BIO TECNOLOGIE
RICERCA DI BASE
INTERDISCIPLINARE
TRASLAZIONALE
IN AMBITO BIOMEDICO

3° Meeting

IBIM-CNR

STEBICEF-UNIPA
UNIVERSITÀ DEGLI STUDI DI PALERMO

BIOINFORMATICA IMMUNOLOGIA
MALATTIE APPARATO RESPIRATORIO
MALATTIE METABOLICHE
MICROORGANISMI NELLE BIOTECNOLOGIE
NANOTECNOLOGIE NEUROSCIENZE
ONCOLOGIA SVILUPPO E DIFFERENZIAMENTO

LIBRO degli ABSTRACT

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Area della Ricerca di Palermo Via Ugo La Malfa 153

Progetto grafico:
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resource software, able to manage the sharing of data collected and processed by different equipes, allowing to trace a specific clinical profile for each monitored patient. The platform allowed health professionals, signed up, to retrive the data and different professionals in different geographic areas to access the data (Second Opinion).

MM4
Molecular modeling studies on dopamine-amino acid conjugates as potential dopaminergic modulators

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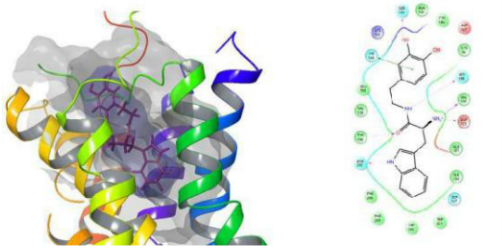

DA-Trp interactions with D1DR after Induced Fit Docking analysis.

In the last years, prodrug strategy was used with the aim to increase drugs selectivity especially in CNS reducing systemic and/or organ-specific toxicity. The dopamine-amino acid conjugate DA-Phen was first designed in order to obtain a useful prodrug for Parkinson's disease therapy, but experimental evidence shows that it effectively interacts with D1 dopamine receptors (D1DRs), leading to an enhancement in cognitive flexibility and to the development of adaptive strategies in front of an aversive environment[1]. In the attempt to identify new compounds with potential dopaminergic activity, we performed a molecular modeling study on other dopamine conjugates. In order to find a method able to give the best predictions of the D1DR binding, we used three different approaches. Molecular Dynamics (MD) simulation was first carried out to analyze D1DR behavior during the interaction with DA-Phen. Cluster Analysis of MD trajectory snapshots was then employed to select the most significant conformations to be used in semi-flexible docking with known agonists and antagonists. Then, we performed semi-flexible docking on the original model, and Induced Fit Docking (IFD). This last method gave the most interesting results, therefore it was the preferred one to perform computational studies on new DA conjugates. Other 19 dopamine-amino acid conjugates were screened. IFD poses of the new conjugates were used to perform MM-GBSA analysis to calculate the ΔG binding energy values, and the most promising compound resulted DA-Trp, followed by DA-Leu and DA-Pro. On the basis of these results, we deem that DA-Trp, DA-Pro and DA-Leu could be potential D1DR agonists, suggesting a possible use for further in vivo studies.

[1] De Caro V., Sutera F.M., Gentile C., Tutone M., et al. Studies on a new potential dopaminergic agent. In vitro BBB permeability, in vivo behavioural effects and molecular docking. J. Drug Target. 2015, 10, 910-925.

MM5
Ex-Vivo model for the evaluation of drugs and micellar systems permeation across cornea

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A.

Nowadays, diseases affecting posterior eye segment are increasing at an alarming rate. These include age-related macular degeneration, diabetic macular edema and diabetic retinopathy. Currently, the intravitreal administration is widely used, even if frequent injections can lead to retinal detachment, endophthalmitis and increased intraocular pressure. To overcome these problems, the topical administration of nanotechnology-based drug delivery systems is a strategy presently used. In particular, polymeric micelles are proposed as an