UNIVERSITÉ DE GENÈVE

PRESS RELEASE

Geneva | 7 July 2016

A new wave of antimalarial drugs in preparation

Malaria caused by the parasite *Plasmodium falciparum* remains a major public health problem worldwide. As a continuation of previous research targeting Hsp90, a universal molecular chaperone performing vital functions both in the parasite and in human cells, researchers from the universities of Geneva (UNIGE) and Basel, Switzerland, have developed a strategy to identify molecules capable of inhibiting the parasite's protein and causing the destruction of the pathogen, without affecting mammalian cells. The study is published in *the Journal of Medicinal Chemistry*.

More than 600,000 people die each year from malaria caused by *Plasmodium falciparum*, the most dangerous member of this family of parasites. The development of new treatments becomes urgent because of arising parasite resistance against current anti-malarial drugs. One of the most promising targets is the *heat shock protein 90* (Hsp90), which plays a central role in the pathogen's life cycle and survival, as well as its resistance to treatments. This protein, which is also present in human cells, functions as a 'molecular chaperone', by assisting other proteins.

'Two years ago, we discovered that the parasite's Hsp90 is slightly different from the human form, because it harbors a "pocket" which is able to bind certain molecules and which is missing in human Hsp90', notes Didier Picard, professor at the Department of Cell Biology of UNIGE Faculty of Science. His team also identified a group of inhibitors targeting this pocket, which are awaiting optimisation in order to perform clinical tests.

An innovative 'real time' modelling technology

Using the customised computerised modelling tools they developed to study the *Plasmodium*'s Hsp90, the biologists have developed an innovative approach to isolate other types of molecules to fight against the parasite and which may be of clinical interest: 'We started by testing 172 compounds from a library of molecules already known to exert a toxic effect on cultures of *Plasmodium*. We then identified compounds whose three-dimensional structure fits the pocket of the pathogen's Hsp90', says Tai Wang, a researcher from the Genevan group and first author of the study.

'By using a "real time" modelling technology, we were able to

examine how the candidate-molecules behave when in contact with the pocket of the pathogen's chaperone. This allowed us to isolate several compounds, all related to aminoalcohol-carbazoles, interacting in a very stable and sustained manner with the pocket, and causing the destruction of the pathogen without affecting the mammalian cells tested', explains Didier Picard.

The results of this study are essential for the elaboration of a therapeutic strategy, thanks to the identification of several substances as serious candidates for future developments. Indeed, inhibitors of parasites' chaperones offer great prospects as next generation drugs. A new path for the fight against malaria.

contact

Didier Picard
+41 22 379 68 13
Didier.Picard@unige.ch

UNIVERSITÉ DE GENÈVE
Service de communication
24 rue du Général-Dufour
CH-1211 Genève 4

Tél. 022 379 77 17

media@unige.ch
www.unige.ch