Short Communication

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Salivary biomarkers in the control of mosquito-borne diseases

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Introduction

Because of the negative impact of blood-sucking insects on vertebrates and the lack of effective control means, many studies aim to identify their salivary proteins. The majority of these researches have focused on mosquitoes as a model in medical entomology. Females exert direct damage by their bites but also indirectly by carrying many pathogens transmissible to humans such as malaria, parasitosis due to a protozoan of the genus *Plasmodium* transmitted by the bite of Anopheles mosquitoes.[1] Saliva is injected several times during penetration of the mouthparts into the skin of the host to the blood capillaries. Different salivary components induce local anesthesia and prevent the blood from clotting in the trunk. Most of these salivary compound have been identified by studies to develop the transcriptome and proteome of salivary glands from several adult female mosquito species. It has thus been possible to identifie new transcrits associated with mosquito nutrition and new salivary protein and peptide séquences.[2] Disposition of databases containing such sequences is a prerequisite for establishing salivary protein profiles of mosquitoes, studying their characteristics and properties, checking their roles and developing strategies to block them.

On the other hand, the evaluation of the efficacy of vectors control strategies is based more generally on entomological methods for the vector, such as the evaluation of vector abundance, their aggressiveness and their infection rate or in humans on detection of pathogens. However, these reference methods have many limitations in their ability to truly and individually evaluate the degree of punctures received by humans and thus the actual effectiveness of vectors control measurements tested. These limits are particularly encountered in a context of low exposure to vectors. The Study of human-vector immunological relationship could lead to several applications for the control of vector-borne diseases. In fact, some salivary proteins of hematophagous arthropods can induce a specific immune response in human populations exposed to arthropod vector stings. One hypothesis is that the antibody response of human specific to salivary peptides of *Aedes* vectors could be an epidemiological biomarker measuring the level of exposure to the humans with the bites of these vectors of arboviruses. Peptide sequences derived from a saliva protein specific for *Aedes aegypti* were selected by combining an immuno-proteomic and bioinformatic approach and taking into account their potential antigenic properties and the absence of cross-reactivity with other arthropodes or organisms.[3] At the present time, a single peptide (N-term-34 kDa) has been validated as a biomarker candidate relevant to evaluate human exposure to *Aedes*. Several studies have demonstrated the main applications of this specific biomarker in the assessment of the risk of transmission of arboviroses in urban and rural contexts and measurements of the effectiveness of vector control on human-vector contact. This new "salivary" biomarker of human exposure to *Aedes* bites could be used as an epidemiological indicator of the risk of arbovirus transmission. It could also be a direct and individual indicator for evaluating the effectiveness of the vector control strategies implemented against this vector.

In Senegal, *Anopheles* anti-saliva antibody levels measured in children of less than five years, which is the population most at risk of malaria, appears proportional to the degree of exposure.[4] All children included in the study had a higher rate during the highest transmission period of the disease. Antibody levels were also associated with the risk of onset of malaria in the next 3 months. These anti-saliva antibodies therefore appear to be an indicator of the risk of malaria transmission in endemic areas, which can be used to improve prevention strategies and management of young patients in the context of seasonal transmission of the disease. From immunogenic salivary proteins, simple and effective prevention tools (immunoassays) can be developed to assess the exposure of individuals or to be used in endemic areas to estimate the effectiveness of preventive strategies against malaria existing vector such as mosquito nets. The analysis of the host-vector relationship is now an important avenue for finding new surveillance and prevention strategies.

This type of immunological biomarker will make it possible to accurately evaluate the operational effectiveness of vector control methods. To this end, the study of the human-vector immunological relationship during sting has made it possible to identify a new immunological biomarker measuring human-vector contact.[5] This biomarker is based on the evaluation, in humans exposed to vector bites, of IgG antibody responses specific to *Anopheles* saliva proteins/peptides. The intensity of this specific anti-saliva antibody response is proportional to the number of punctures (infective or non-infective) received by exposed individuals.[6] This salivary biomarker allows, by qualitative (presence/absence) and quantitative (intensity) evaluation of the specific antibody response to salivary proteins from vectors, identify those exposed to vector bites and measure their level of exposure to vectors. Among all *Anopheles*-specific salivary proteins, a specific salivary peptide (gSG6-P1 peptide of the *Anopheles* gSG6 protein) has been identified and specific IgG responses have been shown to the gSG6-P1 peptide represent biomarkers evaluating human exposure to *Anopheles gambiae* and *Anopheles funestus* bites.[7–11] Interestingly, the gSG6 peptide -P1 is more particularly biomarker of a very weak exposure to vectors of the genus *Anopheles*, conditions where the entomological methods have strong limits of evaluation of the exposure.[8,10] Concerning the anti-vector control against *Anopheles*, specific IgG responses have been demonstrated the total saliva of *Anopheles* and this salivary peptide gSG6-P1 also represented individual biomarkers for evaluate the effectiveness of deployed vector control methods (insecticide-treated nets or non-insecticide-treated nets) and compare the effectiveness of different control methods with each other.[12] The gSG6-P1 peptide also appears to be a relevant biomarker for an operational evaluation of the effective use of impregnated mosquito nets distributed by health actors to populations and whose use is evaluated by standardized questionnaires.[5]

The invention relies on the use of such immunologic biomarkers to provide a methods for evaluating the efficacy of a vector control strategy based on measuring antibody levels against salivary proteins and peptides, specific biomarkers of exposure to *Anopheles* and *Aedes* mosquito bites. It is particularly aimed at the application of this method for vector control to reduce the transmission of malaria and major arboviruses.

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Conflict of interest

The author declares that there is no conflict of interest.

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