Poster Presentation

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The crystal structure of the active domain of AAPP, a powerful anti-coagulant, in complex with an antibody

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Blood clotting is a vitally important process that must be carefully regulated to prevent blood loss on one hand and thrombosis on the other. Severe injury and hemophilia may be treated with pro-coagulants, whereas risk of obstructive clotting or embolism may be reduced with anti-coagulants. Anti-coagulants are an extremely important class of drug, one of the most widely used types of medication, but there remains a pressing need for novel treatments however as present drugs such as warfarin have significant drawbacks. Nature provides a number of examples of anti-coagulant proteins produced by blood-sucking animals, which may provide templates for the development of new small molecules with similar physiological effects. We have therefore studied an Anopheles anti-platelet protein (AAPP) from a malaria vector mosquito, and report its crystal structure in complex with an antibody. Overall the protein is extremely sensitive to proteolysis, but the crystal structure reveals a stable domain built from two helices and a turn, which corresponds to the functional region. The antibody raised against AAPP prevents it from binding collagen. Our work therefore opens new avenues to the development of both novel small molecule anti-clotting agents and anti-malarials.

[1] *K.sugiyama et al. , the journal of biological chemistry, 2014*

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