OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Neurology & Therapeutics

May 14-16, 2012 Embassy Suites Las Vegas, USA

Identification of effective inhibitors of enterovirus replication

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Enteroviruses are a diverse family of small, non-enveloped RNA viruses. While the poliovirus is its most prominent member, enteroviruses are not only responsible for poliomyelitis and encephalitis but also acute heart failure or severe hepatitis in newborns, and other life threatening infections. Although immunization has nearly eliminated circulation of the polioviruses, other enteroviruses continue to cause substantial morbidity and mortality in the United States and throughout the world. Epidemics of enterovirus-71 (EV71) have occurred in Europe and the Asia-Pacific Region over the last 15 years and the many deaths due to fatal brainstem encephalitis and non-cardiogenic pulmonary edema have led to the inclusion of EV71 on NIAID's list of "re-emerging pathogens." A recent outbreak (2007) of infections with coxsackievirus B1 (CVB1) in the United States in newborns also highlighted the mutability of enteroviruses and their epidemic potential. Unfortunately, no antiviral agents are available to treat enterovirus infections. Here, we present results from a high throughput screening campaign of more than 85,000 drug like molecules at the UCLA's Molecular Screening Shared Resource on live virus: We have succeeded in the identification of various pharmacophores with single digit micromolar anti-viral activity and were able to establish excellent structure-activity relationship around these pharmacophores. Our compounds suppress the replication of the coxsackievirus strain used for screening by several orders of magnitude and we are currently evaluating the mode of action and specificity profiles of these compounds.

Biography

Dr. Robert Damoiseaux's main interests are at the interface of chemistry, biology and engineering and include the development of novel assay technology platforms, High Throughput Screening, High Content Screening and nanotechnology. After having earned a Ph.D. degree at the University of Lausanne (Switzerland) where he worked on directed molecular evolution of antibodies he joined the Novartis Institute for Functional Genomics (GNF) in La Jolla, CA in 2001. Since 2004 he is the Scientific Director of the Molecular Shared Screening Resources (MSSR) at the California NanoSystems Institute of UCLA and directs all drug discovery as well as the functional genomics projects at the MSSR. His private research focuses on biofilm assay systems and toxicological issues of nano-materials. He is a grant reviewer for the King's College in London and the Foundation for Innovation in Canada and consults for the pharmaceutical industry.

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