

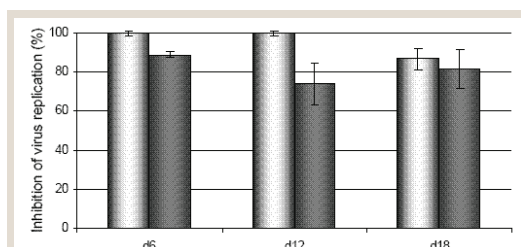
Piperidone derivatives for treatment of HIV and HTLV infections and of Chronic Myeloid Leukemia

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Challenge

An estimated 39.5 million people are living with HIV, the retrovirus causing AIDS, and 2.9 million people died of AIDS-related illnesses in 2006 (source: WHO).

Current antiretroviral therapies primarily rely on virus enzyme inhibitors and



Inhibition of HIV-1 replication by two piperidone derivatives: The percentage of inhibition of virus replication in the drug-treated cell culture as compared to the untreated controls is shown for new substances after 6, 12 and 18 days.

molecules that inhibit virus-cell fusion. The Highly Active Anti-Retroviral Therapy (HAART) is based on a combination of these different drug classes. Although HAART significantly improved morbidity and mortality of HIV-patients, long-term treatment often is accompanied by severe side effects in patients and development of highly resistant HIV-strains. Therefore novel therapy options, especially for patients with multiple HAART-resistant HIV strains have to be developed.

Technology

An alternative target for antiretroviral therapy is the biosynthesis of the eukaryotic initiation factor 5A (eIF-5A). eIF-5A is an essential cofactor of the HIV regulatory protein Rev and the HTLV protein Rex which are important for replication of the respective retroviruses. The biological activity of eIF-5A depends on a posttranslational modification of a single specific lysine that is transformed into the unusual amino acid hypusine. The formation of hypusine is a two-step process involving the enzyme deoxyhypusine hydroxylase (DOHH). The inventors synthesized new substances that specifically target DOHH and that have very low cytotoxic effects. The inventors were able to show that these DOHH-inhibitors strongly inhibit virus replication.

Commercial Opportunity

These new substances can be developed as new active agents for the treatment of HIV-1 and HTLV infections. The technology is offered for co-development or licensing.

Developmental Status

So far, *in vitro* data are available. Additional therapeutic fields in which inhibition of DOHH via the new substances have been shown to have beneficial effects *in vitro* is the treatment of Chronic Myeloid Leukemia (CML) and trypanosomiasis.

Patent Situation

A priority establishing European patent application was filed in 2007.

Further Reading

T. Goebel et al. 2007. 'In search for novel agents in therapy of tropical diseases and human immunodeficiency virus'. Journal of Medicinal Chemistry, J Med Chem. 2008 Jan 24;51(2):238-50.



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