

New substances for treatment of trypanosomiasis

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Challenge

Trypanosomatids are parasitic protozoans that are the causative agents of African sleeping sickness (*Trypanosoma brucei gambiense* and *T. b. rhodiense*) and of South American Chagas' disease (*Trypanosoma cruzi*). Sleeping sickness occurs in 36 sub-Saharan countries



Trypanosomes in a blood sample.

and according to recent estimates over 60 million people are at risk of contracting the disease. There are about 300 000 new cases each year (WHO, 1998). The case fatality rate in untreated patients is 100%. Chagas' disease occurs throughout Mexico and central and southern America. The overall prevalence of human *T. cruzi* infection is estimated at 16-18 million cases. Approximately 120 million people, i.e. 25% of the inhabitants of Latin America, are at risk of contracting the infection (WHO, 2007). The case fatality rate in untreated patients is up to 10%. Available medication against these diseases is very limited

and unsatisfactory due to the emerging levels of resistance against drugs and severe side effects caused by the treatment. Therefore novel effective and safe therapy options have to be developed.

Technology

A potential therapeutic target for trypanosomiasis is the biosynthesis of the eukaryotic initiation factor 5A (eIF-5A). 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 are active against trypanosomatids with an ED₅₀ in the lower micromolar concentration range.

Commercial Opportunity

These new substances can be developed as new active agents for the treatment of trypanosomiasis. Additional therapeutic fields in which inhibition of DOHH via the new substances has been shown to have beneficial effects *in vitro* are retroviral infections (e.g. HIV-1 and HTLV). The technology is offered for co-development or licensing.

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, in press

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