



UNIVERSITÀ DEGLI STUDI
MAGNA GRÆCIA DI CATANZARO



DOTTORATO DI RICERCHE
IN SCIENZE DELLA VITA

UNIVERSITÀ DEGLI STUDI MAGNA GRÆCIA DI CATANZARO
- DIPARTIMENTO DI SCIENZE DELLA SALUTE -
- DOTTORATO DI RICERCHE IN SCIENZE DELLA VITA -
- SCUOLA DI SPECIALIZZAZIONE IN FARMACIA OSPEDALIERA -

SEMINARIO CORSO CV_S_038

THE FIRST MOLECULE INTERACTING WITH A HOST PROTEIN FOR THE INHIBITION OF MULTIPLE VIRUSES



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The cellular helicase DEAD-box 3 (DDX3) is known to be an essential host factor for major human viral pathogens such as HIV-1 and Hepatitis C viruses as well as for the replication of viral agents responsible for orphan diseases such as Dengue virus (DENV), West-Nile virus (WNV), Human T-cell leukemia Virus (HTLV)-1 and Japanese Encephalitis Virus (JEV). No specific and effective pharmacological treatment is currently available for these latter pathogens, despite being an increasing threat to EU citizens that may eventually lead to sustained epidemics in Europe. Additionally, all compounds that are currently approved for the treatment of other viral infections target viral proteins. Targeting a unique viral function has an important the Achilles' heel: viral resistance to the drugs, an important threat to the efficacy of current therapy. Conversely, the alternative strategy, targeting a cellular factor that is required for viral replication, should help to overcome this problem. Theoretically, a drug targeting a cellular factor could also inhibit all viruses that are dependent on the same host factor. Recently, it has been revealed that the cellular ATPase/RNA helicase X-linked DEAD-box polypeptide 3 (DDX3) is an essential host factor for the replication of several viruses.¹ Accordingly, our research group is working in targeting both the ATPase and RNA binding regions of DDX3.²⁻⁶ Most of the synthesized derivatives were able to inhibit the DDX3 helicase activity at submicromolar concentration. Furthermore, these compounds showed anti-HCV and anti-HIV activity in cells, as well as a good inhibitory activity against JEV, DENV and WNV infections. Our results clearly demonstrated that DDX3 inhibitors could be exploited in order to treat HIV/HCV co-infections, emerging infectious diseases such as Dengue and West Nile and HIV-1 patients carrying drug resistant strains. Each of these three medical conditions currently represents a major challenge for clinical treatment.

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