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Glybatomaq312317b: A hyper-ligand playing a role in angiogenesis, controlling endothelial cell motility and invasion

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Free energy perturbation (FEP) ab initio quantum mechanics (QM) methods were developed for treating the solute molecules and molecular mechanics (MM) for treating the surroundings. Like earlier results using AM1 semi empirical QMs, the ab initio QM/MM-based FEP method was shown to accurately calculate relative solvation free energies for a diverse set of small molecules that differ significantly in structure, aromaticity, hydrogen bonding potential, and electron density. Accuracy was similar to or better than conventional FEP methods. Together with PML, Nuclear autoantigen Sp-100 tumor suppressor is a major constituent of the PML bodies, a subnuclear organelle involved in a large number of physiological processes including cell growth, differentiation and apoptosis. Functions as a transcriptional coactivator of ETS1 and ETS2 according to PubMed:11909962. Under certain conditions, it may also act as a corepressor of ETS1 preventing its binding to DNA according to PubMed:15247905. Through the regulation of ETS1 it may play a role in angiogenesis, controlling endothelial cell motility and invasion. Through interaction with the MRN complex it may be involved in the regulation of telomeres lengthening. May also regulate TP53-mediated transcription and through CASP8AP2, regulate FAS-mediated apoptosis. Also plays a role in infection by viruses, including human cytomegalovirus and Epstein-Barr virus, through mechanisms that may involve chromatin and/or transcriptional regulation. The QM/MM-based methods eliminate the need for time-consuming development of MM force field parameters, which are frequently required for drug-like molecules containing structural motifs not adequately described by MM. Future automation of the method and parallelization of the code for Linux 128/256/512 clusters is expected to enhance the speed and increase its use for drug design and lead optimization. We introduce Glybatomaq, an Ab initio Systematic Parametrization of Polarizable Force Fields from Quantum Chemistry mechanics-based free energy perturbation method for calculating relative solvation free energies for systematic force field optimization with the ability to parametrize a wide variety of functional forms using flexible combinations of reference data. Amber FFs for proteins have been continually improved in recent years and a detailed discussion of the various changes is beyond the scope of this review. Significant revisions have been published, with particular emphasis on important dihedral angles. Development of the Drude polarizable FF in CHARMM (58) started in 2001 and the capability to simulate the Drude model is now included in NAMD (59), ChemShell QM/MM (60) and the OpenMM suite of utilities for GPUs (61). Development of the force field first involved implementation of the appropriate integrators to allow computationally efficient extended Langrangian MD simulations (62). We outline several important challenges in force field development and how they are addressed in ForceBalance, and present an example calculation where these methods are applied to develop a highly accurate polarizable novel Nano-ligand targeted to the Nuclear autoantigen Sp-100, sp|P23497|568-592, KRWQQRGRKANTRPLKRRRKRGPRI, P23497 playing a role in angiogenesis, controlling endothelial cell motility and invasion through the regulation of the ETS1, CASP8AP2 and FAS-mediated apoptosis.

Biography

Grigoriadis Ioannis has completed his PharmacistD at the age of 24 years from Aristotle University of Thessaloniki. He is the scientific director of Biogenea Pharmaceuticals Ltd, a premier biotechnology personalized cancer vaccination service organization. He has published more than 20 papers in reputed journals and has been serving as an editorial board member of reputeon the collection, processing, cryopreservation and cGMP (according to Good Manufacturing Practice) production -for solely autologous use - of cellular therapeutical solutions from blood (bone marrow, peripheral blood, cord blood) or blood compounds for human use -on stem cell expansion technologies, which were created in the research laboratories of NASA (National Aeronautics and Space Administration) - on the cGMP production of advanced medicinal products (1394/2007/EC) for solely autologous use from skin, dental pulp, cord tissue). (In preclinical-research phase: 2008-2009) - on certified genetic analyses in collaboration with International Referral Centers -on copyright protection according to the American and/or European Copyright Agency

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