TECHNOLOGY SUMMARY

New structural class of phosphononucleosides as broad antiviral agents

SUMMARY

Collaborative research involving University College Cork (Chemistry) and KU Leuven (Virology) has led to the design, synthesis and evaluation of a new structural class of phosphononucleosides with a novel distinctive functional feature with potential as broad antiviral agents against both DNA and RNA viruses
The new compounds: • have a strong anti-viral polymerase activity • have a proven new mechanism of action • are drug-like • have clear IP position

ADVANTAGES OF THE TECHNOLOGY

- Novel original class of compounds with extensive analytical and structural characterisation and broad patent coverage
- Novel synthetic methodology to access these compounds
- Selective inhibitors of viral polymerases including HCMV, HSV-1, HSV-2, HIV-1, HIV-2, HTLV-I or II, VZV), INF, RSV), flaviviruses (i.e. Dengue virus, hepatitis C virus), hepatitis B virus and coronavirus.
- Antiviral activity at cellular level demonstrated as proof of concept
- Unique mode of action which does not require metabolism to phosphorylated derivatives prior to action against the polymerases
- A variety of compounds show subtle differences in anti-polymerase activity which offers potential to overcoming drug resistance
- Activity of the series against a broad variety of widely occurring NRTI/NNRTI-characteristic mutations in HIV RT

PUBLICATIONS

Design and synthesis of α-carboxy nucleoside phosphonate (α-CNP) analogues and evaluation as HIV-1 reverse transcriptasetargeting agents. S. J. Keane, A. Ford, N. D. Mullins, N. M. Maguire, T. Legigan, J. Balzarini and A. R. Maguire, J. Org. Chem. 2015, 80, 2479−2493.

Alpha-carboxy nucleoside phosphonates as universal nucleoside triphosphate mimics. J. Balzarini, K. Das, J. A. Bernatchez, S. E. Martinez, M. Ngure, S. Keane, A. Ford, N. Maguire, N. Mullins, J. John, Y. Kim, W. Dehaen, J. Vande Voorde, S. Liekens, L. Naesens, M. Götte, A. R. Maguire and E. Arnold, Proc. Natl. Acad. Sci. USA 2015, 112 (11), 3475-3480.

Pronounced inhibition shift from HIV reverse transcriptase to herpetic DNA polymerases by increasing the flexibility of α-carboxy nucleoside phosphonates (α-CNP). J. John, Y. Kim, K. Das, S. Liekens, L. Naesens, E. Arnold, A. R. Maguire, M. Götte, W. Dehaen and J. Balzarini, J. Med. Chem. 2015, submitted (May 2015).

DEVELOPMENT OBJECTIVES

- Seeking enterprise partners with world leading expertise in antiviral drug discovery and development to develop this technological platform with the Analytical and Biological Chemistry Research Facility (ABCRF) in University College Cork (Prof. Maguire) & The Laboratory of Virology and Chemotherapy (Rega Institute, Prof. Balzarini)

INTELLECTUAL PROPERTY

- WO2014079903: Phosphonucleosides useful in the treatment of viral disorders
- WO201517735: Phosphonate nucleosides useful in the treatment of viral diseases

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PARTNERS

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