsteanu



M.Ghiordunescu, E.Ilica, N.Moldoveanu, M.Zamfir M.Lungu, L.Botoşeneanu, S.Mihăescu, Ţache, M Cârsteanu, C.Motaş T.Benţia, L.Buzilă, R.Bârnescu, M.Muşolan, S.Vasu



Mircea Mateescu, Ofelia Gozia, Stelian Niculescu, Jana Ciopraga, Anca Roşeanu, Irina Cornoiu

Annu. Rev. Biochem. 2014. 83:1-44

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## Journeys in Science: Glycobiology and Other Paths

Raymond A. Dwek

Oxford Glycobiology Institute, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom; email: raymond.dwek@exeter.ox.ac.uk

#### Romania: Courage in Science Inspires Us All

Biochemistry suffered in Romania under Nicolae Ceauşescu (1974–1989) from lack of financial support and a complete blockade of scientific contacts with Western universities. Cecilia Motas, a highly cultured and courageous biochemist, challenged the rules and attempted to promote international collaboration. After the collapse of the communist regime, Cecilia immediately took action to revive biochemistry in Romania by reestablishing an institute, of which she was director, under the auspices of the Romanian Academy.

I met Cecilia at a conference at Göteborg in 1992. She asked me to help her train her young scientists. I was moved by her example and dedication. In January 1993, Stefana and Andrei Petrescu, both postdoctoral students, came to Oxford in the first step of a lasting collaboration between Oxford's Institute of Glycobiology and Bucharest's Institute of Biochemistry. This partnership was enthusiastically supported by both the Royal Society and the Wellcome Trust, which saw the importance of trying to rebuild and promote Romanian science. This was a difficult transition in Romania for science, and the collaboration was very important. My colleagues in Oxford helped in the training of many Romanian biochemistry students.





Corina Mihail, Silvia Mihăescu, Cecilia Motaș, Lucia Buzilă, Ecaterina Ilica, Zina Moldoveanu, Daniela Bratosin



The visit in IBAR of *Prof. Jean Montreuil*, *hon.member Romanian Academy featured along with*: F.Mihăilescu, V.Gheordunescu, V.Cişmaşiu, S.Mihăescu, Ş.Szedlacsek, M.Lungu, V.Oprea, E.Ilica, A.Roşeanu, C.Motaş, M.Trif and D.Bratosin - IBAR



Prof. Raymond Dwek, Fellow of the Royal Society awarded by the President of Romania Emil Constantinescu in the presence of the Preisdent of the Romanian Academy Eugen Simion featured also: Prof. Tim Bloch, USA, Cecilia Motaş & Ştefana Petrescu, IBAR





FEBS Advanced Course 2003: Attendants and IBAR Tutors



FEBS-IUBMB Meeting & FEBS Course 2005
Featuring: *Prof.* **P.Cresswell** FRS, Yale; *Prof.* **R.A.Dwek** FRS, Oxford; *Prof.* **H.Ploegh**, Harvard



Diaspora Worksop 2008 in IBAR
Featured: *Prof.* Adrian Salic, Harvard; *Prof.* Dan Duda Harvard; *Acad.* Irinel Popescu



FEBS Visit 2010: Head of FEBS **Prof. Israel Pecht**, Weizman Inst. and **Daniel Funeriu**, *Minstry of Education*Featured also: Norica Nichita and Ştefana Petrescu IBAR



# 2010 Romanian Academy Award Recipients Conference "Chemistry and Life"



Visit in IBAR of
Nobel Price **Baruch Blumberg**, *NASA*; Prof. **Richard Lerner**, *Scripps.Institute* & Prof. **Raymond Dwek**, Oxford discussing with: Ştefan Szedlaczek and Ştefana Petrescu, IBAR



Nobel Price Baruch Blumberg; Prof. Richard Lerner & Prof. Raymond Dwek along with IBAR team members



.Nobel Price Baruch Blumberg, Prof. Richard Lerner & Prof. Raymond Dwek received by the President of Romanian Academy - Acad. Ionel Haiduc





2012 Inauguration of PROCERA - Core Facility of IBAR in the presence of the *President of the Romanian Academy* **Ionel-Valentin Vlad,** *Prof.* **Raymond A.Dwek**; *Prof.* **Adrian Curaj**, UEFISCDI and *Prof.* **Dragoş Ciuparu**, State Secretary of Research



2014 Workshop " Pathogen-informed strategies for sustainable crop resistance " organised by IBAR



2016 IBAR Visit: *Prof.* **Pedro Romero**, *UNIL Lausanne* and *Prof.Asist.* **Calmilla Jandus**, U.Geneve discussing with: Stefana Petrescu, Gabriela Chiritoiu and Cristian Munteanu IBAR



## 25 years anniversary

# Romanian Society of Biochemistry and Molecular Biology



Address of Acad. Bogdan Simionescu, vicepresident of the Romanian Academy



# Romanian Society of Biochemistry and **Molecular Biology 1990-2015**



presidents, vicepresidents, secretaries





Ştefan



Ştefana



Cecilia



Tavi



















Ştefan



Norica



Alexandra

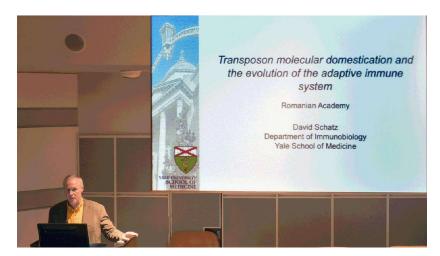




Prof. Vivek Malhotra, CRG Barcelona



2018 IBAR — EMBL-EBI Course "Training Romainan Bionformatic Trainers" featured: Andrew Cowley, EBI Cambridge & Andrei-J Petrescu IBAR



2019 - The IBAR vistit of **Prof**. **David Schatz**, Yale - National Academy of Science USA Address to the Romanian Academy



# **IBAR Publications**

https://www.biochim.ro/publications/

## **IBAR Research in Images**

#### **Molecular Cell Biology**

Glycosylation and Glycoprotein folding



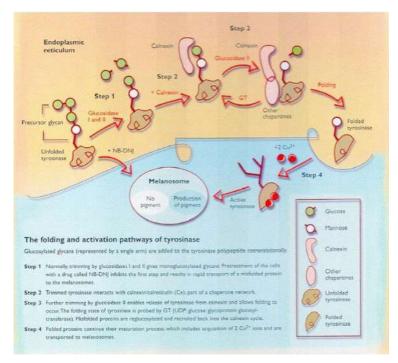












Cell, Vol. 88, 29-38, January 10, 1997, Copyright @1997 by Cell Press

#### Conformation-Independent Binding of Monoglucosylated Ribonuclease B to Calnexin

André Zapun,\*† Stefana M. Petrescu,†§ Pauline M. Rudd,‡ Raymond A. Dwek,‡ David Y. Thomas,\*†∥ and John J. M. Bergeron\*

Biochemical and Biophysical Research Communications 261, 720-725 (1999) Article ID bbrc.1999.1030, available online at http://www.idealibrary

#### Tyrosinase Folding and Copper Loading in Vivo: A Crucial Role for Calnexin and $\alpha$ -Glucosidase II

N. Branza-Nichita, \*† A. J. Petrescu, \*† R. A. Dwek, \* M. R. Wormald, \*
F. M. Platt, \* and S. M. Petrescu \*† †
\*\*. A. Dwek, \* M. R. Wormald, \*
\*\*. M. Polatt, \* and S. M. Petrescu \*† †
\*\*. Oxford Glycobiology Institute, Department of Biochemistry, University of Oxford, South Parks Road,
Oxford OXI, 30U, United Kingdom: and †Institute of Biochemistry of the Romanian Academy,
Splatul Independentei 296, 77700 Bucharest 17, Romania

# **Biochemistry**

Volume 39, Number 18 Current Topics

Tyrosinase and Glycoprotein Folding: Roles of Chaperones That Recognize Glycans efana M. Petrescu,\*,‡ Norica Branza-Nichita,‡ Gabriela Negroiu,‡ Andrei J. Petrescu,‡ and Raymond A. Dw Oxford Glycobiology Institute, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, U.K., and Institute of Biochemistry, Romanian Academy, Splaiul Independentei 296, 77700 Bucharest 17, Romania Received January 19, 2000

The Journal of Biological Chemistry © 2000 by The American Society for Biochemistry and Molecular Biology, Inc.

Inhibition of N-Glycan Processing in B16 Melanoma Cells Results in Inactivation of Tyrosinase but Does Not Prevent Its Transport to the Melanosome\*

Stefana M. Petrescu‡§, Andrei-J. Petrescu‡¶, Haralambie N. Titu‡, Raymond A. Dwek, and Frances M. Platt|

From the Glycobiology Institute, University of Oxford, South Parks Road, OX1 3QU Oxford, United Kingdom and the Institute of Biochemistry, Splain Independentei 296, 77700 Bucharest 17, Romania

Vol. 275, No. 11, Issue of March 17, pp. 8169-8175, 2000 Printed in U.S.A.

#### Mutations at Critical N-Glycosylation Sites Reduce Tyrosinase Activity by Altering Folding and Quality Control\*

(Received for publication, November 25, 1999)

Norica Branza-Nichita‡\$, Gabriela Negroiu‡, Andrei J. Petrescu‡\$, Elspeth F. Garman¶, Fran M. Platts, Mark R. Wormalds, Raymond A. Dweks, and Stefana M. Petrescu‡8\*\*

From the ‡Institute of Biochemistry of the Romanian Academy, Splaiul Independentei 296, 77700 Bucharest 17, Romania, the §Oxford Glycobiology Institute, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OXI 3QU, United Kingdom, and the ¶Laboratory of Biophysics, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, United Kingdom



#### **Molecular Cell Biology**

#### Glycosylation and Glycoprotein folding



The Journal of Biological Chemistry  $\odot$  2003 by The American Society for Biochemistry and Molecular Biology, Inc.

# The Inhibition of Early N-Glycan Processing Targets TRP-2 to Degradation in B16 Melanoma Cells\*

Received for publication, March 27, 2003, and in revised form, April 25, 2003 Published, JBC Papers in Press, April 28, 2003, DOI 10.1074/jbc.M303167200

#### Gabriela Negroiu‡, Raymond A. Dwek§, and Stefana M. Petrescu‡¶

From the ‡Institute of Biochemistry of the Romanian Academy, Splaiul Independentei 296, 77700 Bucharest, Romania and the \$Oxford Glycobiology Institute, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, United Kingdom

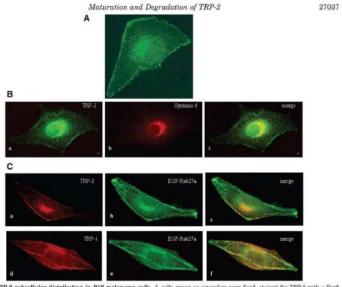


Fig. 1, TRP-2 subcellular distribution in B16 melanoma cells. A, cells grown on coveralips were fixed, stained for TRP-2 with a-Pept antibody, and detected using Alexa 488 goat anti-rabbit secondary antibodies. B, cells grown on coveralips were fixed and stained for TRP-2 (FRP-2 grown on the coverage of the processor) and a syntaxio for TRP-2 with the TRP-2 grown on coveralips were fixed and stained for TRP-2 with the TRP-2 with the TRP-2 with the TRP-2 with the TRP and syntaxion 6. C, cells were transiently transfected with EGFP-Reb27a (panels & and e), fixed after 24 h, and stained for either TRP-2 or TRP-1 with or-Pep8 and o-Pep1, respectively. TRPs were detected with anti-rabbit IgG bioxinylated followed by streptavidin Texas Red (and d). The merges mages (c and b) show that unlike TRP-1 (f), TRP-2 poorly co-localizes with Rab27a in periferal punctate or filamentous structures (panel c).

The Journal of Biological Chemistry  $\odot$  2005 by The American Society for Biochemistry and Molecular Biology, Inc.

Vol. 280, No. 14, Issue of April 8, pp. 13833–13840, 2005 Printed in U.S.A.

# Soluble Tyrosinase is an Endoplasmic Reticulum (ER)-associated Degradation Substrate Retained in the ER by Calreticulin and BiP/GRP78 and Not Calnexin\* Soluble Tyrosinase is an Endoplasmic Reticulum (ER)-associated Degradation Substrate Retained in the ER by Calreticulin and BiP/GRP78 and Not Calnexin

Received for publication, November 19, 2004, and in revised form, January 26, 2005 Published, JBC Papers in Press, January 27, 2005, DOI 10.1074/jbc.M413087200

Costin I. Popescu‡, Crina Paduraru§, Raymond A. Dwek‡, and Stefana M. Petrescu§¶
From the §Institute of Biochemistry, Splaiul Independentei 296, 060031 Bucharest 17, Romania and ‡Department of Biochemistry, Oxford Glycobiology Institute, South Parks Road, OX1 3QU Oxford, United Kingdom

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 281, NO. 31, pp. 21682–21689, August 4, 2006

# Productive Folding of Tyrosinase Ectodomain Is Controlled by the Transmembrane Anchor\*

Received for publication, April 21, 2006, and in revised form, May 31, 2006 Published, JBC Papers in Press, May 31, 2006, DOI 10.1074/jbc.M603841200

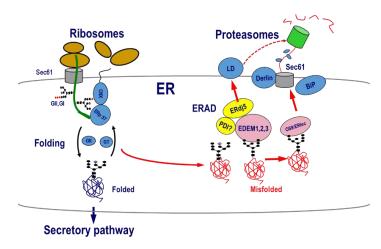
Costin I. Popescu<sup>†</sup>, Alina Mares<sup>†</sup>, Livia Zdrentu<sup>†</sup>, Nicole Zitzmann<sup>§</sup>, Raymond A. Dwek<sup>§†</sup>, and Stefana M. Petrescu<sup>‡1,2</sup> From the <sup>‡</sup>Institute of Biochemistry, Splaiul Independentei 296, 060031 Bucharest 17, Romania and <sup>§</sup>Oxford Glycobiology Institute, Department of Biochemistry, South Parks Road, OX1 3QU Oxford, United Kingdom



#### **Molecular Cell Biology**

#### ER Associated Degradation Pathways and Antigen Presentation





OPEN & ACCESS Freely available online



MDPI

# Tyrosinase Degradation Is Prevented when EDEM1 Lacks the Intrinsically Disordered Region

Marioara B. Marin<sup>1</sup>, Simona Ghenea<sup>1</sup>, Laurentiu N. Spiridon<sup>2</sup>, Gabriela N. Chiritoiu<sup>1</sup>, Andrei-Jose Petrescu<sup>2\*</sup>, Stefana-Maria Petrescu<sup>1\*</sup>

1 Department of Molecular Cell Biology, Institute of Biochemistry of Romanian Academy, Bucharest, Romania, 2 Department of Bioinformatics and Structural Biochemistry, Institute of Biochemistry of Romanian Academy, Bucharest, Romania

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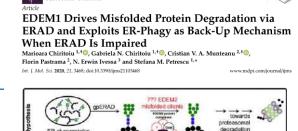
Integrative ERAD Network

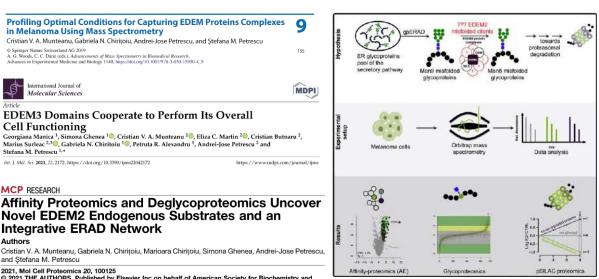
Authors

August 2012 | Volume 7 | Issue 8 | e42998



. Mol Cell Proteomics 20, 100125
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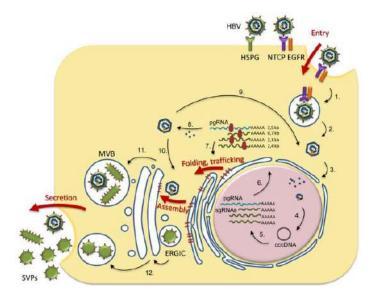




#### **Molecular Virology**

#### Hepatitis B research and terapy strategies







## Polyunsaturated liposomes are antiviral against hepatitis B and C viruses and HIV by decreasing cholesterol levels in infected cells

Stephanie Pollock<sup>a</sup>, Norica Branza Nichita<sup>b</sup>, Annette Böhmer<sup>a</sup>, Cristina Radulescu<sup>b</sup>, Raymond A. Dwek<sup>a</sup>, and Nicole Zitzmann<sup>a,1</sup>

<sup>a</sup>Oxford Antiviral Drug Discovery Unit, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom; and <sup>b</sup>Institute of Biochemistry, Romanian Academy, Bucharest 060031, Romania

17176–17181 | PNAS | October 5, 2010 | vol. 107 | no. 40

www.pnas.org/cgi/doi/10.1073/pnas.1009445107

#### The FASEB Journal • Research Communication

# Uptake and trafficking of liposomes to the endoplasmic reticulum

Stephanie Pollock,\* Robin Antrobus,\* Laura Newton,\* Bettina Kampa,\* Jan Rossa,\* Sally Latham,\* Norica Branza Nichita,<sup>†</sup> Raymond A. Dwek,\* and Nicole Zitzmann\*,<sup>1</sup>

\*Oxford Antiviral Drug Discovery Unit, Department of Biochemistry, University of Oxford, Oxford, UK; and †Institute of Biochemistry, Romanian University, Bucharest, Romania

1866 0892-6638/10/0024-1866 © FASEB

Journal of Virology, Dec. 2011, p. 13373–13383 0022-538X/11/\$12.00 doi:10.1128/JVI.05423-11 Copyright © 2011, American Society for Microbiology. All Rights Reserved. Vol. 85, No. 24

Cholesterol Depletion of Hepatoma Cells Impairs Hepatitis B Virus Envelopment by Altering the Topology of the Large Envelope Protein<sup>∇</sup>

Cristina Dorobantu, <sup>1</sup> Alina Macovei, <sup>1</sup>† Catalin Lazar, <sup>1</sup>† Raymond A. Dwek, <sup>2</sup> Nicole Zitzmann, <sup>2</sup> and Norica Branza-Nichita <sup>1</sup>\*

JOURNAL OF VIROLOGY, Jan. 2010, p. 243–253 0022-538X/10/\$12.00 doi:10.1128/JVI.01207-09 Copyright © 2010, American Society for Microbiology. All Rights Reserved. Vol. 84, No. 1

Hepatitis B Virus Requires Intact Caveolin-1 Function for Productive Infection in HepaRG Cells<sup>▽</sup>

Alina Macovei,¹ Cristina Radulescu,¹ Catalin Lazar,¹ Stefana Petrescu,¹ David Durantel,² Raymond A. Dwek,³ Nicole Zitzmann,³ and Norica Branza Nichita¹\*



#### **Molecular Virology**

#### Hepatitis B research and terapy strategies

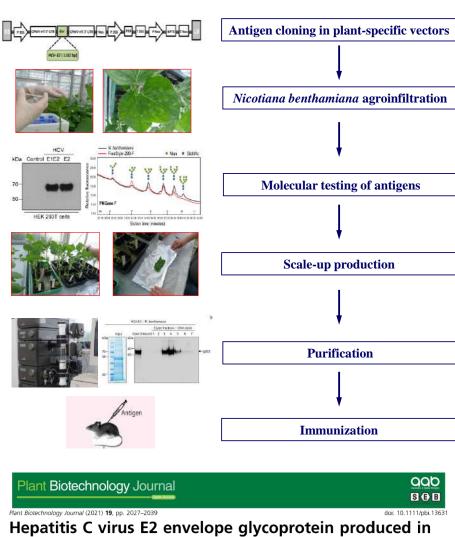




Lettuce-produced hepatitis C virus E1E2 heterodimer triggers immune responses in mice and antibody production after oral vaccination

Jihong Liu Clarke<sup>1,\*</sup>, Lisa Paruch<sup>1</sup>, Mihaela-Olivia Dobrica<sup>2</sup>, Iuliana Caras<sup>3</sup>, Catalin Tucureanu<sup>3</sup>, Adrian Onu<sup>3</sup>, Sonya Ciulean<sup>3</sup>, Crina Stavaru<sup>3</sup>, Andre Eerde<sup>1</sup>, Yanliang Wang<sup>1</sup>, Hege Steen<sup>1</sup>, Sissel Haugslien<sup>1</sup>, Catalina Petrareanu<sup>2</sup>, Catalin Lazar<sup>2</sup>, Costin-loan Popescu<sup>2</sup>, Ralph Bock<sup>4</sup>, Jean Dubuisson<sup>5</sup> and Norica Branza-Nichita<sup>2,\*</sup>

# Viral antigen production in plants



Hepatitis C virus E2 envelope glycoprotein produced in *Nicotiana benthamiana* triggers humoral response with virus-neutralizing activity in vaccinated mice

Mihaela-Olivia Dobrica<sup>1</sup> , André van Eerde<sup>2</sup>, Catalin Tucureanu<sup>3</sup>, Adrian Onu<sup>3</sup>, Lisa Paruch<sup>2</sup>, Iuliana Caras<sup>3</sup>, Ene Vlase<sup>3</sup>, Hege Steen<sup>2</sup>, Sissel Haugslien<sup>2</sup>, Dominic Alonzi<sup>4</sup>, Nicole Zitzmann<sup>4</sup>, Ralph Bock<sup>5</sup> , Jean Dubuisson<sup>6</sup>, Costin-Ioan Popescu<sup>1</sup>, Crina Stavaru<sup>3</sup>, Jihong Liu Clarke<sup>2</sup>, and Norica Branza-Nichita<sup>1</sup>, a



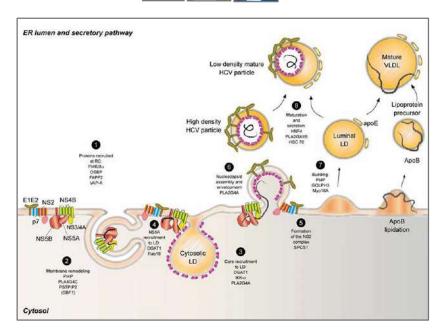
#### **Molecular Virology**

#### Hepatitis C research and terapy strategies









Viruses 2011, 3, 2238-2254; doi: 10.3390/v3112238

#### **Hepatitis C Virus Assembly Imaging**

Costin-Ioan Popescu 1,\*, Yves Rouillé 2 and Jean Dubuisson 2

viruses

ISSN 1999-4915

www.mdpi.com/journal/viruses

OPEN & ACCESS Freely available online

PLOS PATHOGENS

# NS2 Protein of Hepatitis C Virus Interacts with Structural and Non-Structural Proteins towards Virus Assembly

Costin-Ioan Popescu<sup>1,2</sup>, Nathalie Callens<sup>1</sup>, Dave Trinel<sup>3</sup>, Philippe Roingeard<sup>4</sup>, Darius Moradpour<sup>5</sup>, Véronique Descamps<sup>6</sup>, Gilles Duverlie<sup>6</sup>, François Penin<sup>7</sup>, Laurent Héliot<sup>3</sup>, Yves Rouillé<sup>1</sup>, Jean Dubuisson<sup>1</sup>\*



February 2011 | Volume 7 | Issue 2 | e1001278

Biology 2014, 3, 892-921; doi:10.3390/biology3040892

www.mdpi.com/journal/biology

# Hepatitis C Virus Life Cycle and Lipid Metabolism Costin-Ioan Popescu <sup>1</sup>, Laura Riva <sup>2</sup>, Ovidiu Vlaicu <sup>1</sup>, Rayan Farhat <sup>2</sup>,

Costin-Ioan Popescu <sup>1</sup>, Laura Riva <sup>2</sup>, Ovidiu Vlaicu <sup>1</sup>, Rayan Farhat <sup>2</sup>, Yves Rouillé <sup>2</sup> and Jean Dubuisson <sup>2,\*</sup>



Journal of Virological Methods 246 (2017) 42–50

Contents lists available at ScienceDirect



Journal of Virological Methods

journal homepage: www.elsevier.com/locate/jviromet



Novel replicons and *trans*-encapsidation systems for Hepatitis C Virus proteins live imaging and virus-host interaction proteomics

Ovidiu Vlaicu<sup>a</sup>, Tudor Selescu<sup>a,b</sup>, Florin Pastrama<sup>a</sup>, Cristian Munteanu<sup>a</sup>, Laura Riva<sup>c</sup>, Jean Dubuisson<sup>c</sup>, Yves Rouille<sup>c</sup>, Costin-Ioan Popescu<sup>a,\*</sup>





#### **Enzymology**

#### The structure of protein tyrosin phosphataes and cellular signaling

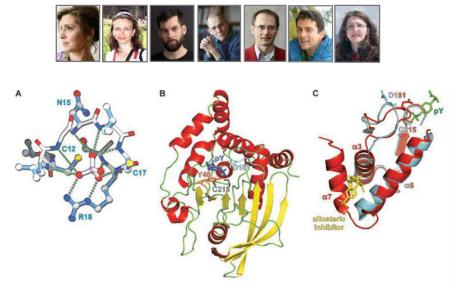


Fig. 1. (A) Structure of the phosphate-binding loop (P-loop). Stick representation of the consensus signature motif (CX<sub>6</sub>R) that forms the Ploop present in the active site of PTPs. The P-loop from bovine LMW-PTP (1PNT) [79] is represented and the catalytic Cys12 and Arg18 are labelled. The amide nitrogens form hydrogen-bond interactions (dotted green lines) with the phosphatase bound showing network of interactions that involve the catalytic Arg. The cradle-like conformation of the P-loop is conserved in the structures of all PTPs

doi:10.1006/jmbi.2001.4890 available online at http://www.idealibrary.com on IDE L 1"J. Mol. Biol. (2001) 311, 557-568

#### IMB



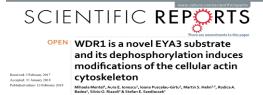
Crystal Structure of PTP-SL/PTPBR7 Catalytic Domain: Implications for Map Kinase Regulation Stefan E. Szedlacsek'\*, Alexandru R. Aricescu¹, Tudor A. Fulga¹ Louis Renault³ and Axel J. Scheidig²

#### MINIREVIEW

#### Protein tyrosine phosphatases: structure-function relationships



Lydia Tabernero<sup>1</sup>, A. Radu Aricescu<sup>2</sup>, E. Yvonne Jones<sup>2</sup> and Stefan E. Szedlacsek<sup>3</sup> FEBS Journal 275 (2008) 867-882 @ 2008 The Authors Journal compilation @ 2008 FEBS







#### Analysis of EYA3 Phosphorylation by Src Kinase Identifies Residues Involved in Cell Proliferation

Aura E. Ionescu 10, Mihaela Mentel 1,†, Cristian V.A. Munteanu 2, Livia E. Sima 30, Eliza C. Martin <sup>2</sup>, Georgiana Necula-Petrareanu <sup>1</sup> and Stefan E. Szedlacsek <sup>1,\*</sup>

Int. J. Mol. Sci. 2019, 20, 6307; doi:10.3390/ijms20246307

www.mdpi.com/journal/ijms

Journal of Structural Biology 207 (2019) 85-102



Contents lists available at ScienceDirect

#### Journal of Structural Biology

journal homepage: www.elsevier.com/locate/yjsbi



Crystal structure of a xylulose 5-phosphate phosphoketolase. Insights into the substrate specificity for xylulose 5-phosphate

A.J. Scheidig<sup>a</sup>, D. Horvath<sup>b</sup>, S.E. Szedlacsek<sup>c,a</sup>

Received: 24 October 2019 | Accepted: 31 October 2019

DOI: 10.1002/jcp.29397

#### Cellular Physiology WILEY

#### ORIGINAL RESEARCH ARTICLE

## Regulation of TRPM8 channel activity by Src-mediated tyrosine phosphorylation

Alexandra Manolache<sup>1</sup> | Tudor Selescu<sup>1</sup> | G. Larisa Maier<sup>1</sup> | Mihaela Mentel<sup>2</sup> | Aura Elena Ionescu<sup>2</sup> | Cristian Neacsu<sup>1</sup> | Alexandru Babes<sup>1</sup> | Stefan Eugen Szedlacsek<sup>2</sup>

J Cell Physiol. 2019;1-12.

wileyonlinelibrary.com/journal/jcp

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#### Structural Imunobiology. The adaptative systemul Structura și evoluția Complexului Sinaptic în Recombinarea V(D)J













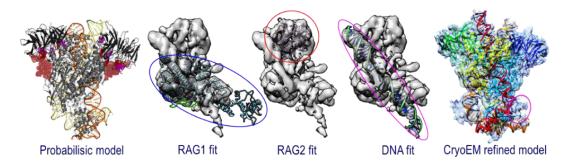
# ARTICLE

https://doi.org/10.1038/s41586-019-1093-7

# Transposon molecular domestication and the evolution of the RAG recombinase

 $\label{eq:changless} Yuhang Zhang^{1,8}, Tat Cheung Cheng^{2,8}, Guangrui Huang^3, Qingyi Lu^3, Marius D. Surleac^4, Jeffrey D. Mandell^1, Pierre Pontarotti^{5,6}, Andrei J. Petrescu^4, Anlong Xu^{3,7*}, Yong Xiong^{2*} \& David G. Schatz^{1*}$ 

NATURE | www.nature.com/nature



Martin et al. Mobile DNA (2020) 11:17 https://doi.org/10.1186/s13100-020-00214-y

Mobile DNA

#### RESEARCH

**Open Access** 

# Identification of RAG-like transposons in protostomes suggests their ancient bilaterian origin



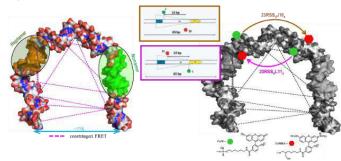
Eliza C. Martin<sup>1†</sup>, Célia Vicari<sup>2†</sup>, Louis Tsakou-Ngouafo<sup>2</sup>, Pierre Pontarotti<sup>2,3\*</sup>, Andrei J. Petrescu<sup>1\*</sup> and David G. Schatz<sup>4</sup>

Published online 4 January 2013

Nucleic Acids Research, 2013, Vol. 41, No. 4 2437–2454 doi:10.1093/nar/gks1294

# RAG and HMGB1 create a large bend in the 23RSS in the V(D)J recombination synaptic complexes

Mihai Ciubotaru<sup>1,2,3</sup>, Adam J. Trexler<sup>4</sup>, Laurentiu N. Spiridon<sup>5</sup>, Marius D. Surleac<sup>5</sup>, Elizabeth Rhoades<sup>4</sup>, Andrei J. Petrescu<sup>5</sup> and David G. Schatz<sup>1,4,6,\*</sup>





# Structural Imunobiology. The innate system Structure function relation in plant host-pathogen systems







# Coiled-Coil Domain-Dependent Homodimerization of Intracellular Barley Immune Receptors Defines a Minimal Functional Module for Triggering Cell Death

Takaki Maekawa,<sup>1,8</sup> Wei Cheng,<sup>2,3,8</sup> Laurentiu N. Spiridon,<sup>4</sup> Armin Töller,<sup>1</sup> Ewa Lukasik,<sup>5</sup> Yusuke Saijo,<sup>1</sup> Peiyuan Liu,<sup>3</sup> Qian-Hua Shen,<sup>5</sup> Marius A. Micluta,<sup>4</sup> Imre E. Somssich,<sup>1</sup> Frank L.W. Takken,<sup>5</sup> Andrei-Jose Petrescu,<sup>4</sup> Jijie Chai,<sup>3,7,\*</sup> and Paul Schulze-Lefert<sup>1,\*</sup>

Cell Host & Microbe 9, 187-199, March 17, 2011 @2011 Elsevier Inc. 187

# Structural Determinants at the Interface of the ARC2 and Leucine-Rich Repeat Domains Control the Activation of the Plant Immune Receptors Rx1 and Gpa2<sup>1[C][W][OA]</sup>

Erik J. Slootweg<sup>2\*</sup>, Laurentiu N. Spiridon<sup>2</sup>, Jan Roosien, Patrick Butterbach, Rikus Pomp, Lotte Westerhof, Ruud Wilbers, Erin Bakker, Jaap Bakker, Andrei-José Petrescu, Geert Smant, and Aska Goverse

Plant Physiology®, July 2013, Vol. 162, pp. 1510–1528, www.plantphysiol.org © 2013 American Society of Plant Biologists. All Rights Reserved.

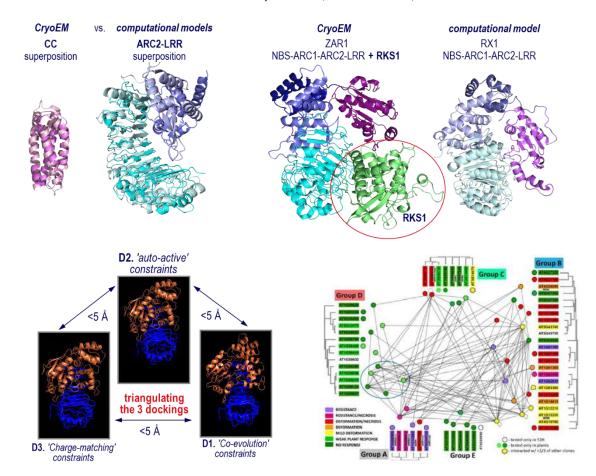


OPEN ACCES

Citation: Wróblewski T., Spiridon L., Martin E.O., Petrescu A.-J., Cavanaugh K., Truco M.J., et al. (2018) Genome-wide functional analyses of plant colledcoil NLR-type pathogen receptors reveal essential roles of their N-terminal domaria in oligomerization, networking, and immunity. PLoS Biol 16(12): e2005521. https://doi.org/10.1371/journal. pbib.2005521. RESEARCH ARTICLE

Genome-wide functional analyses of plant coiled-coil NLR-type pathogen receptors reveal essential roles of their N-terminal domain in oligomerization, networking, and immunity

Tadeusz Wróblewski. \*, Laurentiu Spiridon², Eliza Cristina Martin², Andrei-Jose Petrescu², Keri Cavanaugh¹, Maria José Truco¹, Huaqin Xu¹, Dariusz Gozdowski³, Krzysztof Pawłowski³, Richard W. Michelmore¹.4.5, Frank L.W. Takken⁵.





#### **Structural Glycobiology**

#### Glycan and Glycoprotein Bioinformatics & Molecular modeling

Chem. Rev. 2002, 102, 371-386

371

## Conformational Studies of Oligosaccharides and Glycopeptides: Complementarity of NMR, X-ray Crystallography, and Molecular Modelling

Mark R. Wormald,\*,† Andrei J. Petrescu,†,‡ Ya-Lan Pao,† Ann Glithero,†,§ Tim Elliott,§,# and Raymond A. Dwek†

372 Chemical Reviews, 2002, Vol. 102, No. 2

Wormald et al



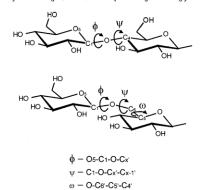
Dr. Mark Wormald is a University Research Lecturer in the Department of Biochemistry, Oxford University, and is a Fellow in Biochemistry and Chemistry at Corpus Christi College, Oxford. He graduated with a degree in chemistry from Oxford University in 1985, followed by a D.Phil. in the Inorganic Chemistry Laboratory (doing a mixture of physics, biophysics, and bioinorganic chemistry) with Prof. R. J. P. Williams, FRS. He moved to the then Oxford Oligosaccharide Group in 1989 to work with Prof. R. A. Dwek, FRS, on the conformations of oligosaccharides by NMR spectroscopy. From 1990 to 1993, he held a Junior Research Fellowship at Corpus Christi College, Oxford. He is currently running the structural glycobiology group in the Oxford Glycobiology Institute, his main interests being in the conformations and dynamics of oligosaccharides, glycopeptides, and glycoproteins.



Dr. Andrei-J. Petrescu is a graduate in biophysics from the University of Bucharest. This was followed by postdoctoral positions in the Department of Biochemistry, University of Oxford, UK, and at the Centre de Etudes Atomique, Saclay, France. He is a member of the Oxford Glycobiology Institute and head of the Structural Biochemistry Group of the Biochemistry Institute of the Romanian Academy. He has been involved in developing physical methods for the study of unfolded states of proteins. He determined the structures of glucosylated oligomannose glycans specific to the early glycosylation stages in the ER and has contributed to the characterization of the glycan recognition elements of glycoproteins by lectin-like chaperones during glycoprotein folding. Currently, he is working on the development of a database of structural information on glycoproteins



Professor Raymond Dwek is Professor of Glycobiology, Director of the Glycobiology Institute, and Head of the Department of Biochemistry, Oxford University. He is a Professorial Fellow at Exeter College, Oxford. He obtained his B.Sc. (1963) and M.Sc. (1964) degree at Manchester University and his D.Phil. (1966) degree in Oxford. He founded the Glycobiology Institute at Oxford University in 1991 and has received several awards for his work on glycobiology, including the 7th Wellcome Trust Award for Research in Biochemistry Related to Medicine and the First Scientific Leadership Award, Hepatitis B Foundation, Philadelphia, PA. He is a member of the European Molecular Biology Organization and Fellow of the Royal Society. In 1996, Professor Dwek was awarded a Doctoris Honoris Causa by the Katholieke Universiteit, Leuven, Belgium, for his research contributions to NMR, antibodies, and glycobiology. In 2000, he was awarded the National Romanian Order for merit with rank of Commander for his major contribution to the Romanian—British cooperation in biochemistry and molecular biology, and this year has been awarded the Doctor Philosophiae Honoris Causa from the Ben-Gurion University of the Negev, Israel, for his pioneering work in glycobiology.



**Figure 1.** Schematic diagrams of a 1-4 linkage (upper) and 1-6 linkage (lower) showing the torsion angles that need to be determined to characterize the linkage conformation



# Structural aspects of glycomes with a focus on *N*-glycosylation and glycoprotein folding

Andrei-José Petrescu<sup>1</sup>, Mark R Wormald<sup>2</sup> and Raymond A Dwek<sup>2</sup>

Current Opinion in Structural Biology 2006, 16:1-8



#### **Structural Biology**

#### Modeling molecular structures and interactions in Biology









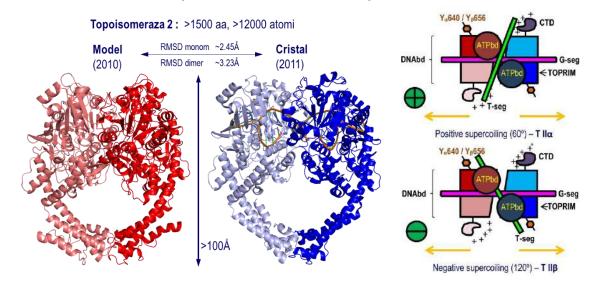


Published online 2 May 2017

Nucleic Acids Research, 2017, Vol. 45, No. 10 5995-6010

# Roles of the C-terminal domains of topoisomerase II $\!\alpha$ and topoisomerase II $\!\beta$ in regulation of the decatenation checkpoint

Toshiyuki Kozuki<sup>1,†</sup>, Kenichi Chikamori<sup>1,†</sup>, Marius D. Surleac<sup>2,†</sup>, Marius A. Micluta<sup>2</sup>, Andrei J. Petrescu<sup>2</sup>, Eric J. Norris<sup>3</sup>, Paul Elson<sup>1</sup>, Gerald A. Hoeltge<sup>4</sup>, Dale R. Grabowski<sup>1</sup>, Andrew C.G. Porter<sup>5</sup>, Ram N. Ganapathi<sup>3,\*</sup> and Mahrukh K. Ganapathi<sup>3,\*</sup>







Analysis of decapping scavenger cap complex using modified cap analogs reveals molecular determinants for efficient cap binding

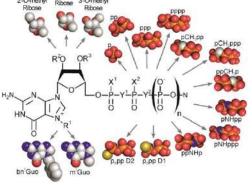
Anna Wypijewska del Nogal<sup>1</sup>, Marius D. Surleac<sup>2</sup>, Joanna Kowalska<sup>1</sup>, Maciej Lukaszewicz<sup>1</sup>, Jacek Jemielity<sup>1,3</sup> Martin Bisaillon<sup>4</sup>, Edward Darzynkiewicz<sup>1</sup>, Adina L. Milac<sup>2</sup> and Elzbieta Bojarska<sup>1</sup>

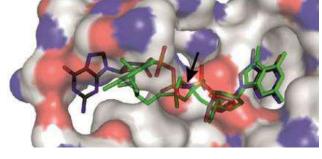
Biochimica et Biophysica Act. 1830 (2014) 453-462
Contents lists available at ScienceDirect
Biochimica et Biophysica Acta

ELSEVIER journal homepage: www.elsevier.com/locate/bbagrm

Decapping Scavenger (DepS) enzyme: Advances in its structure, activity and roles in the cap-dependent mRNA metabolism. Adina L Milar, Elzbieta Bojarska \*\*, Anna Wypijewska del Nogal \*\*\*









#### **Biocomputing and Bioinformatics**

#### Software Development



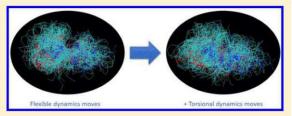


pubs.acs.org/JCTC

### Hamiltonian Monte Carlo with Constrained Molecular Dynamics as **Gibbs Sampling**

Laurentiu Spiridon\*,†,‡ and David D. L. Minh\*,†©

ABSTRACT: Compared to fully flexible molecular dynamics, simulations of constrained systems can use larger time steps and focus kinetic energy on soft degrees of freedom. Achieving ergodic sampling from the Boltzmann distribution, however, has proven challenging. Using recent generalizations of the equipartition principle and Fixman potential, here we implement Hamiltonian Monte Carlo based on constrained molecular dynamics as a Gibbs sampling move. By mixing Hamiltonian Monte Carlo based on fully flexible and torsional dynamics,



we are able to reproduce free energy landscapes of simple model systems and enhance sampling of macrocycles.



DOI: 10.1021/acs.jctc.7b00570 J. Chem. Theory Comput. 2017, 13, 4649–4659





Contents lists available at ScienceDirect

#### **BBA** - General Subjects

journal homepage: www.elsevier.com/locate/bbagen



Robosample: A rigid-body molecular simulation program based on robot



Laurentiu Spiridon<sup>a,\*</sup>, Teodor Asvadur Şulea<sup>a</sup>, David D.L. Minh<sup>b,\*</sup>, Andrei-Jose Petrescu<sup>a,\*</sup>

\*Department of Bioinformatics and Structural Biochemistry, Institute of Biochemistry of the Romanian Academy, Splaiul Independentei 296, Bucharest 060031, Romania

b Department of Chemistry, Illinois Institute of Technology, Chicago, IL 60616, USA





# LRRpredictor—A New LRR Motif Detection Method for Irregular Motifs of Plant NLR Proteins Using an **Ensemble of Classifiers**

Eliza C. Martin <sup>1</sup>, Octavina C. A. Sukarta <sup>2</sup>, Laurentiu Spiridon <sup>1</sup>, Laurentiu G. Grigore <sup>3</sup>, Vlad Constantinescu<sup>1</sup>, Robi Tacutu<sup>1</sup>, Aska Goverse<sup>2</sup>,\* and Andrei-Jose Petrescu<sup>1</sup>,\*

- Department of Bioinformatics and Structural Biochemistry, Institute of Biochemistry of the Romanian Academy, Splaiul Independentei 296, 060031 Bucharest, Romania; eliza.martin@biochim.ro (E.C.M.); laurentiu.spiridon@biochim.ro (L.S.); vlad.ion.constantinescu@gmail.com (V.C.); robi.tacutu@gmail.com (R.T.)
- Laboratory of Nematology, Wageningen University and Research, 6700ES Wageningen, The Netherlands; octavina.sukarta@wur.nl
- Space Comp SRL, 041512 Bucharest, Romania; laur@itprod.eu



#### **Biocomputing and Bioinformatics**

#### **Database Development**



Nucleic Acids Research, 2018, Vol. 46, Database issue D1083-D1090

### Human Ageing Genomic Resources: new and updated databases

Robi Tacutu<sup>1,2,†</sup>, Daniel Thornton<sup>1,†</sup>, Emily Johnson<sup>1,†</sup>, Arie Budovsky<sup>3,4,†</sup>, Diogo Barardo<sup>5,6</sup>, Thomas Craig<sup>1</sup>, Eugene Diana<sup>1</sup>, Gilad Lehmann<sup>3</sup>, Dmitri Toren<sup>3</sup>, Jingwei Wang<sup>1</sup>, Vadim E. Fraifeld<sup>3</sup> and João P. de Magalhães<sup>1,\*</sup>



# SCIENTIFIC DA

OPEN SynergyAge, a curated database DATA DESCRIPTOR for synergistic and antagonistic interactions of longevity-associated genes

> Gabriela Bunu 61,7, Dmitri Toren1,2,7, Catalin-Florentin Ion1, Diogo Barardo3, Larisa Sârghie1, Laurentiu Gabriel Grigore⁴, João Pedro de Magalhães⁵, Vadim E. Fraifeld 62 & Robi Tacutu 61,6 ⊠

Biogerontology (2020) 21:763-771 https://doi.org/10.1007/s10522-020-09892-w



#### RESEARCH ARTICLE

## MetaboAge DB: a repository of known ageing-related changes in the human metabolome

Teodora Bucaciuc Mracica · Anca Anghel · Catalin Florentin Ion · Corina Violeta Moraru · Robi Tacutu 📵 · Gligor Andrei Lazar



#### **Bionanotechnologies**

#### Biocompatibility, Nanocarriers, Effectors



Journal of Liposome Research, 17:237-248, 2007 ISSN: 0898-2104 print / 1532-2394 online DOI: 10.1080/08982100701530027



## **Designing Lipid Nanostructures for Local Delivery** of Biologically Active Macromolecules

MIHAELA TRIF,<sup>1</sup> ANCA ROSEANU,<sup>1</sup> JEREMY H. BROCK,<sup>2</sup> AND JAMES M. BREWER<sup>2</sup>

Biometals (2010) 23:485-492 DOI 10.1007/s10534-010-9312-6

#### Liposomalization of lactoferrin enhanced its anti-tumoral effects on melanoma cells

Anca Roseanu · Paula E. Florian · Magdalena Moisei · Livia E. Sima · Robert W. Evans · Mihaela Trif

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#### Differentiation of mesenchymal stem cells onto highly adherent radio frequency-sputtered carbonated hydroxylapatite thin films

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# Dermal cells distribution on laser-structured ormosils

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#### **Human Mesenchymal Stem Cell Response to Lactoferrin-based Composite Coatings**

Madalina Icriverzi 1,20, Anca Bonciu 3,40, Laurentiu Rusen 30, Livia Elena Sima 10, Simona Brajnicov 3, Anisoara Cimpean <sup>2</sup>, Robert W. Evans <sup>5</sup>, Valentina Dinca <sup>3,\*</sup> and Anca Roseanu <sup>1,\*</sup>

Materials 2019, 12, 3414; doi:10.3390/ma12203414

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#### Salecan-Clay Based Polymer Nanocomposites for Chemotherapeutic Drug Delivery Systems; Characterization and In Vitro **Biocompatibility Studies**

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Materials 2020, 13, 5389; doi:10.3390/ma13235389

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Nanoformulation of Natural Bioactive Compounds as Efficient



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#### **Functionalized Graphene Oxide Thin** Films for Anti-tumor Drug Delivery to Melanoma Cells

Oana Craciunescu 1, Madalina Icriverzi 2, Paula Ecaterina Florian 2, Anca Roseanu 2 and Mihaela Trif 2,\* Pharmaceutics 2021, 13, 1108. https://doi.org/10.3390/pharmaceutics13081108

Delivery Systems in the Therapy of Osteoarthritis

https://www.mdpi.com/journal/pharmaceutics