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Molecular docking and *in vitro* assay of isoindolina-1,3-dione amine derivative as novel HDAC8 inhibitor for cancer treatment

Garcia Gamez Jesus, Bahena Herrera José Raul, Sixto López Yudideth, Trujillo Ferrera José Guadalupe and Andrade Jorge Erik
Escuela Superior de Medicina del Instituto Politécnico Nacional, Mexico

Cancer is an uncontrolled process of growth and dissemination that can appear ubiquitously. Genetic and epigenetic mutations in cancer cells elicit protection of tumor cells like overexpression of histone deacetylase (HDAC). HDAC inhibitors (HDACi) have shown that over acetylated state induce anticancer effects like apoptosis, cytostasis, differentiation and angiogenesis inhibition. HDAC8 is overexpressed in different types of cancer such as colon, breast, lung, pancreas, ovary, etc. Therefore, we modeled a serie of isoindoline-1,3-dione due to their homology with thalidomide's metabolites and also similar to HDACi previously reported just as sodium butyrate, sodium valproate, phenylbutanoic acid, etc. Docking results showed our ligand DxD2-15 interacting with HDAC8 in the catalytic site with the amino acid residues Phe208, Phe152, His180, Met214, Asp178, Tyr306, Gly303 and Gly304 suggesting possible inhibitory effect. Anti-tumoral capacity of DxD2-15 was tested in different concentrations at 24 and 48 h on L5178-Y murine leukemia cells with MTT assay. Cellular viability decreased importantly after 24 and 48 h of culture. There was a significant decrease in cell viability caused by DxD2-15 at all times and concentrations of 1×10^{-4} M, 1×10^{-5} M and 1×10^{-6} M showing DxD2-15 as a potent anti-tumoral drug compared with control cells ($P < 0.05$). With these important results we propose to perform more experiments on other cell lines such as HeLa, Vero and prostate cancer cells and also perform *in vivo* experiments in male Balb/C mice.

Biography

Garcia Gamez Jesus is a medical student of Escuela Superior de Medicina at Instituto Politécnico Nacional. He is a junior researcher who has been working at Biochemistry Department since 2013 on different research lines such as asthma, Parkinson's and obesity. His recent research is focused on drug design for cancer treatment.

jjcgg2330@hotmail.com

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