Extended biography

Name: Juan Bautista Rodriguez

Nationality: Argentinean

Marital status: Married, two children.

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Education/Training

Institution: Universidad de Buenos Aires, Degree: Licenciado (1982) major in Organic Chemistry.
Institution: Universidad de Buenos Aires, Degree: Ph. D. (1990) major in Organic Chemistry
Institution: National Institutes of Health, Bethesda, USA, Postdoctoral (January 1992–December 1993)

A. Personal Statement

The interest of our research is to develop new antiparasitic agents effective against toxoplasmosis and American trypanosomiasis (Chagas disease) based on the metabolic differences between *Toxoplasma gondii* and *Trypanosoma cruzi* the etiologic agents of these diseases, and the mammalian host. The isoprenoid pathway constitutes a major target for the treatment of toxoplasmosis and other parasitic diseases. Based on these facts, it has been considered to investigate the effect of pyrophosphate analogues (bisphosphonates) against the enzymatic activity of *T. gondii* and *T. cruzi* farnesyl diphosphate synthase, and to perform structure-activity relationship studies to assist drug design; second, to study the effect of aryloxyethyl selenocyanate derivatives against squalene synthase, and against *T. gondii* and *T. cruzi* cells. Our laboratory has a vast experience in this area of research and has developed very potent drugs against these molecular targets. I have a strong background in Synthetic Organic Chemistry and in Medicinal Chemistry. Since my postdoctoral studies at the NIH (Bethesda campus), I have been involved in projects aimed at searching new carbanucleosides targeting different viruses as well as selenocyanates aganist *T. cruzi* whose molecular target is squalene synthase (SQS) and diverse linear bisphosphonates as growth inhibitors either of *T. cruzi* or *T. gondii* cells. The mode of action of these linear bisphosphonates turns out to be parasitic farnesyl diphosphate synthase (FPPS), a key enzyme of isoprenoid biosynthesis that catalyzes farnesyl diphosphate formation.

Ongoing Research Support

– Faculty Resources Grant, University of Buenos Aires 20020170100067BA Rodriguez (PI) − 01/01/18-12/06/23. Isoprenoid biosynthesis as a target for the development of antiparasitic agents. The goal of this study is to design and synthesize growth inhibitors of pathogenic parasites. Role: PI
– ANPCyT, FONCyT, PICT-2018-03888 − Rodriguez (PI) – 06/2020−06/2023. Design, synthesis and biological evaluation of antiparasitic agents. The goal of this study is to design and synthesize growth inhibitors of pathogenic parasites. Role: PI.
– ANPCyT, FONCyT, PICT-2021-I-A-00887 − Rodriguez (PI) – 06/2023−06/2026. Design, synthesis and biological evaluation of antiparasitic agents. The goal of this study is to design and synthesize growth inhibitors of pathogenic parasites. Role: PI
– CONICET PIP 11220200101544 CO − Rodriguez (PI) − 10/2021−09/2023. Medicinal Chemistry: Design of antiparasitic agents and agonists and antagonists of adenosine receptors. The goal of this study is to design and synthesize growth inhibitors of pathogenic parasites. Role: PI.

Completed Research Support

– European Commission Contract Nº ERBIC18 CT98 − Haemers (PI) − 01/01/1999−12/31/2001. Rational Drug Design in Leishmaniasis. Mechanism based on Inhibitors of Trypanothione Biosynthesis. International Collaboration Award. The goal was to develop inhibitors of trypanothione biosynthesis. Role: Co-PI.
– World Health Organization TDR ID A00044 − Docampo (PI) − 07/01/2000-06/30/2001. Pyrophosphate analogs against trypanosomiasis and leishmaniasis. The goal was to employ bisphosphonates as lead drugs targeting farnesyl pyrophosphate synthase. Role: Co-PI.

– ANPCyT, FONCyT, PICT 06-00000-00579 (1998–1999). Role: PI.
– ANPCyT, FONCyT, PICT PICT2004 21897 (2005–2007). Role: PI.
– ANPCyT, FONCyT, PICT PICT-2008-1690 (2010–2012). Role: PI.
– ANPCyT, FONCyT, PICT PICT-2012-0457 (2013–2015). Role: PI.
– ANPCyT, FONCyT, PICT-2015-1349 (2016–2018). Role: PI.
– Antorchas Foundation A-13434/1-000124 (1997–1998). Role: PI
– Antorchas Foundation A-13532/1-78 (1998–1999). Role: PI
– Antorchas Foundation 14116 – 77 (2002–2003). Role: PI
– Antorchas Foundation 14264 (2003–2004). Role: PI
– Faculty Resources Grant, University of Buenos Aires EX017 (1995–1997). Role: PI.
– Faculty Resources Grant, University of Buenos Aires TX073 (1997–1998). Role: PI.
– Faculty Resources Grant, University of Buenos Aires X080 (2001–2003). Role: PI.
– Faculty Resources Grant, University of Buenos Aires X-252 (2004–2007). Role: PI.
– Faculty Resources Grant, University of Buenos Aires X-191 (2008–2010). Role: PI.
– Faculty Resources Grant, University of Buenos Aires 20020100100380 (2011–2014). Role: PI.
– Faculty Resources Grant, University of Buenos Aires 20020130100223BA (2014–2017). Role: PI.
– CONICET PIP 0635/98 (1999–2001). Role: PI.
– CONICET PIP 5508 CO (2005–2006). Role: CoPI.
– CONICET PIP 112-200801-01888 (2009–2011). Role: PI.
– CONICET PIP 112-201101-00797 (2012–2014). Role: PI.
– CONICET PIP 112-201501-00631 CO (2015–2017). Role: PI.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1986–1991; Teaching Assistant at the Department of Organic Chemistry, FCEyN−University of Buenos Aires.
1992–1993; Visiting Fellow at the National Institutes of Health, Bethesda, Maryland.
1995–2000; Adjunct Investigator at the National Research Council of Argentina (CONICET).
1997–2004; Assistant Professor at the Department of Organic Chemistry, FCEyN−University of Buenos Aires.
Oct 1999–Nov 1999; Guest Researcher at the National Cancer Institute, NIH, Bethesda, Maryland, USA
2000–2006; Independent Investigator at the National Research Council of Argentina (CONICET).
2004–2005; Associate Professor at the Department of Organic Chemistry, FCEyN−University of Buenos Aires.
2005–present; Full Professor at the Department of Organic Chemistry, FCEyN−University of Buenos Aires.
2006–2019; Principal Investigator at the National Research Council of Argentina (CONICET).
2019–present; Superior Investigator at the National Research Council of Argentina (CONICET).

Other Experience and Professional Memberships

2015–2022; Member of the Editorial Advisory Board of the *Journal of Medicinal Chemistry* (American Chemical Society).
2022–2023 Member of the “Search Committee for *Editor-in-Chief*” for an American Chemical Society Journal.
2001–present; Editorial Advisory Board *Mini Reviews in Medicinal Chemistry*
2005–2006; Editorial Advisory Board *Medicinal Chemistry Reviews – on Line*
2006–present; Editorial Advisory Board *Recent Patent Reviews on Anti -Infective Drug Discovery*
2001; Executive Guest Editor *Current Pharmaceutical Design* "hot topic issue" (vol 7, issue 12).
2015–2018; Editorial Advisory Board, Section Editor (Metabolic Agents) *Immunology, Endocrine and Metabolic Agent in Medicinal Chemistry*.
1993–present; Member *American Chemical Society*.
2011–present; Member *Argentinean Society of Protozoology*.
1986–present; Sociedad Argentina de Investigaciones en Química Orgánica (*Argentinean Society of Research in Organic Chemistry*, SAIQO)

Honors

2023 Merit Diploma in Organic Chemistry, Fundación Konex
2012 Outstanding Reviewer of the *Journal of Medicinal Chemistry*, American Chemical Society.
1991 "Dr. Luis Guglialmelli Prize", Argentinean Chemical Association (AQA)

C. Contributions to Science

1. Studies on the chemotherapy of antiviral agents.

During my stay at NIH carrying out postdoctoral studies under the guidance of Dr. V. E. Marquez, we were pioneers in the synthesis and design of carboxyclic nucleosides, particularly, those structurally related to the naturally occurring neplanocin C (a,b). These studies lead to the development of one of the most effective antiherpetic drug, the carbanucleoside *N*-methano-*carba*-T (c−e), which turns out to be more potent than the currently used in the clinic acyclovir and ganciclovir. The sulfur-containing analogue employing a thiirane ring to fix the Northern conformation, which was envisioned and designed in our laboratory (f), exhibit a similar efficacy as *N*-methano-*carba*-T (g). In our lab, we accomplished the first total synthesis of (–)-neplanocin C (h), which turned out to be a potent agonist in A_3 adenosine receptor and a selective one towards the other subtypes (i). We also carried out the first enantioselective synthesis of (+)-neplanocin F (j,k) and the DNA analogues (2′-deoxy derivatives) of neplanocin C (l). Significant contributions in the synthesis of the pseudosugar ring for carbanucleosides have also been made (m−o).

a– Synthesis of cyclopropane-fused dideoxycarbocyclic nucleosides structurally related to neplanocin C. Rodriguez, J. B.; Marquez, V. E.;* Nicklaus, M. C.; Barchi Jr., J. J. *Tetrahedron Lett*. **1993**, *34*, 6233–6236.

b– Conformationally locked nucleosides analogues. Synthesis of dideoxycarbocyclic nucleosides analogues structurally related to neplanocin C. Rodriguez, J. B., Marquez, V. E.;* Nicklaus, M. C.; Mitsuya, H.; Barchi, Jr., J. J. *J. Med. Chem*. **1994**, *37*, 3389–3399.

c– Synthesis of cyclopropane-fused dideoxy-carbocyclic nucleosides locked in the Northern conformation." Marquez, V. E. Rodriguez, J. B.; Nicklaus M. C.; Barchi Jr., J. J.; Siddiqui, M. *U. S. Patent* 5,629,454 (May 13, 1997). Filed September 23, 1994.

d– Conformationally locked nucleoside analogs as antiherpetic Agents. Marquez, V. E.; Nicklaus, M. C.; Barchi Jr., J. J.; Rodriguez, J. B.; Siddiqui, M. *U. S. Patent* 5,840,728 (Nov. 24, 1998). Filed August 7, 1997.

e– Conformationally locked nucleoside analogues. Marquez, V. E.; Rodriguez, J. B.; Nicklaus, M. C.; Barchi Jr., J. J. and M. Siddiqui. *U. S. Patent* 5,869,666 (Feb. 9, 1999). Filed March 14, 1997.

f– Synthesis of conformationally locked carbocyclic nucleosides built on a thiabicyclo[3.1.0]hexane system as a pseudosugar surrogate. Elhalem, E.; Comin, M. J.; Rodriguez, J. B.* *Eur. J. Org. Chem*. **2006**, 4473–4482.

g– Synthesis and biological evaluation of *N*-thia-*carba*-thymidine as an antiherpetic agent. Elhalem, E.; Pujol, C. A.; Damonte, E. B. Rodriguez, J. B.* *Tetrahedron* **2010**, *66*, 3332–3340.

h– First synthesis of (–)-neplanocin C. Comin, M. J.; Rodriguez, J. B.* *Tetrahedron* **2000**, *56*, 4639–4649.

i– Structural determinants of efficacy at A_3 adenosine receptors: Modification of the ribose moiety. Gao, Z. –G.; Jeong, L. S.; Moon, H. R.; Kim, H. O.; Choi, W. J.; Shin, D. H.; Elhalem, E.; Comin, M. J.; Melman, N.; Mamedova, L.; Gross, A. S.; Rodriguez, J. B.; Jacobson, K. A.* *Biochem. Pharmacol*. **2004**, *67*, 893–901.

j– Enantioselective synthesis of (+)-neplanocin F. Comin, M. J.; Leitofuter, J.; Rodriguez, J. B.* *Tetrahedron* **2002**, *58*, 3129–3136.

k– New progresses in the enantioselective synthesis and biological properties of carbocyclic nucleosides. Rodríguez, J. B.;* Comin, M. J. *Mini Rev. Med. Chem.* **2003**, *3*, 95–114.

l– Synthesis of conformationally locked carbocyclic nucleosides built on an oxabicyclo[3.1.0]hexane system. Comin, M. J.; Rodriguez, J. B.;* Russ, P.; Marquez, V. E.* *Tetrahedron* **2003**, *59*, 295–301.

m– Synthetic studies towards the preparation of (4*R*,5*R*)-(–)-3-[(benzyloxy)methyl]-4,5-*O*-isopropylidene-cyclopenten-2-one. An important synthetic intermediate for carbanucleosides. Elhalem, E.; Comin, M. J.; Leitofuter, J.; García-Liñares G.; Rodriguez, J. B.* *Tetrahedron : Asymmetry* **2005**, *16*, 425–431.

n– Cerium ammonium nitrate: A new catalyst for regioselective protection of glycols. Comin, M. J.; Elhalem, E.; Rodríguez, J. B.* *Tetrahedron* **2004**, *60*, 11851–11860.

o– Chiral 1,4-dicarbonyl-2,3-*O*-isopropylidene derivatives. Rapid racemization on standing. Rodríguez, J. B. *Tetrahedron* **1999**, *55*, 2157–2170.

2. Studies on the chemotherapy of antiparasitic agents targeting squalene synthase.

Development of **WC-9** (4-phenoxyphenoxyethyl thiocyanate) an effective inhibitor of *Trypanosoma cruzi* proliferation (a,b). **WC-9** was more potent than nifurtimox under similar assays conditions and a rigorous structure-activity relationship was established (c–g). The mechanism of action of **WC-9** is the inhibition of the enzymatic activity of *T. cruzi* squalene synthase at the nanomolar range (h). Work that led to **WC-9** appearance was the first Medicinal Chemistry project conducted in Argentina (i). The progresses made on this subject can be reviewed in (j–l). **WC-9** and closely related compounds are also effective against apicomplexan parasites such as *Toxoplasma gondii* (m,n). Selenium-containing analogues of **WC-9** resulted to be two orders of magnitude more potent than their sulfur-containing counterpart with excellent therapeutic index values (o–q).

a– Structure-activity relationship of new growth inhibitors of *Trypanosoma cruzi.* Cinque, G. M.; Szajnman, S. H.; Zhong, L.; Docampo, R.; Schvartzapel, A. J.; Rodriguez, J. B.;* Gros, E. G. *J. Med. Chem*. **1998**, *41*, 1540–1554.

b– Design, synthesis and biological evaluation of new growth inhibitors of *Trypanosoma cruzi* (epimastigotes). Schvartzapel, A. J.; Zhong, L.; Docampo, R.; Rodriguez, J. B.;* Gros, E. G. *J. Med. Chem*. **1997**, *40*, 2314–2322.

c– Design and synthesis of aryloxyethyl thiocyanate derivatives as potent inhibitors of *Trypanosoma cruzi* proliferation. Szajnman, S. H.; Yan, W.; Bailey, B. N., Docampo, R.; Elhalem, E.; Rodriguez, J. B.* *J. Med. Chem*. **2000**, *43*, 1826–1840.

Commentary in ***Science*** (interview with Dan Ferber) "Infectious Disease: New Weapons in the Battle of the Bugs". *Science* **2002**, *295(5554)*, 433–434.

d– Design, synthesis and biological evaluation of aryloxyethyl thiocyanate derivatives against *Trypanosoma cruzi*. Elhalem, E.; Bailey, B. N.; Docampo, R.; Ujváry, I.; Szajnman, S. H.; Rodriguez, J. B.* *J. Med. Chem*. **2002**, *45*, 3984–3999.

e– Aryloxyethyl thiocyanates are potent growth inhibitors of *Trypanosoma cruzi* and *Toxoplasma gondii*. Chao, M. N.; Exeni Matiuzzi, C.; Storey, M.; Li, C.; Szajnman, S. H.; Docampo, R.; Moreno, S. N.; Rodríguez, J. B.* *ChemMedChem* **2015**, *10*, 1094–1108.

f– Design, synthesis and biological evaluation of WC-9 analogues as antiparasitic agents. P. D. Elicio, M. N. Chao, M. Galizzi, C. Li, S. H. Szajnman, R. Docampo, S. N. J. Moreno and J. B. Rodriguez.* *Eur. J. Med. Chem*. **2013**, *69*, 480–489.

g– Fluorine-containing aryloxyethyl thiocyanate derivatives are potent inhibitors of *Trypanosoma cruzi* and *Toxoplasma gondii* proliferation. García Liñares, G.; Gismondi, S.; Osa Codesido, N.; Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem. Lett*. **2007**, *17*, 5068–5071.

h**–** Mechanism of action of 4-phenoxyphenoxy derivatives against *Trypanosoma cruzi*, the causative agent of Chagas disease. Urbina, J. A.;* Concepcion, J. L.; Montalvetti, A.; Rodriguez, J. B.; Docampo, R. *Antimicrob. Agents Chemother*. **2003**, *47*, 2047–2050.

i– Synthesis and biological activity of synthetic juvenile hormone analogues for *Trypanosoma cruzi*. Rodriguez, J. B.; Gros, E. G.;* Stoka, A. M. *Bioorg. Med. Chem. Lett*. **1991**, *1*, 679–682.

j– Design, synthesis and anti-*Trypanosoma cruzi* evaluation of a new class of cell growth inhibitors structurally related to fenoxycarb. Schvartzapel, A. J.; Fichera, L.; Esteva, M.; Rodriguez, J. B.; Gros, E. G.* *Helv. Chim. Acta* **1995**, *78*, 1207–1214.

k– Progresses in the field of drug design to combat tropical protozoan parasitic diseases. García Liñares, G.; Ravaschino, E. L.; Rodriguez, J. B.* *Curr. Med. Chem*. **2006**, *13*, 335–360.

l– Current status and progresses made in malaria chemotherapy. García Liñares, G.; Rodriguez, J. B.* *Curr. Med. Chem*. **2007**, *14*. *14*, 289–314.

m– New antibacterials for the treatment of toxoplasmosis; a patent review. Rodriguez, J. B.;* Szajnman, S. H. *Expert Opinion Ther. Patents* **2012**, *22*, 311–334.

n– Activity of fluorine–containing analogues of WC-9 and structurally related analogues against two intracellular parasites: *Trypanosoma cruzi* and *Toxoplasma gondii*. Chao, M. N.; Li, C.; Storey, M.; Falcone, B. N.; Szajnman, S. H.; Bonesi, S. M.; Docampo, R.; Moreno, S. N. J.; Rodríguez, J. B.* *ChemMedChem* **2016**, *11*, 2690–2702.

o– Selenium-containing analogues of WC-9 are extremely potent inhibitors of *Trypanosoma cruzi* proliferation. Chao, M. N.; Storey, M.; Li, C.; Rodríguez, M. G.; Di Salvo, F.; Szajnman, S. H;* Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B.;* *Bioorg. Med. Chem.* **2017**, *25*, 6435–6449.

p– Further insights of selenium-containing analogues of WC-9 against *Trypanosoma cruzi*. Chao, M. N.; Lorenzo Ocampo, M. V.; Szajnman, S. H.;* Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem*. **2019**, *27*, 1350–1361.

q– Synthetic and mechanistic studies on 2,3-dihydrobenzo[*b*][1,4]oxaselenines formation from selenocyanates. M. N. Chao, S. H. Szajnman,* M. Cattaneo, J. Sánchez González, S. M. Bonesi and J. B. Rodríguez.* *Synthesis* **2020**, *52*, 1643–1658

3. Studies on the chemotherapy of antiparasitic agents targeting farnesyl diphosphate synthase.

We developed linear bisphosphonates as efficient and selective antiparasitic agents either against *T. cruzi* or *T. gondii* proliferation. We have begun the design of antiparasitic bisphosphonates many years ago finding that non functionalized bisphosphonates exhibited a modest antiparasitic activity against *T. cruzi* (a) whose primary target resulted to be farnesyl diphosphate synthase (b,c). 2-Alkylaminoethyl bisphosphonates have proven to be extremely potent inhibitors of *T. cruzi* proliferation targeting *Tc*FPPS at the low nanomolar concentration (d,e).

We were able to crystallize these bisphosphonate with the target enzyme, a fact that will be very useful for drug design (f). Some 2-alkylaminoethyl bisphosphonates also behaved as potent inhibitor of the enzymatic activity of *Tc*SQS (g). Some structural variations on linear bisphosphonates led to potent molecules against *T. gondii* growth, particularly fluorine and sulfur-containing derivatives (h–l). It is worth mentioning sulfone-containing bisphosphonates are unusually potent inhibitors of *T. gondii* and *Plasmodium falciparum*. One of them turns out to be very effective against the extremely virulent RH strain of *T. gondii* in *in vivo* assays (j). We have published the recent advances about the design of FPPS modulators (m,n).

a– Bisphosphonates derived from fatty acids are potent growth inhibitors of *Trypanosoma cruzi*. Szajnman, S. H.; Bailey, B. N.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem. Lett*. **2001**, *11*, 789–792.

b– Bisphosphonates derived from fatty acids are potent inhibitors of *Trypanosoma cruzi* farnesyl pyrophosphate synthase. Szajnman, S. H.; Montalvetti, A.; Wang, Y.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem. Lett*. **2003**, *13*, 3231–3235.

c– Synthesis and biological evaluation of 1-amino-1,1-bisphosphonates derived from fatty acids against *Trypanosoma cruzi* targeting farnesyl pyrophosphate synthase. Szajnman, S. H.; Ravaschino, E. L.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem. Lett*. **2005**, *15*, 4685–4690.

d– Synthesis and biological evaluation of 2-alkylaminoethyl-1,1-bisphosphonic acids against *Trypanosoma cruzi* and *Toxoplasma gondii* targeting farnesyl diphosphate synthase. Szajnman, S. H.; García Liñares, G.; Li, Z. –H.; Galizzi, M.; Jiang, C.; Bontempi, E.; Ferella, M.; Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem.* **2008**, *16*, 3283–3290.

e– Synthesis and biological evaluation of new 2-alkylaminoethyl-1,1-bisphosphonic acids against *Trypanosoma cruzi* and *Toxoplasma gondii* targeting farnesyl diphosphate synthase. Rosso, V. S.; Szajnman, S. H.; Malayil, L.; Galizzi, M.; Moreno, S. N. J.; Docampo, R. Rodriguez, J. B.* *Bioorg. Med. Chem.* **2011**, *19*, 2211–2217.

f– Design, synthesis, calorimetry and crystallographic analysis of 2-alkylaminoethyl-1,1-bisphosphonates as inhibitors of *Trypanosoma cruzi* farnesyl diphosphate synthase. Aripirala, S.; Szajnman, S. H.; Jakoncic, J.; Rodriguez, J. B.; Docampo, R.; Gabelli, S. B.;* Amzel, L. M.* *J. Med. Chem*. **2012**, *55*, 6445–6454.

g– *Trypanosoma cruzi* squalene synthase is a major target for 2-alkylaminoethyl-1,1-bisphosphonates. Rodrígues-Poveda, C. A.; González-Pacanowska, D.; Szajnman, S. H.; Rodríguez, J. B.* *Antimicrob. Agents Chemother*. **2012**, *56*, 4483–4486.

h– Design, synthesis and biological evaluation of 1-(fluoroalkylidene)-1,1-bisphosphonic acids against *Toxoplasma gondii* targeting farnesyl diphosphate synthase. Szajnman, S. H.; Rosso, V. S.; Malayil, L.; Smith, A.; Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B.* *Org. Biomol. Chem*. **2012**, *10*, 1424–1433.

i– Design, synthesis and biological evaluation of sulfur-containing 1,1-bisphosphonic acids as antiparasitic agents. Recher, M.; Barboza, A. P.; Malayil, L.; Smith, A.; Szajnman, S. H.; Moreno, S. N. J.; Docampo, R. Rodriguez J. B.* *Eur. J. Med. Chem*. **2013**, *60*, 431–440.

j– *In vitro* and *in vivo* activity of sulfur-containing linear bisphosphonates against Apicomplexan parasites. Szajnman, S. H.; Galaka, T.; Li, Z. –H.; Li, C.; Storey, M.; Howell, N. M.; Muralidharan, V.; Chao, M. N. Moreno, S. N. J.;* Rodríguez, J. B.* *Antimicrob. Agents Chemother*. **2017**, *61*, e01590–16.

k– Synergistic activity of statins and bisphosphonates against acute experimental toxoplasmosis. Li, Z. –H.; Li, C.; Szajnman, S. H.; Rodríguez, J. B.; Moreno, S. N. J.* *Antimicrob. Agents Chemother*. **2017**, *61*, e02628–16

l– Synthesis and biological evaluation of 1-alkylaminomethyl-1,1-bisphosphonic acids against *Trypanosoma cruzi* and *Toxoplasma gondii* targeting farnesyl diphosphate synthase. Galaka, T.; Falcone, B. N.; Li, C.; Szajnman, S. H.; Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B.* *Bioorg. Med. Chem*. **2019**, *27*, 3663–3673.

m– Approaches for designing new potent inhibitors of farnesyl pyrophosphate synthase, Rodriguez, J. B.;* Falcone, B. N.; Szajnman, S. H.; *Expert Opinion on Drug Discovery* **2016**, *11*, 307–320.

n– The role of the phosphorus atom in drug design. Rodriguez, J. B.;* Gallo-Rodriguez, C. *ChemMedChem* **2019**, *14*, 190–216.

4. Studies on the chemotherapy of antiparasitic agents targeting trypanothione synthase

We were also involved in the design and synthesis of inhibitors of trypanothione synthase (TryS), a unique enzyme present in trypanosomatids but absent in the mammalian host. We have developed tetrahedral transition state mimics of the reaction catalyzed by TryS, a typical C:N ligase (a,b).

a– Glutathione-like tripeptides as inhibitors of glutathionylspermidine Synthetase: 1. Substitution of the glycine carboxylic acid group. Amssoms, K.; Oza, S. L.; Ravaschino, E.; Yamani, A.; Lambeir, A. –M.; Rajan, P.; Bal, G.; Rodriguez, J. B.; Fairlamb, A. H.; Augustyns, K.; Haemers, A.* *Bioorg. Med. Chem. Lett*. **2002**, *12*, 2553–2556.

b– Design, synthesis and biological evaluation of phosphinopeptides against *Trypanosoma cruzi* targeting trypanothione biosynthesis. Ravaschino, E. L.; Docampo, R.; Rodriguez, J. B.* *J. Med. Chem*. **2006**, *49*, 426–435.

5. Synthetic studies to access the core of Aristotelia-type alkaloids

Taking advantage of the ability of the Ritter reaction on terpenes to enantioselectively produce 3-aza-bicyclo [3.3.1] non-2-ene systems, we have studied this reaction to access Aristotelia-type alkaloids.

a– Ritter reaction on terpenoids. III. Stereospecific preparation of bicyclic[3.3.1]substituted piperidines. Samaniego, W. N.; Baldessari, A.; Ponce, M. A.; Rodriguez, J. B.;* Gros, E. G.; Caram, J. A.; Marschoff, C. M. *Tetrahedron Lett*. **1994**, *35*, 6967–6970.

b– Ritter reaction on terpenoids. IV. Remarkable tendency to produce 3-aza-bicyclo [3.3.1] non-2-ene systems from mono and sesquiterpenes. Rodriguez, J. B.;* Gros, E. G.; Caram, J. A.; Marschoff, C. M. *Tetrahedron Lett*. **1995**, *36,* 7825–7828.

6. Design, synthesis, and biological evaluation of inhibitors of the enzymatic activity of Acyl-CoA synthetase 4

Acyl-CoA synthetase 4 (ACSL4) is an isoenzyme of the fatty acid ligase-coenzyme-A family taking part in arachidonic acid metabolism and steroidogenesis. ACSL4 is involved in the development of tumor aggressiveness in breast and prostate tumors through the regulation of various signal transduction pathways.

a– New inhibitor targeting Acyl-CoA synthetase 4 reduces breast and prostate tumor growth, therapeutic resistance and steroidogenesis. Castillo, A. F.; Orlando, U. D.; Maloberti, P. M.; Prada, J. G.; Dattilo, M. A.; Solano, A. R.; Bigi, M. M.; Ríos Medrano, M. A.; Torres, M. T.; Indo, S.; Caroca, G.; Contreras, H. R.; Marelli, B. E.; Salinas, F. J.; Salvetti, N. R.; Ortega, H. H.; Lorenzano Menna, P.; Szajnman, S.; Gomez, D. E.; Rodríguez, J. B.; Podesta, E. J.* *Cellular and Molecular Life Sciences* **2021**, *78*, 2893–2910.

Patents

1– "Synthesis of cyclopropane-fused dideoxy-carbocyclic nucleosides locked in the Northern conformation." Marquez, V. E.; Rodriguez, J. B.; Nicklaus, M. C.; Barchi, Jr. J. J.; Siddiqui, M. *U. S. Patent* 5,629,454 (13 May 1997). Filed on 23 September 1994.

2– "Conformationally locked nucleoside analogs as antiherpetic agents." Marquez, V. E.; Nicklaus, M. C.; Barchi, Jr. J. J.; Rodriguez, J. B.; Siddiqui, M. *U. S. Patent* 5,840,728 (24 November 1998). Filed on 7 de agosto de 1997.

3– "Conformationally locked nucleoside analogues." V Marquez, V. E.; Rodriguez, J. B.; Nicklaus, M. C.; Barchi, Jr. J. J.; Siddiqui, M. *U. S. Patent 5,869,666* (9 February 1999). Filed on 14 de marzo de 1997.

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Complete list of published work:
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