

New anticoagulant discovered based on the same used by malaria vectors to feed on

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An international project lead by the Molecular and Cell Biology Institute of Porto University with the participation of researchers from IMIM (Hospital del Mar Medical Research Institute) has, for the first time ever, deciphered the mechanism by which a substance called anophelin binds to an enzyme (thrombin) involved in the process of blood coagulation. This discovery was published in the last issue of the *PNAS* journal and opens the door to, on the one hand, designing a new generation of anticoagulant drugs with a totally different functioning to current ones and, on the other hand, fighting against the spreading of malaria by designing inhibitors for this substance.

Anophelin is a substance playing a crucial role in the nutrition of a large number of parasites like malaria-carrying *Anopheles* [mosquitoes](#) or [vampire bats](#). These animals need to feed on fresh blood and stop it from coagulating while they are eating. To make this possible, they use powerful inhibitors of the coagulation process mainly affecting thrombin. Researchers have discovered that "anophelin blocks thrombin in a new and different way than other substances: it's like a key fitting in a lock of a door, but in this case the key fits in the other side" explains Ricardo Gutiérrez Gallego, a member of the IMIM Bioanalysis research group.

The project is based on two recent studies which led to the discovery of thrombin inhibitors presenting new structures. For the inhibitor produced by [Anopheles mosquitoes](#) (anophelin), it was seen that after binding to thrombin, proteins did not degrade, so a systematic study was

launched for all coagulants in the several variants of the Anopheles mosquito. By using very powerful and sensitive [analytical techniques](#) it was possible to determine and monitor in real time the molecule interactions in both anophelin and thrombin, leading to a detailed characterization of their structure and interaction. Researchers also performed mutations on this protein, i.e. they changed the amino acid at each time, so as to discover the crucial components of the molecule when it interacted with thrombin.

[Blood coagulation](#) is a complex mechanism to prevent bleeding after an injury. However, in some cases, the formation of blood clots can lead to a myocardial infarction, a cerebral infarction etc. In these cases, administering anticoagulants is essential. Anticoagulants are drugs that prevent blood from coagulating, thus avoiding cardiovascular events, which are the leading cause of death in Spain. In recent years, one of the most active fields of research has been the search for the ideal anticoagulant since the ones available today may have side effects and must be administered under strict medical control. "The discovery of this new interaction could be useful in the future to create new generation anticoagulant drugs that improve these aspects and also to fight against the spreading of malaria" concludes Dr. Gutiérrez Gallego.

More information: "Unique thrombin inhibition mechanism by anophelin, an anticoagulant from the malaria vector". Ana C. Figueiredo, Daniele de Sanctis, Ricardo Gutiérrez-Gallego, Tatiana B. Cereija, Sandra Macedo-Ribeiro, Pablo Fuentes-Prior, Pedro José Barbosa Pereira. www.pnas.org/content/early/201.../1211614109.abstract

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