2017

medicina

BUENOS AIRES VOL. 77 Supl. I - 2017

MEDICINA

Volumen 77, Supl. I, págs. 1-620

medicina

BUENOS AIRES, VOL. 77 Supl. I - 2017

La Tapa (Ver p. IV)
Imagen ígnea, 1996.
María Esther Gené

MEDICINA (Buenos Aires) – Revista bimestral – ISSN 1669-9106 (En línea)

REVISTA BIMESTRAL
Registro de la Propiedad Intelectual N° 5324261
Personería Jurídica N° C-7497
Publicación de la Fundación Revista Medicina (Buenos Aires)
Propietario de la publicación: Fundación Revista Medicina
Queda hecho el depósito que establece la Ley 11723

Publicada con el apoyo del Ministerio de Ciencia, Tecnología e Innovación Productiva.
MEDICINA no tiene propósitos comerciales. El objeto de su creación ha sido propender al adelanto de la medicina argentina. Los beneficios que pudieran obtenerse serán aplicados exclusivamente a este fin.
Aparece en *MEDLINE (PubMed), ISI-THOMSON REUTERS (Journal Citation Report, Current Contents, Biological Abstracts, Biosis, Life Sciences), CABI (Global Health), ELSEVIER (Scopus, Embase, Excerpta Medica), SciELO, LATINDEX, BVS* (Biblioteca Virtual en Salud), *DOAJ, Google Scholar y Google Books.*
Incluida en el Núcleo Básico de Revistas Científicas Argentinas del CONICET.

Directores Responsables:
Basilio A. Kotsias, Damasia Becú Villalobos, Isabel Narvaiz Kantor, Guillermo B. Semeniuk

Secretaría de Redacción: Ethel Di Vita, Instituto de Investigaciones Médicas Alfredo Lanari, Combatientes de Malvinas 3150, 1427 Buenos Aires, Argentina
Tel. 5287-3827 Int. 73919 y 4523-6619
e-mail: revmedbuenosaires@gmail.com – http//: www.medicinabuenosaires.com

Vol. 77, N° 5, Noviembre 2017

Edición realizada por
GRAFICA TADDEO – Charrúa 3480 – Buenos Aires – Tel: 4918.6300 l 4918.1675 l 4918.0482
e-mail: ctp@graficataddeo.com.ar – www.graficataddeo.com.ar

medicina
BUENOS AIRES, VOL 77 Supl. I - 2017

REUNIÓN CONJUNTA DE SOCIEDADES DE BIOCIENCIAS

LXII REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

LIII REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN BIOQUÍMICA Y BIOLOGÍA MOLECULAR (SAIB)

LXV REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INMUNOLOGÍA (SAI)

REUNIÓN DE LA SOCIEDAD ARGENTINA DE ANDROLOGÍA (SAA)

XLVI REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE BIOFÍSICA (SAB)

XIX REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE BIOLOGÍA (SAB)

XLIX REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE FARMACOLOGÍA EXPERIMENTAL (SAFE)

REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE FISIOLOGÍA (SAFIS)

REUNIÓN DE LA SOCIEDAD ARGENTINA DE HEMATOLOGÍA (SAH)

XXIX REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE PROTOZOOLOGÍA (SAP)

13-17 de noviembre de 2017
Palais Rouge– Buenos Aires

1 Mensaje de Bienvenida de los Presidentes
2 Conferencias, Simposios y Presentaciones a Premios
92 Resúmenes de las Comunicaciones presentadas en formato E-Póster

medicina
BUENOS AIRES, VOL 77 Supl. I - 2017

JOINT MEETING OF BIOSCIENCE SOCIETIES

LXII ANNUAL MEETING OF ARGENTINE SOCIETY OF CLINICAL INVESTIGATION (SAIC)

LIII ANNUAL MEETING OF ARGENTINE SOCIETY OF BIOCHEMISTRY AND MOLECULAR BIOLOGY (SAIB)

LXV ANNUAL MEETING OF ARGENTINE SOCIETY OF IMMUNOLOGY (SAI)

MEETING OF ARGENTINE SOCIETY OF ANDROLOGY (SAA)

XLVI ANNUAL MEETING OF ARGENTINE SOCIETY OF BIOPHYSICS (SAB)

XIX ANNUAL MEETING OF ARGENTINE SOCIETY OF BIOLOGY (SAB)

XLIX ANNUAL MEETING OF ARGENTINE SOCIETY OF EXPERIMENTAL PHARMACOLOGY (SAFE)

ANNUAL MEETING OF ARGENTINE SOCIETY OF PHYSIOLOGY (SAFIS)

MEETING OF ARGENTINE SOCIETY OF HEMATOLOGY (SAH)

XXIX ANNUAL MEETING OF ARGENTINE SOCIETY OF PROTOZOOLOGY (SAP)

November 13 -17, 2017
Palais Rouge– Buenos Aires

1 **Welcome Message from Presidents**
2 **Lectures, Symposia and Award Presentations**
92 **Abstracts of E-Poster Presentations**

The $GABA_A$Rs, γ-Aminobutyric acid type A receptors, belong to the family of pentameric ligand gated ion channels and are the main mediators of fast inhibitory transmission in the mammalian CNS. They are the target of a variety of compounds such as GABA, benzodiazepines (BZDs), anaesthetics, β-carbolines and neurosteroids, and have a fundamental role in neurological health.

In this work we aim to elucidate the binding modes of relevant ligands of the BZDs' binding site, which include classical BZDs, imidazo-BZDs, zolpidem and eszopiclone. We applied computational biophysics methods, namely molecular docking and molecular dynamics (MD) simulations, to undertake this study. We employed a previously developed homology model of the $\alpha1\beta2\gamma2$ subtype (based on a β3 homopentamer as a template, PDBID: 4COF) in a closed desensitized state.

We approached molecular docking through different methods: we used HADDOCK which introduces experimental data as ambiguous interaction restraints and AutoDock Vina which runs a local optimization from random starting conformations. While the highest ranked binding modes were not necessarily the best predictions, some of the docking poses obtained could be related to the experimental data.

In order to assess the stability of the complexes, we performed 100ns MD simulations of the systems with GROMACS (using gromos53a6 force field and SPC water model). The receptor was embedded in a POPC membrane. RMSD calculations of the backbone show that the receptors did not suffer major global changes, although the presence of the ligands and relaxation of the side chains caused local modifications.

With the aid of experimental information we could predict the binding modes for ligands of the BZDs' site in $GABA_A$Rs. These compounds remained bound in the cavity during all MD simulations and improved their contacts with the receptor. Taking these results into account, we can confirm that our model can be used for further investigation of ligand binding.

Keywords: GABAARs, molecular docking, benzodiazepines, molecular dynamics.

(1045) **APLICATION OF COMPUTER-AIDED DRUG REPURPOSING IN THE SEARCH OF NEW THYPANOTHIONE SYNTETHASE INHIBITORS FOR THE TREATMENT OF CHAGAS DISEASE.**

Juan Ignacio Alice (1), María Laura Sbaraglini (1), Juan Francisco Morales (1), Carolina Leticia Bellera (1), Catalina Dirney Alba Soto (2), Alan Talevi (1)
(1) Laboratory of Research and Development of Bioactives (LIDeB), Faculty of Exact Sciences, National University of La Plata, (2) Institute of Research Medical in Microbology and Parastiology (IMPaM) Faculty of Medicine, University of Buenos Aires (UBA)-CONICET.

Chagas disease is an endemic parasitic disease that mainly affects Latin America. The currently available medication display a high incidence of adverse effects and low efficacy in the chronic phase of infection in adults. Thus, it is very important to find new therapies with higher clinical efficacy and safety profiles.

Computer-aided drug repositioning may contribute to the systematic identification of new pharmacological applications for existing drugs, thus allowing the development of innovative therapeutic solutions in a cost- and time-efficient manner.

Here, we report the development and validation of ligand-based *in silico* models aimed at the identification of trypanothione sintethase (*TryS*) inhibitors. Such enzyme is essential for the biosynthesis of trypanothione, a key metabolite for the maintenance of the redox balance and defense against oxidative stress in *the parasite.* The models were inferred and validated from the molecular structures of 109 compounds previously assayed against *TryS*.

We built 1000 individual classificatory models capable of differentiating molecules with and without inhibitory effect against *TryS*. For model validation, a pilot virtual screening *in silico* campaign was performed against a drug library containing a small proportion of known inhibitors spread among decoys generated through the enhanced Directory of Useful Decoys. Based on the results, we resort to ensemble learning to obtain a 10-model combination which was later applied in the *in silico* screening of DrugBank 3.0 and Sweetlead. Twenty-one hits were classified as potential *TryS* inhibitors. 10 of them were acquired and assayed against *T. cruzi* trypomastigotes.

(1563) **CHARGE DENSITY AS A MOLECULAR DESCRIPTOR TO UNRAVEL STRUCTURE-ACTIVITY RELATIONSHIPS OF CRUZAIN INHIBITORS**

Adriano Martín Luchi, Angel Ramirez, María Lucrecia Bogado, Emilio Luis Angelina, Nelida María Peruchena
LEMYP-IQUIBA-NEA-FaCENA-UNNE

Chagas disease is endemic to South and Central America caused by the parasite *Tripanosoma cruzi.* Actually just two drugs like nifurtimox and benznidazole are available, however they are highly toxic and drug resistance has been reported. Cruzain (Cz), the major cysteine protease of T. cruzi, is one attractive drug target; since, it is required for all the major proteolytic activities of the parasite life circle.

Cysteine protease inhibitors containing a vinyl sulfone warhead can exhibit good selectivity and a favorable in vivo safety profile despite the irreversible nature of inhibition.

K-777, a vinyl sulfone inhibitor of Cz has shown to be safe and efficacious in animal models of acute and chronic Chagas disease but the project was stopped due to tolerability issues at low dose in primates and dogs.

Jaishankar et al. synthesized and determined the inhibition constant of a series of vinyl sulfone analogs closely related to K-777 with substitutions at P2 and P3. Unfortunately, 3-D structures of these complexes are not available yet. However, there are several solved structures of Cz complexed with vinyl sulfone analogs available in the PDB. Moreover, all these irreversible inhibitors mimic the well known binding mode of classical substrate-like peptidic inhibitors. This structural information allowed us to make a reasonably good initial guess of the binding mode of these K-777 analogues at the Cz active site. Complexes were then subjected to MD simulations. Reduced model systems comprising inhibitor and residues from the Cz binding pocket were constructed from the MD simulation. Charge density topological analysis based in QTAIM was performed on these reduced models to evaluate the inhibitor/Cz interactions.

By carefully inspecting the electron density values at the interactions bond critical points, we found out what are the key interactions that explain the activity differences (Ki values) among K-777 analogues.

Keywords: QTAIM, MD, K-777

(740) **HUMAN TELOMERASE PROTEIN/RNA/DNA COMPLEX: THEORETICAL STUDY OF KEY CONSERVED RESIDUES BY MOLECULAR DYNAMICS SIMULATIONS**

Fernando Herrera (1), Sferco Silvano (2)
(1) Dpto. De Física, Facultad De Bioquímica Y Ciencias Biológicas, Universidad Nacional Del Litoral, Santa Fe, Argentina. Conicet. (2) Ifis Litoral (Unl-Conicet), Santa Fe, Argentina.

Telomerase adds several nucleotides to the 3' terminal of a DNA strand. It is a protein/RNA complex, formed by the Telomerase protein and a RNA strand. Inside the protein, in a Reverse Transcriptase (RT) catalytic pocket, there are several conserved residues: a triad of aspartates (D712, D868, D869, for the human case) whose crucial role in the telomerase activity is quite well understood, as well as other residues (K626, R631, K902) the two latter, also bringing the catalytic activity to zero when mutated. But a molecular model description is still lacking. This work aims to study, using molecular dynamics simulations, the role of all these residues in the activity of the human telomerase protein at atomic level. A chimeric model of the complex, constituted by the RT domain of the Telomerase protein, a double strand DNA/RNA, an incoming dNTP and two Mg^{2+} ions was studied in two configurations: i) before the catalytic reaction, with the dNTP at the reaction site, and ii) after the catalytic reaction, were the dNTP was broken in a nucleotide and an inorganic pyrophophate (PPi). Additionally to the wild type (WT) protein, 5 mutants (D712A, D868A, D869A, K902N and R631Q) were also