

Name: Galina I. Lepesheva

Office Address: 622A RRB

Office Phone Number: 615-343-1373

Date and Place of Birth: November 3, 1960, Grodno, Belarus

PERSONAL DATA: citizen of the USA since 2013

Home Address 320 Old Hickory Blvd, Unit 111, Nashville, TN, 37221

Home Phone Number 615-476-3132

Marital Status, Spouse's Name Married, Igor A. Ges

Children, names, dates of birth son Igor I. Ges, 1987

Military Service no

Education:

- **College: school (city, state), degree, date**

1978-1983 Belarusan State University, Minsk, Belarus (*rated #1 in Belarus*), 1983 B.S./M.S. in Biochemistry (summa cum laude)

- **Professional or graduate: School(s) (city, state), degree(s), date(s), dissertation title.**

Fellowship in Bioorganic Chemistry, Institute of Bioorganic Chemistry National Academy of Sciences of Belarus, Minsk, Belarus (IBOCH, NAS), PhD in Bioorganic Chemistry, Mentors: Turko IV, PhD, Chashchin VL, PhD, DSc.

Dissertation: "Physico-chemical and immunological properties of Langmuir-Blodgett films of immunoglobulin G." (Defended in IBOCH, NAS in 1993; Ph.D degree conferred by Supreme Attestation Committee, Russian Academy of Sciences, Moscow, Russia).

- **Postgraduate Training: residency, fellowship, etc.**

Institute of Bioorganic Chemistry National Academy of Sciences of Belarus, Minsk, Belarus, Laboratory of Protein Chemistry (Prof. Usanov S.A., PhD, D.Sc., 1993-1997)

- **Visiting Scientist**

1999, April – May: Prof. Christiana Jung lab, Max Delbrück Center for Molecular Medicine, Berlin, Germany (INTAS funding).

2000, January – February: Prof. Rita Bernhard lab, Biochemistry, University of Saarland, Saarbrücken, Germany INCO-Copernicus funding.

Academic Appointments:

1987 -1992	Junior Research Scientist, Laboratory of Protein Chemistry, IBOCH, NAS, Belarus;
1992-1996	Research Scientist, Laboratory of Protein Chemistry, IBOCH, NAS, Belarus;
1996- 2000	Senior Research Scientist, Laboratory of Protein Chemistry, IBOCH, NAS, Belarus; since 1997 – research group leader
2000-2002	Research Fellow, Vanderbilt University, School of Medicine, Department of Biochemistry
2002-2006	Research Instructor, Vanderbilt University, School of Medicine, Department of Biochemistry
2006 - 2009	Research Assistant Professor of Biochemistry, Vanderbilt University, School of Medicine
2009 - 2018	Research Associate Professor of Biochemistry, Vanderbilt University, School of Medicine
2018-Present	Research Professor of Biochemistry, Vanderbilt University, School of Medicine

Professional Organizations:

- 2012 - Present Member, Vanderbilt Institute for Global Health
2012 - Present Core Faculty Member, Vanderbilt Center for Structural Biology
(<https://wp0.vanderbilt.edu/csb/faculty-core/galina-lepesheva/>)
2013 – Present Structural Biology Grid at Harvard Medical School (SBGrid) Member
(<https://sbgrid.org/members/>)
2018 – Present Member, Vanderbilt Ingram Cancer Center
(<https://www.vicc.org/member/galina-i-lepesheva>)
2018 – Present Member, Vanderbilt Institute of Chemical Biology
(<https://www.vanderbilt.edu/vicb/research.html#members>)
American Chemical Society, since 2003, American Heart Association (2005-2012), American Oil Chemists' Society (AOCS), since 2007, American Society of Biochemistry and Molecular Biology, since 2015

Professional Activities:

- EDITORIAL BOARD MEMBER: ISRN Structural Biology (2012-2015), Journal of Cytology & Molecular Biology (current)
- GRANTS REVIEW:
 - 2004-2007 National Science Foundation (ad hoc)
 - 2013, Nov 7 National Institutes of Health (XNDA, ad hoc)
 - 2014, Aug 24 NIAID review meeting for R13 conference grant applications
 - 2016, May 10 NIAID ZAI1 LR-M (S1) 1
 - 2018, June 6-7 National Institutes of Health (XNDA)ZRG1 DKUS N Special Emphasis Panels
 - 2019, July 16, NIH study section ZRG1 IDM S (02)
- PAPERS REVIEWED FOR:
ACS Med Chem Lett, ACS Infect. Dis., Anal Biochem; Antimicrob Agents Chemother; Arch Biochem Biophys; Biochem Biophys Acta; Biochem Soc Trans; Biochemistry (Mosc); Bioorg Med Chem; Curr Top Med Chem; Current Cancer Therapy Reviews, Enzyme Microb Technol; Eur J Biochem; Future Med Chem; J. Infect. Dis; J. Inorg. Bioch. J. Med. Chem; Adv Parasitol; Int J Parasitol Drug Drug Resist; Lipids; Med.Chem.Comm.; Molecules, PLoS Negl Trop Dis; PLoS One; PLOS pathogens; Scientific Reports, Science

Teaching Activities:

- **Teaching:** 1982-1983, Chemistry and Biology, High School # 42, Minsk, Belarus
- **Research Supervision:**
 - PREDOCTORAL STUDENTS:
 - 1997-2000: Natalya Strushkevich, Igor Bespalov (PhD Supervisor, IBOCH, NAS, Minsk, Belarus)
 - 2003-2013: Cornelia Virus, Charles Knutson, Matej Seliskar, Urshka Zelenko, (training, Vanderbilt University); Laura Friggeri (PhD Supervisor)
 - RESEARCH FELLOWS:
 - 2016- 2019: Dr. Laura Friggeri (postdoctoral trainee)

Research Program:

Cytochrome P450 structure/function, structure-based drug design

Cumulative listing of all grants: title, source, dollar amount, inclusive dates, percent effort.

RESEARCH SUPPORT (past)

1996-1999 INTAS, grant # 96-1343, role: co-PI

1997-2000, INCO-Copernicus, grant #ERBIC15CT960810, role: co-PI

1997-1998, Foundation of Fundamental Research of Belarus, grant # B97-154, role: co-PI

1998-1999, Foundation of Fundamental Research of Belarus, grant # B98-162, role: PI

2005 -2009, American Heart Association (National Scientist Development Grant) #0535121N, role: PI

2008-2019 NIH/NIGMS (R01) #GM067871, role: MPI; since 2012 - PI

2010, NIH/NIGMS (ARRA supplement) #GM067871S; role: PI

2010-2011, Vanderbilt Institute of Chemical Biology Pilot Project grant, role: PI

2013, NIH/NIGMS (Administrative supplement) #GM067871-10S1, role: PI

2014, NIH/NIGMS (Administrative supplement) #GM067871-11S1, role: PI

2014-2017 Viamet Pharmaceutical; role: PI

2018, NIH/NIGMS (Administrative supplement) #3R01GM067871-15S1, role: PI

RESEARCH SUPPORT (current)

01/01/2020 -30/12/2023, NIH/NIGMS (R01) #GM067871, role: PI

Competitively Renewed: Structural requirements for sterol 14 α -demethylases,

Total Budget: \$363,400 per year

Publications and Presentations:

Peer Reviewed Research Papers (* - corresponding author)

1. Pikulev, A.T., Khripchenko, I.P., **Lepesheva, G.I.** Effect of low-intensity laser radiation on the brain cholinesterase activity of rats. *Radiobiologia* 1984 24(4):565-568
2. Martsev, S.P, **Lepesheva, G.I.**, Gapeeva, E.V., Cheykina, A.V., Kirillova, N.M., Zhorov, O.V., Preygerzon, V.A., Chashchin, V.L. Antibodies labeled with isotope and enzyme label in immunometric analysis of ferritin. *Immunology*, Moscow (Rus) 1990, 1, 64-66.
3. **Lepesheva, G.I.***, Martsev, S.P. Application of biotin-streptavidin systems for the improvement of parameters of the immunometric assay. *Zh Mikrobiol Epidemiol Immunobiol.* 1990, Oct;(10):121-125
4. Turko, I.V., **Lepesheva, G.I.**, Chashchin, V.L. Direct fluoroimmuno-assay in Langmuir-Blodgett films of immunoglobulin *SPIE Proceeding.* 1991, 1572,419-423.
5. **Lepesheva, G.I.***, Martsev, S.P. Modification of the rabbit IgG hinge disulfide bond and study of interaction of the modified IgG with polyvalent antigen ferritin, protein A and anti-IgG. *Biochemistry* (Moscow, Rus.,Engl.). 1992, 7, 1089-1099
6. Turko, I.V., **Lepesheva, G.I.**, Chashchin, V.L. Direct antigen detection in Langmuir-Blodgett films of IgG modified with coproporphyrin I. *Analytica Chimica Acta.* 1992, 265, 21-26
7. Turko, I.V., **Lepesheva, G.I.**, Chashchin, V.L. Stability and stabilization of immunoglobulin G Langmuir-Blodgett films. *Thin Solid Films.* 1993, 230, 70-72.
8. **Lepesheva, G.I.***, Turko, I.V., Shestakov, V.L., Chashchin, V.L. IgG modified by coproporphyrin and possibility of direct antigen detection. *Biochemistry* (Moscow ,Rus., Engl)), 1993, 58, 6, 938-943.

9. **Lepesheva, G.I.***, Turko, I.V., Ges, I.A., Chashchin, V.L. Direct detection of antigens in Langmuir-Blodgett films of IgG formed by the method of surface plasmon resonance and in a piezo-electric system. *Biochemistry* (Moscow, Rus., Engl.), 1994, 59, 7, 701 - 705.
10. **Lepesheva, G.I.***, Usanov, S.A Using of selective chemical modification of cytochrome P450_{sc} with FITS for the estimation of intramolecular distances and conformational changes by fluorescence resonance energy transfer. *Biochemistry* (Moscow, Rus., Engl.), 1996, 8, 1395-1407.
11. **Lepesheva, G.I.***, Usanov, S.A. Dynamics and functional activity of cytochrome P450_{sc} selectively labelled with fluorescein isothiocyanate-*Biochemistry* (Moscow, Rus, Engl.), 1997, 6, 558 - 568.
12. **Lepesheva, G.I.***, Usanov, S.A. Comparative structural and immunochemical characterization of recombinant and natural cytochrome P450_{sc} (CYP11A1) *Biochemistry* (Moscow, Rus, Engl.), 1998, 2, 224-234.
13. **Lepesheva, G.I.***, Ges, I.A. Chashchin, V.L Piezoelectric Sensor for Protein Antigens on Base of Langmuir-Blodgett Films, In Proceedings of the 13th European Conference on Solid-State Transducers (EUROSENSORS XIII), The Hague, The Netherlands, 12-15 September, 1999, pp.189-192.
14. **Lepesheva, G.I.***, Azeva, T.N., Strushkevich, N.V., Adamovich, T.B., Cherkesova, T.S., Usanov, S.A. Comparative structural-functional characterization of recombinant and natural adrenodoxin. Interaction with cytochrome P450_{sc}. *Biochemistry* (Mosc) 1999 Sep;64(9):1079-1088
15. **Lepesheva, G.I.***, Strushkevich, N.V., Usanov, S.A Conformational dynamics and molecular interaction reactions of recombinant cytochrome P450_{sc} (CYP11A1) detected by fluorescence energy transfer. *Biochim Biophys Acta*. 1999,1434(1):31-43.
16. **Lepesheva, G.I.***, Azeva, T.N., Knyukshto, V.N., Chashchin, V.L., Usanov, S.A. A model of optical immunosensor for hemoproteins based on Langmuir-Blodgett films of FITC-labelled immunoglobulin G. *Sensors and Actuators* 2000, B68, 27-33.
17. **Lepesheva, G.I.***, Azeva, T.N., Strushkevich, N.V., Gilep, A.A., Usanov, S.A. .Site-directed mutagenesis of cytochrome P450_{sc} (CYP11A1). Effect of lysine residue substitution on its structural and functional properties. *Biochemistry* (Mosc). 2000 65(12):1409-1418.
18. Azeva, T.N., Gilep, A.A., **Lepesheva, G.I.**, Strushkevich, N.V., Usanov, S.A. Site-directed mutagenesis of cytochrome P450_{sc}. II. Effect of replacement of the Arg425 and Arg426 residues on the structural and functional properties of the cytochrome P450_{sc}. *Biochemistry* (Mosc). 2001;66(5):564-575
19. **Lepesheva, G.I.***, Podust, L.M., Bellamine, A., Waterman, M.R. Folding requirements are different between sterol 14 α -demethylase (CYP51) from *Mycobacterium tuberculosis* and human or fungal orthologs. *J Biol Chem*. 2001;276(30):28413-28420
20. Usanov, S.A., Graham, S.E., **Lepesheva, G.I.**, Azeva, T.N., Strushkevich, N.V., Gilep, A.A., Estabrook, R.W., Peterson, J.A. Probing the interaction of bovine cytochrome p450_{sc} (CYP11A1) with adrenodoxin: evaluating site-directed mutations by molecular modeling *Biochemistry* 2002 Jul 2;41(26):8310-20
21. **Lepesheva, G.I.***, Virus, C, Waterman, M.R. Conservation in the CYP51 family. Role of the B' helix/BC loop and helices F and G in enzymatic function. *Biochemistry*. 2003 Aug 5;42(30):9091-101.
22. **Lepesheva, G.I.***, Waterman, M.R. CYP51 – the omnipotent P450. *Mol Cell Endocrinol*, 2004, 215, 165-170.
23. **Lepesheva, G.I.***, Nes W.D., Zhou, W., Hill G.C., Waterman M.R. CYP51 from *Trypanosoma brucei* is obtusifoliosol specific. *Biochemistry*, 2004 43, 10789-10799.

24. Bellamine A, **Lepesheva G.I.**, Waterman MR. Fluconazole binding and sterol demethylation in three CYP51 isoforms indicate differences in active site topology. *J. Lipid Res.* 2004, 45 (11), 2000-2007.
25. Podust, L.M., Yermalitskaya, L.V., **Lepesheva, G.I.**, Podust, V.N., Dalmasso, E.A., Waterman, M.R. Estriol bound and ligand-free structure of sterol 14 α -demethylase (CYP51) *Structure*, 2004, 12, 1937-1945.
26. Strushkevich, N. V., Azeva, T. N., **Lepesheva G. I.**, Usanov S. A. Role of Positively Charged Residues Lys267, Lys270, and Arg411 of Cytochrome P450_{sc} (Cyp11A1), *Biochemistry (Moscow)*, 2005, 70 (6), 664-671
27. Lamb DC, Kim Y, Yermalitskaya LV, Yermalitsky VN, **Lepesheva GI**, Kelly SL, Waterman MR, Podust LM. A second FMN binding site in yeast NADPH-cytochrome P450 reductase suggests a mechanism of electron transfer by diflavin reductases. *Structure*. 2006 Jan;14(1):51-61.
28. **Lepesheva, G.I.***, Zaitseva, N.G., Nes, W.D., Zhou, W. Arase, M Liu, G., Hill, G., Waterman, M.R. CYP51 from *Trypanosoma cruzi*. A phyla-specific residue in the B' helix defines substrate preferences of sterol 14 α -demethylase *J. Biol. Chem.* 2006 Feb 10;281(6):3577-3585.
29. Zhou, W., **Lepesheva, G.I.**, Waterman, M.R, Nes, W.D. Mechanistic analysis of a multiple product sterol methyltransferase implicated in ergosterol biosynthesis in *trypanosoma brucei*. *J. Biol. Chem.* 2006 Mar 10;281(10):6290-6.
30. Strushkevich NV, Harnastai IN, **Lepesheva GI**, Usanov SA. Role of C-terminal sequence of cytochrome P450_{sc} in folding and functional activity. *Biochemistry (Mosc)*. 2006 Sep;71(9):1027-34.
31. **Lepesheva G.I.***, Hargrove TY, Ott RD, Nes WD, Waterman MR. Biodiversity of CYP51 in trypanosomes. *Biochem Soc Trans.* 2006 Dec;34(Pt 6):1161-4.
32. **Lepesheva G.I.***, Seliskar M, Knutson CG, Stourman NV, Rozman D, Waterman MR. Conformational Dynamics in the F/G Segment of CYP51 from *Mycobacterium tuberculosis* Monitored by FRET. *Arch. Biochem Biophys* 2007 Aug 15;464(2):221-7. PMID: 17585868.868
33. **Lepesheva G.I.***, Ott RD., Hargrove TY, Kleshchenko YY, Schuster I, Nes, W.D., Hill, GC, Villalta F, Waterman MR. Sterol 14 α -demethylase as a potential target for antitrypanosomal therapy: enzyme inhibition and cellular effects. *Chemistry & Biology* 2007 Nov;14(11):1283-93.
34. **Lepesheva G.I.***, Hargrove, Villalta, F, Nes, W.D Waterman, MR. CYP51, a major drug target in the cytochrome P450 superfamily. *Lipids* 2008, 43(12):1117-25, 2008 PMID: 18769951
35. **Lepesheva, G.I.***, Villalta, F., Hargrove, T., Nes, D., Waterman, M CYP51 as a Potential Target for Treatment of Human Infections with Trypanosomatidae The Proceedings of the 17th International Symposium on Microsomes and Drug Oxidations. July 2008 Saratoga Springs, NY, K706R9026 invited review
36. Buckner FS, Kraus JM, Verlinde J, Karimi M, **Lepesheva GI**, Gelb MH Rational Modification of a Candidate Cancer Drug for Use Against Chagas Disease, *J. Med Chem*, 2009, 52(6):1639-47. PMID: 19239254 .
37. Konkle M.E., Hargrove TY Kleshchenko Y.Y., von Kries JP, Marnett LJ, Nes, W.D, Villalta F., Waterman MR, **Lepesheva GI***. Indomethacin Amides As a Novel Molecular Scaffold for Targeting *Trypanosoma cruzi* Sterol 14 α -Demethylase *J. Med Chem* 2009 52(9):2846-53. PMID: 19239254
38. Lamb DC, Lei L, Warrillow AG, **Lepesheva GI**, Mullins JG, Waterman MR, Kelly SL. The first virally encoded cytochrome p450. *J Virol.* 2009 83 (16):8266-8269. *J Virol.* 2009 Jun 10. PMID: 19515774
39. **Lepesheva GI***, Park HW, Hargrove TY, Wawrzak, Z, Harp, J, Sundaramoorthy, M, Vanhollebeke B, Nes, WD, Pays E, Chaudhuri, M, Villalta, F, Waterman MR. Crystal structures of *Trypanosoma brucei* sterol 14 alpha-demethylase and implications for selective treatment of human infections *J Biol Chem.* 2010, 285 (3):1773-1780 (**Paper of the Week, cover page image**)

40. **Lepesheva GI***, Hargrove TY, Anderson S, Kleshchenko Y, Futak V, Wawrzak Z, Villalta F, Waterman M Structural insights into inhibition of sterol 14 α -demethylase in the human pathogen *Trypanosoma cruzi* *J Biol Chem* 2010 285 (33):25582-25590
41. Hargrove TY., Wawrzak Z, Liu JL, Nes W.D, Waterman MR, **Lepesheva, G.I***. Substrate preferences and catalytic parameters determined by structural characteristics of CYP51 from *Leishmania infantum* *J Biol Chem*. 2011 286(30):26838-48. PMID:21632531; PMCID:PMC3143644
42. Hargrove TY., Liu JL, Wawrzak Z, Waterman MR, Nes W.D, **Lepesheva, G.I***. Structural complex of sterol 14 α -demethylase (CYP51) with 14 α -methylenecyclopropyl- Δ 7-24, 25-dihydrolanosterol. *J Lipid Res*. 2012 53(2):311-20. PMID: 22135275; PMCID:PMC3269163
43. Nes CR, Singha UK, Liu J, Ganapathy K, Villalta F, Waterman MR, **Lepesheva GI**, Chaudhuri M, Nes WD. Novel Sterol Metabolic Network of *Trypanosoma brucei* Procylic and Bloodstream Forms. *Biochem J*. 2012 443(1):267-77. PMID:22176028, PMCID:PMC3491665
44. Buckner FC, Bahia MT, Suryadevara PK, White K, Chennamaneni NK, Hulverson M, Laydbak J, Verlinde CL, Charman SA, **Lepesheva GI**, Gelb MH Pharmacological characterization, structural studies, and *in vivo* Activity of Lead Anti-Chagas Disease Compounds Derived from Tipifarnib. *Antimicrob. Agents Chemother*. 2012 56, 4914-4921 PMID:22777048; PMCID:PMC3421879.
45. Dobish MC, Villalta F, Waterman MR, **Lepesheva GI**, Johnston JN. Organocatalytic, enantioselective synthesis of VNI: a robust therapeutic development platform for Chagas, a neglected tropical disease. *Org. Lett*, 2012, Dec 21;14 (24):6322-52012 PMID:23214987
46. Hargrove T., Kim K., Soeiro M.de N., da Silva C., Batista D., Batista M., Yazlovitskaya Y., Waterman M, Sulikowski G., **Lepesheva G***. CYP51 structures and structure-based development of novel, pathogen-specific inhibitory scaffolds. *Int. J Parasitol Drugs Drug Resist*, 2012; 2 178-186. PMID:23504044.
47. Andriani G, Amata E, Coffey B, Juda C, Erath J, Devine W, Wawrzak Z, Courtemanche G, **Lepesheva GI***, Rodriguez A, Pollastri MP. Antitrypanosomal lead discovery: Identification of a ligand-efficient inhibitor of *Trypanosoma cruzi* CYP51 and parasite growth. *J. Med. Chem*. 2013 Mar 28;56(6):2556-2567; PMID:23448316.
48. Villalta F, Dobish MC, Nde P, Kleshchenko Y, Hargrove TY, Johnson CA, Waterman MR, Johnston JN, **Lepesheva GI***. VNI cures the acute and chronic experimental Chagas disease. *J. Infect. Dis* 2013; 208(3), 504-511 PMID:23372180 PMCID:3698996 (cover page image, NIH highlights: Research news from NIGMS))
49. Soeiro MN, Soura EM, Silva CF, Batista DG, Batista MM, Pavão PP, Lionel J, Hargrove T, Kim K, Sulikowski G, Waterman MR, **Lepesheva GI**. Antiparasitic Activity of Sterol 14 α -Demethylase (CYP51) Inhibitor VNI Against Drug-Resistant Strains of *Trypanosoma cruzi*: *In vitro* and *In vivo* Studies *Antimicrob. Agents Chemother*, 2013 57(9), 4151-63. PMID:23774435; PMCID:PMC3754355
50. Suryadevara, P.K., Racherla, K.K., Olepu, S., Norcross, N.R., Tatipaka, H.B., Arif, J.A., Planer, J.D., **Lepesheva, G.I**, Verlinde, C.L.M., Buckner, F.S., Gelb, M.H., Dialkylimidazole inhibitors of *Trypanosoma cruzi* sterol 14 α -demethylase as anti-Chagas disease agents, *Bioorg. Med. Chem. Lett* 2013; 23(23):6492-9. doi: 10.1016/j.bmcl.2013.08.015.
51. Hargrove TY, Wawrzak Z, Alexander PW, Chaplin JH, Keenan M, Charman SA, Waterman MR, Chatelain E, **Lepesheva GI***. Complexes of *Trypanosoma cruzi* sterol 14 α -demethylase (CYP51) with two pyridine-based drug candidates for Chagas disease: Structural basis for pathogen-selectivity. *J Biol Chem*. 2013; 288(44):31602-15 PMID: 24047900
52. Friggeri L, Hargrove TY, Rachakonda G, Wawrzak Z, De Vita D, Waterman MR, Tortorella S, Villalta F, **Lepesheva GI*** Structural Basis for Rational Design of Inhibitors Targeting *Trypanosoma cruzi* Sterol

- 14 α -Demethylase: Two Regions of the Enzyme Molecule Potentiate its Inhibition. *J Med Chem* 2014, Aug 14;57(15):6704-6717 PMID:25033013
53. Cherkesova TS, Hargrove TY, Vanrell MC, Ges I, Usanov SA, Romano PS, **Lepesheva GI*** Sequence variation in the *CYP51A* gene alters drug sensitivity of the Y strain of *Trypanosoma cruzi* *FEBS Lett* 588 (2014), pp. 3878-3885. PMID: 25217832; NIHMSID #627819
54. Papadopoulou MV, Bloomera WD, **Lepesheva GI**, Rosenzweigc, HS, Kaiserd Marcel, Chatelain E, Ioset, JR Novel 3-nitrotriazole-based amides and carbinols as bifunctional anti-Chagasic agents. *J Med Chem*, 2015; 58(3):1307-19. NIHMSID: NIHMS663209
55. Yu X, Cojocar V, Mustafa G, Salo-Ahen O, **Lepesheva GI**, Wade RC Dynamics of CYP51: Implications for Function and Inhibitor Design. *J Mol Recognit*, 2015; 28(2):59-73. NIHMSID: NIHMS663210.
56. **Lepesheva GI***, Hargrove T, Rachakonda G, Cojean S, Nde P, Nes WD, Locuson C, Calcutt MW, Waterman MR, Daniels SJ, Loiseau P, Villalta F. VFV is a new effective CYP51 structure-derived drug candidate for Chagas disease and visceral leishmaniasis, *J. Inf. Dis.* 2015; 212(9):1439-1448. PMID: PMC4601915.
57. Hargrove TY, Wawrzak Z, Lamb DC, Guengerich FP, **Lepesheva GI***. Structure-functional characterization of sterol 14 α -demethylase from *Aspergillus fumigatus* and molecular basis for the development of antifungal drugs. *J Biol Chem*. 2015, 290(39):23916-23934. PMID: PMC4583043.
58. Guedes-da-Silva FH, Batista DG, França CF, Meuser MB, Simões MR, Araújo JS, Ferreira CG, Moreira OC, Britto C, **Lepesheva GI**, Soeiro MN. Different therapeutic outcomes of benznidazole and VNI treatment in distinct genders of mouse experimental models of *Trypanosoma cruzi* infection. *Antimicrob Agents Chemother*. 2015, 59(12):7564-7570. PMID: PMC4649169.
59. Yu X; Nandekar P; Mustafa G; Cojocar V; **Lepesheva GI**; Wade R. Ligand Tunnels in *T. brucei* and human CYP51: Insights for Parasite-specific Drug Design, *Biochim Biophys Acta - General Subjects*, 2016, 1860 (1 Pt A):67-78. NIHMSID: NIHMS744470.
60. Hoekstra W, Hargrove T, Wawrzak Z, Batista D, Silva D Nefertiti ASG, Rachakonda G, Schotzinger R, Villalta F, Soeiro MNC **Lepesheva GI***. Antiparasitic effect in vitro, activity in a murine model of Chagas disease, and structural characterization in complex with the target enzyme CYP51 from *Trypanosoma cruzi* of the potent clinical candidate VT-1161. *Antimicrob Agents Chemother*. 2016, 60 (2) 1058-1066. PMID:26643331.
61. Hargrove T, Friggeri L, Wawrzak Z, Sivakumaran S, Yazlovitskaya E, Hiebert S, Guengerich F, Waterman M, **Lepesheva GI***. Human sterol 14 α -demethylase (CYP51) as a target for anticancer chemotherapy: Towards structure-aided drug design, *J Lipid Res*, 2016, 57 (8): 1552-1563. PMID:27313059.
62. Guedes-da-Silva FH; Batista DGJ; Da Silva, CF; De Araújo JS; Pavão BP; Simões-Silva MR; Meuser MB, Demarque KC, Moreira OC; Britto C; **Lepesheva GI**, Soeiro MNC. Anti-trypanosomal activity of sterol 14 α -demethylase (CYP51) inhibitors VNI and VFV in the Swiss mouse models of Chagas disease induced by the Y strain *Trypanosoma cruzi*. *Antimicrob Agents Chemother* 2017 Mar 24;61-64. PMID: 28167559.
63. EOJ Porta, SN Jäger, I Nocito, **GI Lepesheva**, EC Serra, BL Tekwani, GR Labadie. Antitrypanosomal and antileishmanial activity of prenyl-1,2,3-triazoles. *Medchemcomm*. 2017 May 1; 8(5): 1015-1021 PMID: 28993794.
64. R Mwenechanya, J Kovářová, NJ Dickens, M. Manikhandan, P Herzyk, IM. Vincent, SK. Weidt, K Burgess, RJ.S. Burchmore, A Pountain, TK Smith, DJC, DH Kim, **GI Lepesheva**, MP. Barrett. Sterol 14 α -demethylase mutation leads to amphotericin B resistance in *Leishmania mexicana*. *PLoS Negl Trop Dis*. 2017 Jun 16;11(6):e0005649. doi: 10.1371/journal.pntd.0005649 2/2016) PMID: 28622334.

65. TY Hargrove, L Friggeri, Z Wawrzak, A Qi, WJ Hoekstra, RJ Schotzinger, JD York, FP Guengerich, **GI Lepesheva***. Structure-function and Inhibition of Sterol 14 α -Demethylase (CYP51) from *Candida albicans*. Complexes with Posaconazole and the Tetrazole-based Drug Candidate VT-1161. *J Biol Chem*. 2017 Apr 21;292(16):6728-6743. doi: 10.1074/j. PMID: 28258218.
66. Hargrove TY, Garvey EP, Hoekstra WJ, Yates CM, Wawrzak Z, Rachakonda G, Villalta F, **Lepesheva GI***. Crystal Structure of the New Investigational Drug Candidate VT-1598 in Complex with *Aspergillus fumigatus* Sterol 14 α -Demethylase Provides Insights into Its Broad-Spectrum Antifungal Activity. *Antimicrob Agents Chemother*. 2017 Jun 27;61(7). pii: e00570-17. PMID: 28461309.
67. **Lepesheva G**, Christov P, Sulikowski GA, Kim K. A convergent, scalable and stereoselective synthesis of azole CYP51 inhibitors, *Tetrahedron Lett*, 2017, 58(45): 4248-4250. PMCID: PMC5777588.
68. Friggeri L, Hargrove TY, Wawrzak Z, Blobaum AL, Rachakonda G, Lindsley CW, Villalta F, Nes WD, Botta M, Guengerich FP, **Lepesheva GI***. Sterol 14 α -demethylase structure-based design of VNI derivatives to target fungal infections: synthesis, biological evaluation, and crystallographic analysis. *J. Med.Chem*. 2018 July 12; 61(13):5679-5691. PMID: 29894182; MC6176729.
69. Hargrove TY, Wawrzak Z, Fisher PM, Child SA, Nes WD, Guengerich FP, Waterman MR, **Lepesheva GI***. Binding of a physiological substrate causes large-scale conformational reorganization in cytochrome P450 51. *J. Biol. Chem*. 2018 October 16. 293 (50) PubMed PMID: 30327430.
70. Friggeri L, Hargrove TY, Blobaum A, Fisher P, Oliveira GM, Soeiro MNC, Nes WD, Lindsley CW, Villalta F, Guengerich FP, **Lepesheva GI***. Sterol 14 α -Demethylase Structure-Based Optimization of Drug Candidates for Human Infections with the Protozoan *Trypanosomatidae*. *J. Med. Chem*, 2018 Dec 13;61(23):10910-10921. PubMed PMID: 30451500.
71. da-Silva FHG; Batista DGJ; Da Silva CF; Pavão BP; Meuser MB; Moreira OC; Souza LRQ; Britto C; Villalta F; **Lepesheva GI**, Soeiro MNC. Successful Aspects of the Co-administration of Sterol 14 α -Demethylase Inhibitor VFV and Benznidazole in Experimental Mouse Models of Chagas Disease Caused by the Drug-Resistant Strain of *Trypanosoma cruzi*. *ACS Infect Dis*. 2019 Mar 8;5(3):365-371
72. Friggeri L.; Hargrove T.; Wawrzak Z.; Guengerich FP.; **Lepesheva, GI***. Validation of human sterol 14 α -demethylase (CYP51) druggability: structure-guided design, synthesis and evaluation of stoichiometric, functionally irreversible inhibitors. *J Med Chem*. 2019 Nov 27;62(22):10391-10401 PMID:31663733.
73. Wang X.; Cal M.; Kaiser M.; Buckner F.; **Lepesheva GI**; Sanford A.; Davis P.; Vennerstrom J. A New Chemotype with Promise against *Trypanosoma cruzi* *Bioorg Med Chem Lett*. 2020 Jan 1;30(1):126778. PMID:31706668.
74. Hargrove TY, Wawrzak Z, Guengerich FP, **Lepesheva GI***. A requirement for an active proton delivery network supports a compound I-mediated C-C bond cleavage in CYP51 catalysis. *J Biol Chem*. 2020 Jul 17;295(29):9998-10007. PMID:32493730.
75. Mercorelli B.; Lugini A.; Celegato M.; Palù G.; Gribaudo G.; **Lepesheva GI**; Loregian A. The Clinically Approved Antifungal Drug Posaconazole Inhibits Human Cytomegalovirus Replication. *Antimicrob Agents Chemother*. 2020 Sep 21;64(10):e00056-20. PMID: 32690644.
76. Lamb DC, Hargrove TY, Zhao B, Wawrzak Z, Goldstone JV, Nes WD, Kelly SL, Waterman MR, Stegeman JJ, **Lepesheva GI***. Concerning P450 evolution: Structural Analyses Support Bacterial Origin of Sterol 14 α -Demethylases. *Mol Biol Evol*. 2020 Oct 8:msaa260. doi: 10.1093/molbev/msaa260. Online ahead of print. PMID: 33031537.

Book chapters, invited review articles (* - corresponding author)

1. Waterman, M.R, and **Lepesheva G.I.** Sterol 14 α -demethylase, an abundant and essential mixed-function oxidase. *Biochem Biophys Res Commun.* 2005 Dec 9;338(1):418-422 **(invited review)**
2. **Lepesheva G.I.***, Waterman M.R. Sterol 14 α -demethylase cytochrome P450 (CYP51), a P450 in all biological kingdoms, *Biochim Biophys Acta.* 2007 Mar;1770(3):467-77 **(invited review)**
3. **Lepesheva GI***, Waterman MR Structural basis for conservation in the CYP51 family *Biochim Biophys Acta.*, 2011 Jan;18 14(1):88-93 **(invited review)**
4. **Lepesheva G.I.***, Waterman M.R. Sterol 14 α -Demethylase (CYP51) as a Therapeutic Target for Human Trypanosomiasis and Leishmaniasis. *Cur. Top. Med. Chem.* 2011 11 (16): 2060-2071 **(invited review)**
5. **Lepesheva G.I.***, Villalta F, Waterman MR. Targeting *Trypanosoma cruzi* sterol 14 β -demethylase (CYP51). *Adv Parasitol.* 2011; 75:65-87 **(book chapter)**
6. **Lepesheva GI*** Design or screening of drugs for the treatment of Chagas disease: what shows the most promise? *Expert Opin Drug Discov.* 2013 (8) 12, 1479-89 **(invited review)**
1. **Lepesheva GI***, Friggeri L, Waterman MR. CYP51 as a target for fungi and protozoan parasites: past, present and future. *Parasitology*, 2018 145(14):1820-1836. PMC6185833 **(invited review)**

Presentations at Scientific Meetings:

- July 23-26, 2006, Swansea, UK. 8th International P450 Symposium: “Biodiversity of CYP51 in trypanosomes” **(invited).**
- May 18, 2008, Seattle, Washington, USA, 99th AOCs Annual Meeting & Expo: “CYP51, a major drug target in the cytochrome P450 superfamily” **(invited, session co-Chair).**
- July 7-10, 2008, Saratoga Springs, NY. The 17th International Symposium on Microsomes and Drug Oxidations: “CYP51 as a Potential Target for Treatment of Human Infections with Trypanosomatidae” **(invited).**
- May 17, 2010, Phoenix, OR, USA. 101st AOCs Annual Meeting & Expo: Structural basis for inhibition of sterol 14 α -demethylase” **(invited, session co-Chair).**
- May 25, 2010, Cambridge, MA, USA. Novartis Institute for Biomedical Research: “Structural insights into selective inhibition of sterol 14 α -demethylase (CYP51) in *Trypanosomatidae*” **(invited).**
- October 3-7 2010, Woods Hole MA, USA. 10th International Symposium on Cytochrome P450 Biodiversity and Biotechnology: “Structural basis for the CYP51 family conservation and druggability” **(invited).**
- October 5-7, 2011, Modena, Italy. COST CM0801 Annual Meeting New drugs for neglected diseases: “CYP51 structure and structure-based design of novel, pathogen-specific inhibitory scaffolds” **(invited).**
- November 7-11, 2011, San Paulo, Brazil. Symposium on Drug Design and Development for Neglected Diseases: “Structure-based development of novel sterol 14 α -demethylase inhibitors for treatment of human trypanosomiasis and leishmaniasis” **(invited).**
- April 6, 2012, Texas Tech University, Lubbock, TX. Biochemistry Seminar “Sterol 14 α -demethylase: Structural basis for the development of pathogen-specific drugs” **(invited).**
- April 19-20, 2012, Tres Cantos (Madrid), Spain. Chagas Drug Discovery Consortium Meeting “Sterol 14 α -demethylase (CYP51) as a therapeutic target” **(invited).**
- June 22-26, 2012, Torino, Italy. 11th Symposium on Cytochrome P450 Biodiversity and Biotechnology “Structure-based design of pathogen-specific CYP51 inhibitors” **(invited).**
- November 26, 2012, Vanderbilt Institute for Global Health. “CYP51 structures and structure-based development of novel chemotherapies for neglected tropical diseases” **(invited).**

June 18-22, 2013, Seattle, WA. International Conference on Cytochrome P450: Biochemistry and Biophysics, "Use of Structure/Function for Design of Drugs to Inhibit CYP51" (**invited**).

November 13, 2013, Washington, DC. Chagas Drug Discovery Consortium meeting, "CYP51 structure-based VNI scaffold development for Chagas disease" (**invited**).

November 16–18, 2014. Mar del Plata, Argentina. X Congress of the Argentinean society of protozoology, "New CYP51 inhibitors as potential drug candidates against human infections with Trypanosomatidae"(**invited**).

June 12-15, 2015, Tokyo, Japan. 19th International Conference of Cytochrome P450, "CYP51 structure based VNI scaffold development for treatment of human infections: *Trypanosomatidae* vs. the filamentous fungus *Aspergillus fumigatus*" (**invited**).

October 26-28, 2015, Belgrade Serbia. 2nd COST CM1307 Conference Medicinal Chemistry in Parasitology, "Structure-based development of novel antimicrobial agents targeting sterol 14 α -demethylase" (**invited, opening lecture**).

February 1, 2017, Skype for Business Presentation at the Teleconference with NIH/NIAID "VNI/VFV as drug candidates for Chagas disease" (**invited**).

August 20 – 24, 2017, Washington, DC. Symposium on CYP450 Inhibitors as Drug Discovery Targets, 24th ACS National Meeting. "CYP51 inhibitors for Chagas disease" (**invited**).

August 27-31, 2017, Düsseldorf, Germany. 20th International Conference on Cytochrome P450: Biochemistry, Biophysics and Biotechnology, "CYP51: phyla-specific structural features and structure-based design of antiparasitic, antifungal and anticancer drugs" (**invited**).

July 15-19, 2018, York, UK. 14th International Symposium on Cytochrome P450 Biodiversity and Biotechnology, "Structural dynamics in the CYP51 function: from bacteria to humans" (**invited**).

July 24, 2018, Minsk, Belarus Institute of Bioorganic Chemistry National Academy of Sciences of Belarus: "Substrate binding reveals the essential role of structural dynamics in function of sterol 14 α -demethylase" (**invited**).

June 23-27, 2019, Brisbane, Australia, 21st International Conference on Cytochrome P450: Biochemistry, Biophysics and Biotechnology, "Lineage-specific structural features in CYP51 catalysis and inhibition" (**invited**).

October 6, 2020, via Zoom. Chemical Biology Association of Students/Faculty Seminar Series "Validation of human CYP51druggability: structure-based design of stoichiometric, functionally irreversible inhibitors".

November 16, 2020, Vanderbilt Redox Enzymology Meeting "Structural analyses of CYP51-ferredoxin fusion protein from *Methylococcus capsulatus* support bacterial origin of sterol 14 α -demethylases".