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Chem-Bioinformatics & Nanoinformatics in Neurosciences

Prof. Humberto González-Díaz

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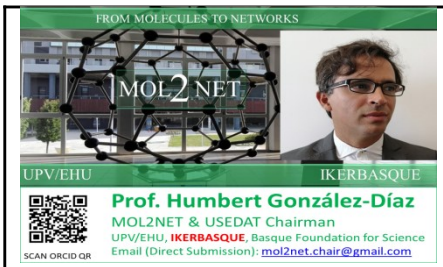

This professor can interact with students in English, Spanish, and Galego,

Euskera can be used as well for written communication.

Description. Welcome to Prof. PhD. Humberto González-Díaz invited talk cover and tutoring channel on Chem-Bioinformatics & Nano-Informatics in Neurosciences. The talk is part of the NEURODAT'21 training program funded by IBRO-PERC Soft Skills Training call of the International Brain Research Organization (IBRO) and the Pan-Europe Regional Committee (PERC). NEURODAT'21 is devoted to promote soft skills on entry level medicine and also STEMS area students interested on neurosciences. On this talk the professor made an introduction to the basic concepts related to Chem-Bioinformatics and Nano-Informatics with applications in Neurosciences.

Description of channel. This channel is part of the NEURODAT'21 training program funded by IBRO-PERC Soft Skills Training call of the International Brain Research Organization (IBRO) and the Pan-Europe Regional Committee (PERC). NEURODAT'21 is a training program devoted to promote soft skills on entry level Medicine and also STEMS area students interested on Neurosciences. In this tutoring channels students will be allowed to do online public questions and comments about different topics of Deep Learning and its applications in Neurosciences. Prof. González-Díaz will answer all questions within his area of expertise.

Talk & Channel Topics. The emphasis is on use in Neurosciences of Chem-Bioninformatics and Nanoinformatics, Molecular Descriptors, Computer Aided Drug Discovery (CADD), Machine Learning, Multi-output models, Multi-label classification, Information Fusion Perturbation-Theory Machine Learning (IFPTML) models, Complex Networks, Protein Interactions Networks (PINs), Metabolic Networks, Brain Cortex Networks, etc.

Instructions for students. The steps for participation are: (1) Wait for channel starting in 2021-Dec-25, you will see a posting comments option/button, (2) Register/login with your email and password to validate your user, (3) Post your question/comment for the Prof. of the channel, (4) Wait for the email advising that professor has answered your question, (5) Make other questions related to this topic or other topics, (6) Request your attendance certificate to mol2net.chair@gmail.com or directly to the email of the professor.

General notes. (1) Students are allowed to made multiple questions following the same discussion threat or open new questions. (2) Some professors may release different materials, slides, etc., that the student can use to study and/or follow the discussion, click the button bellow to see the pdf files. (3) Language note: some professors allow students to select their favorite language of interaction according to professor communications skills, accordingly materials, questions, and answers may appear in these languages. (4) The channel will be open until conference finish the post-publication stage, contact chairpersons for doubts: mol2net.chair@gmail.com

ACS Chemical Neuroscience

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Synthesis, Pharmacological, and Biological Evaluation of 2-Furoyl-Based MIF-1 Peptidomimetics and the Development of a General-Purpose Model for Allosteric Modulators (ALLOPTMLs)

Ivo E. Sampaio-Dias,* José E. Rodríguez-Borges, Víctor Yáñez-Pérez, Sonia Arrasate, Javier Llorente, José M. Brea, Harbil Bediaga, Dolores Viña, María Isabel Loza, Olga Caamaño, Xerardo García-Mera,* and Humberto González-Díaz*

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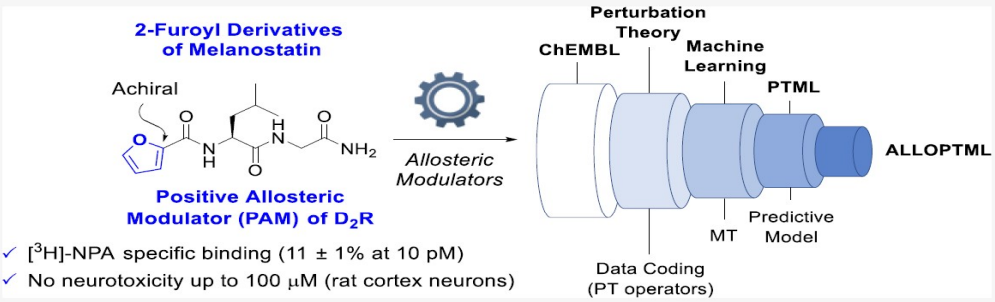

This work describes the synthesis and pharmacological evaluation of 2-furoyl-based Melanostatin (MIF-1) peptidomimetics as dopamine D2 modulating agents. Eight novel peptidomimetics were tested for their ability to enhance the maximal effect of tritiated N-propylapomorphine ([3H]-NPA) at D2 receptors (D2R). In this series, 2-furoyl-L-leucylglycinamide(6a) produced a statistically significant increase in the maximal [3H]-NPA response at 10 pM (11 ± 1%), comparable to the effect of MIF-1 (18 ± 9%) at the same concentration. This result supports previous evidence that the replacement of proline residue by heteroaromatic scaffolds are tolerated at the allosteric binding site of MIF-1. Biological assays performed for peptidomimetic 6a using cortex neurons from 19-day-old Wistar-Kyoto rat embryos suggest that 6a displays no neurotoxicity up to 100 μM.

Overall, the pharmacological and toxicological profile and the structural simplicity of peptidomimetic 6a makes this peptidomimetic a potential lead compound for further development and optimization, paving the way for the development of novel modulating agents of D2R suitable for the treatment of CNS-related diseases. Additionally, the pharmacological and biological data herein reported was used, along with >20 000 outcomes of preclinical assays, to seek a general model to assess the potential of a series of compounds as allosteric modulators for a myriad of receptors targets, organisms, cell lines, and biological activity parameters based on perturbation theory (PT) ideas and machine learning techniques (MLs), abbreviated as ALLOPTMLs. By doing so, ALLOPTML shows specificity Sp = 89.2/89.4% and sensitivity Sn = 71.3/72.2% in training/validation series, respectively. To the best of our knowledge, ALLOPTML is the first general-purpose chemoinformatic tool using a PTML-based model for the multioutput and multicondition prediction of allosteric compounds, which is expected to save both time and resources during the early drug discovery.

KEYWORDS: Allosteric modulators, artificial neural networks, big data, ChEMBL, machine learning, Melanostatin, multitarget models, perturbation theory

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Article

Prediction of Anti-Glioblastoma Drug-Decorated Nanoparticle Delivery Systems Using Molecular Descriptors and Machine Learning

Cristian R. Munteanu [1,2,3,4,*], Pablo Gutiérrez-Asorey [1], Manuel Blanes-Rodríguez [1], Ismael Hidalgo-Delgado [1], María de Jesús Blanco Liverio [5], Brais Castiñeiras Galdo [1,2], Ana B. Porto-Pazos [1,2], Marcos Gestal [1,2,3,4,*], Sonia Arrasate [4,5] and Humbert González-Díaz [4,5,6,7]

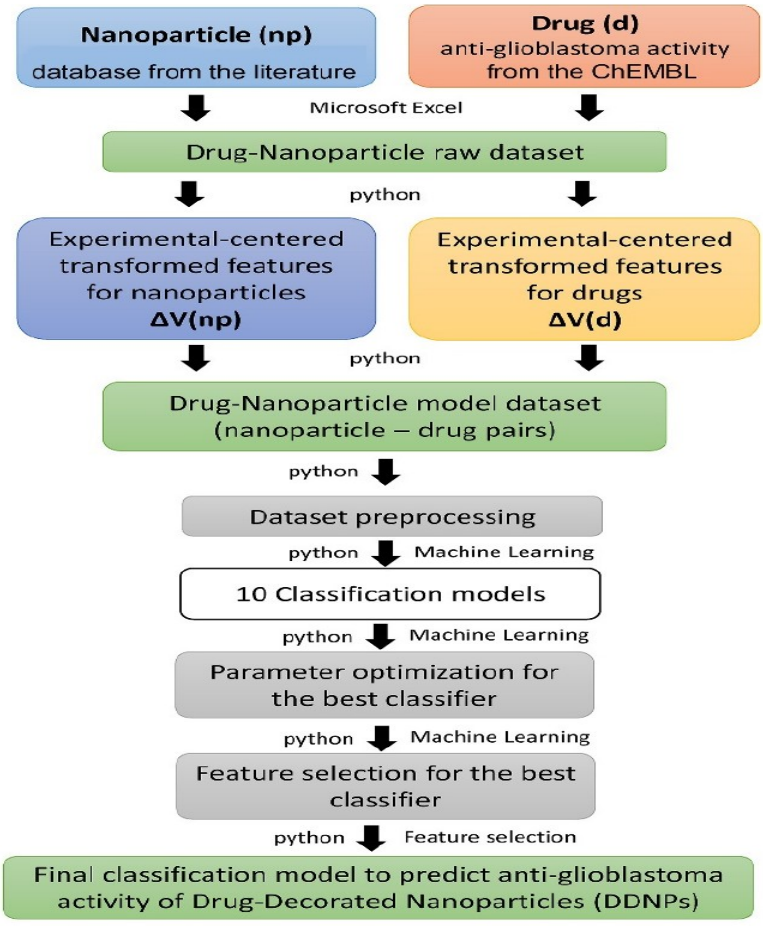

Figure 5. Methodology workflow for building classification models for DDNPs against anti-glioblastoma.

Abstract: The theoretical prediction of drug-decorated nanoparticles (DDNPs) has become a very
important task in medical applications. For the current paper, Perturbation Theory Machine Learning (PTML) models were built to predict the probability of different pairs of drugs and nanoparticles creating DDNP complexes with anti-glioblastoma activity. PTML models use the perturbations of molecular descriptors of drugs and nanoparticles as inputs in experimental conditions. The raw dataset was obtained by mixing the nanoparticle experimental data with drug assays from the ChEMBL database. Ten types of machine learning methods have been tested. Only 41 features have been selected for 855,129 drug-nanoparticle complexes. The best model was obtained with the Bagging classifier, an ensemble meta-estimator based on 20 decision trees, with an area under the receiver operating characteristic curve (AUROC) of 0.96, and an accuracy of 87% (test subset). This model could be useful for the virtual screening of nanoparticle-drug complexes in glioblastoma. All the calculations can be reproduced with the datasets and python scripts, which are freely available as a GitHub repository from authors.

Keywords: decorated nanoparticles; drug delivery; anti-glioblastoma; big data; perturbation theory;