Implementation of the PROTAC targeting strategy to generate a mechanistically new type of antiviral drugs

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

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The current repertoire of antiviral drugs is based on the classical type of direct-acting antivirals. Their limitations, in terms of viral drug resistance and pharmacological constraints, however, have been clearly recognized so that alternatives are urgently needed. An innovative concept aims at the targeting of cellular proteins through host-directed antivirals, which has only rarely been realized so far. This situation prompted the project team to look out for such specified strategies of drug targeting to improve antiviral drug mechanisms and efficacies, particularly against clinically highly relevant human viruses. In this context, the team recently documented initial progress with new ways of chemical drug functionalization specified by 'Proteolysis Targeting Chimeras' (PROTACs). The chemical linkage of PROTAC moieties to bioactive small molecules has been used as a means to induce the proteasomal target protein degradation. This strategy is expected to improve the potency of antiviral drugs in a number of ways, i.e. by an increase of antiviral efficacies, the suppression of viral drug resistance and opening new options of broad-spectrum activities. Thus, the project is focused on the implementation of PROTAC-based targeting to generate a mechanistically new type of antiviral drugs.

Projektbeteiligte

Prof. Dr. Manfred Marschall
Universitätsklinikum Erlangen
Institut für Klinische und Molekulare Virologie
Erlangen

Prof. Dr. Svetlana Tsogoeva
Universität Erlangen-Nürnberg
Institut für Organische Chemie I
Erlangen