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DEVELOPMENT OF NEW ANTIHERPETIC COMPOUNDS

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Background & Aims: Herpes simplex viruses type 1 (HSV-1) and type 2 (HSV-2) are responsible for recurrent oro-labial and genital infections. The seroprevalence of HSV-1 and HSV-2 infections has been estimated at ~54 % and 16 % respectively in North American adults and at ~88 % and 1 % respectively in Saudi Arabian adults. Long-term exposure to antiviral drugs or suboptimal doses selects for mutations leading to drug resistance. The development of new antiviral agents becomes increasingly important to develop combined therapies with increased potency and decreased potential for treatment failure.

Methods: We have used HSV-11-DNA polymerase structure based virtual screening to search for HSV-1 inhibitors and tested potentials molecules on cell culture and on herpes encephalitis mice model.

Results: Using a rational approach that combines computer-generated 3D modeling of viral DNA polymerase and virtual screening of compounds, we discovered that compounds (E)-N-(2-(2-(4-hydroxybenzylidene)hydrazinyl)-2-oxoethyl)-1-naphthamide (C2) and (E)-N-(2-(2-(6-fluoro-2-hydroxybenzylidene) hydrazinyl)-2-oxoethyl)-1-naphthamide (C2-20) inhibit several HSV-1 and HSV-2 strains of clinical isolates resistant to cidofovir and foscarnet while having a low cytotoxicity profile. Treatment with heptanoate C2-20 and C2-20 of herpes encephalitis mice model were encouraging with 62% survival rate.

Conclusion: The discovered molecules have a new mechanism of action against HSV-1 and -2 shows a good potential for further development in preclinical stages

Biography

Arezki Azzi completed his Post-graduation from department of molecular biophysics at Florida State University. He is a Structural Biologist, received his PhD from Laval University in Physiology. At Laval University, he stated working on viruses structures and rational drug design against various viral targets. He pursued his research on Antivirals Compounds when he moved to Al Imam university college of medicine.

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