to a better detection of cases that potentially contributed to improved case management. Furthermore, the expansion of diagnostic testing along with the increase in confirmed cases implies that before 2010, cases were underreported, and that the accuracy of routine data to describe malaria incidence has improved.

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INTEGRATING GENETIC AND ENVIRONMENTAL DATA TO MODEL TRANSMISSION PARAMETERS (MOVEMENT AND HABITAT USE) IN THE MAJOR INSECT VECTOR OF SLEEPING SICKNESS IN UGANDA (*GLOSSINA FUSCIPES*)

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Tsetse flies (genus *Glossina*) are the obligate vectors of the trypanosome parasite that cause animal and human African trypanosomiasis (also known as nagana and sleeping sickness, respectively). One of the most effective strategies in controlling these dangerous and costly diseases is through vector control of tsetse flies. Establishing feasible programs that reduce on-the-ground disease risk require knowledge of vector movement and habitat use. Spatial modeling of these parameters using genetic and ecological data can fill this knowledge gap. However, integrating these two data types remains a challenge in spatial ecology. In this study, we build upon maximum likelihood methods developed by Bouyer et al (2015 in PLoS NTD) to predict movement and habitat use in the insect vector *Glossina fuscipes fuscipes* in Uganda. We use a novel strategy that applies a machine learning algorithm (random forest regression) to model both genetic and ecological parameters (gene flow and fly density, respectively) based on remotely-sensed environmental data (temperature, precipitation, isothermality, altitude, etc.). The final output integrates the two models into a single bivariate map that can identify areas (i) with the highest disease risk and greatest need for medical infrastructure, (ii) with marginal habitat that can be controlled at low cost but also require dedicated monitoring to prevent re-colonization, and (iii) likely to harbor isolated populations that can be effectively eradicated and/or use in the development of novel vector control strategies. To our knowledge, this is the first application of machine learning to integrate genetic and ecological data to predict these important disease transmission parameters (vector gene flow and habitat use). We also apply our approach to forecast future patterns of gene flow and habitat use under alternative global warming and solar geoengineered scenarios. Future forecasting will help to predict changes in parasite transmission dynamics, and can improve strategic planning to reduce human and animal African trypanosomiasis in a changing climate.

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MUTUALISTIC BACTERIA-PROVISIONED RESOURCES IMPACT VECTOR COMPETENCY

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Many symbionts supplement their host's diet with essential nutrients. However, whether these nutrients also enhance parasitism is unknown. In this study, we investigated whether folate (B9) production by the tsetse fly (*Glossina* spp.) essential mutualist, *Wigglesworthia,* aids auxotrophic African trypanosomes in completing their lifecycle within this obligate vector. We show that the expression of *Wigglesworthia* folate biosynthesis genes changes with the progression of trypanosome infection within tsetse. The disruption of *Wigglesworthia* folate production caused a reduction in the percentage of flies that housed midgut (MG) trypanosome infections. However, decreased folate did not prevent MG trypanosomes from migrating to and establishing an infection in the fly's salivary glands, thus suggesting that nutrient requirements vary throughout the trypanosome life cycle. We further substantiated that trypanosomes rely on symbiont-generated folate by feeding this vitamin to *G. brevipalpis*, which exhibits a low trypanosome vector competency and houses *Wigglesworthia* incapable of producing folate. Folate supplemented *G. brevipalpis* were significantly more susceptible to trypanosome infection, further demonstrating that this vitamin facilitates parasite infection establishment. Our cumulative results provide evidence that *Wigglesworthia* provides a key metabolite (folate) that is 'hijacked' by trypanosomes to enhance their infectivity, thus indirectly impacting tsetse species vector competency. Parasite dependence on symbiont-derived micronutrients, which likely also occurs in other arthropod vectors, represents a relationship that may be exploited to reduce disease transmission.

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PARATRANSGENIC MANIPULATION OF MICRORNA275 IN THE TSETSE FLY AND ITS DOWNSTREAM EFFECT ON TRYPANOSOME INFECTIONS

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Tsetse flies (*Diptera Glossina*) are prominent vectors of African trypanosomes, which are the causative agents of "sleeping sickness" in humans and "Nagana" in domesticated animals throughout sub-Saharan Africa. As effective vaccines and affordable treatments for these diseases are still lacking, we investigated alternative methods, such as interfering with trypanosome infection progression in tsetse, as strategies to reduce disease. We discovered previously that trypanosomes manipulate the expression of a host microRNa 275 (*miR275*), which in turn regulates the structural integrity of tsetse's gut associated peritrophic matrix (PM). This outcome promotes the establishment of trypanosome infections in the fly's gut. To investigate the role of *miR275*in tsetse vector competence, we developed a novel system to constitutively manipulate the expression of tsetse *miR275*. We engineered a tsetse commensal endosymbiont, *Sodalis glossinidius,* to express antagomir-275, which binds to *miR275* thus reducing its expression. We subsequently recolonized flies with recombinant (rec)*Sodalis* and evaluated the downstream effects on tsetse midgut physiology as well as trypanosome infection traits. We found that flies colonized with rec*Sodalis*display impaired digestion phenotypes and are highly susceptible to infection with trypanosomes. Our study is a proof of concept that paratransgenic expression is an effective method to regulate microRNa expression levels for downstream functional studies.

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TSETSE CONTROL IN G-HAT *FOCI*: FOR HOW LONG AND HOW TO STOP?

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With the development and the use of tiny targets, implementation of tsetse control in complement to the "screen and treat" strategy has significantly impacted gambiense Human African Trypanosomiasis (g-HAT) incidence in Guinea, Chad, Côte d'Ivoire and Uganda. This combination of methods, in addition to saving lives and reducing/eliminating transmission, is easily accepted by populations that are not anymore disturbed by tsetse bites and that are more protected against g-HAT. However, with the reduction of the tsetse densities together with decrease in disease incidence, and decrease in funding when the number of cases has gone down, the question of sustainability of vector control operations emerges. Tsetse eradication can be contemplated in potentially isolated areas (e.g. like the Mandoul in Chad), but in many HAT *foci* tsetse populations are not isolated, e.g. in areas like the mangrove in Guinea. In these areas, the

question becomes: until when should the vector control be maintained, and by who? If it has to be stopped, what are the conditions to be fulfilled in before stopping? We propose here an algorithm aiming at helping decision on tsetse control in g-HAT *foci* according to the incidence of HAT cases in the focus, which consists in: 1) maintaining vector control as long as new cases are still found, 2) decreasing vector control when number of new cases reaches zero, but keeping a capacity of reaction to be able to implement vector control in the vicinity of new cases, should they be found (« reactive vector control »), and 3) stopping vector control when no cases have been found during 5 consecutive years with similar medical effort. Parallel to these decisions, other tools (xenomonitoring in tsetse, monitoring in animals and tsetse densities surveillance) should be used to help for early response if necessary, using prediction models. Such an approach is useful and will give some common guidelines for decision making, depending on the context, provided stakeholders have the same understanding on the description/definition of the different situations.

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AMBLYOMMA VARIEGATUM, VECTOR OF AFRICAN TICK-BITE FEVER, CONTAINS AN INTEGRATED *RICKETTSIA AFRICAE* CHROMOSOME IN ITS NUCLEAR GENOME

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Amblyomma variegatum, the tropical bont tick, is one of the most important ticks involved in pathogen transmission to humans and livestock in sub-Saharan Africa and the Caribbean, and also has direct impacts on ruminant productivity. It is the primary vector of two bacteria in the Rickettisiales: *Ehrlichia ruminantium*, the aetiological agent of heartwater disease in ruminants, and *Rickettsia africae*, which causes African tick-bite fever in humans. Unusually for a pathogenic *Rickettsia* sp., the prevalence of *R. africae* in *A. variegatum* has been reported to be close to fixation. We confirmed this finding using specimens collected from the Adamawa Region of Cameroon, where 95.3% of ticks (*n* = 192) removed from cattle were positive by qPCR. However, the normalised density of rickettsial to tick single-copy genes was often low (rickettsia:tick ratio of ~0.5 - 5). The Tick Cell Biobank maintains two *A. variegatum* cell lines (AVL/CTVM13 and AVL/CTVM17) that were found to be positive by PCR for several rickettsial genes; Sanger sequencing confirmed that these genes were of *R. africae* origin. Unexpectedly, no microscopic or proteomic evidence of a bacterial infection in these cell lines was evident, and tetracycline treatment of cultures over two months, which was sufficient to eliminate *Rickettsia raoultii* from parallel tick cell cultures, had no significant effect on *R. africae* DNa signal in the *A. variegatum* lines. We extracted high molecular-weight DNa from AVL/CTVM17 cells and a single adult *A. variegatum* male from a colony maintained at the International Livestock Research Institute in Nairobi. Using Chromium 10x libraries, we sequenced these genomes on an Illumina NovaSeq and obtained assemblies of ~6 Gb, the first from an *Amblyomma* sp. The cell line and the tick genomes contained an integrated *R. africae* chromosome, although a large deletion representing ~10% of the rickettsial genome was present in both assemblies. This finding has significant implications for the epidemiology of *R. africae* and suggests that other tick genomes may contain integrated rickettsial DNA.

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A NOVEL GROUP OF SCABIES MITE INACTIVE CYSTEINE PROTEASES WITH PRO-COAGULATORY FUNCTIONS

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Scabies is an infectious skin disease caused by the burrowing mite *Sarcoptes scabiei* affecting an estimated 100-300 million people worldwide and various companion, farm and wild animals. There is no vaccine and the few available broad-spectrum anti-parasitic drugs fail to control the disease. Scabies is not simply an itch; its mechanical damage to the skin allows the entrance of *Staphylococcus aureus* and group a *Streptococcus* leading to serious secondary complications and mite essential secretory / excretory proteins contribute to this bacterial establishment. Scabies mite express cysteine proteases homologous to the group 1 allergen of house dust mites. However, in contrast to their free-living relatives scabies mites express multiple cysteine proteases comprised of 5 proteolytically active (Sars1a-e) and 5 inactive (SMIPP-Ca-e) members. Recombinant, soluble SMIPP-C proteins were successfully expressed and purified from *Escherichia coli*. Localisation studies using immune-histology demonstrated that SMIPP-Cs are present in the mite gut and excreted within the faeces. Gene expression analysis found that SMIPP-Cs are highly expressed in the adult female mite, and less in other life stages. Initial functional investigations showed that SMIPP-Cs bind to calcium ions and the skin protein Dermatopontin, a fibrin formation accelerator. Two SMIPP-Cs were found to accelerate blood coagulation, accelerate fibrin formation during fibrinogen polymerisation and delay plasmin induced fibrinolysis, hence maintaining the fibrin clot for a longer time. Scanning electron micrographs of SMIPP-C induced fibrin clots revealed a complex structure compared to normal fibrin clot structures, suggesting that SMIPP-C proteins are responsible for an aberrant fibrin formation. Immuno-histological localisation of SMIPP-C proteins in the microthrombi within skin biopsies from human scabies lesions further consolidate the SMIPP-C role in the host-pathogen interplay. We propose that scabies mite SMIPP-Cs cause the pathophysiology of the micro-thrombi formation commonly found in scabies infected skin histology.

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RHODNIUS ECUADORIENSIS POPULATION GENOMICS IN SOUTHERN ECUADOR FOR GUIDING VECTOR CONTROL PROGRAMS

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Understanding triatomine population dynamics at a region scale is key for an effective vector control program. Here we aimed to investigate province-wide population structure and gene flow in the main Chagas disease vector in southern Ecuador, *Rhodnius ecuadoriensis*, and provide guidelines for vector control. To achieve this, we genotyped 2,552 SNP markers of 282 *R. ecuadoriensis* samples from 25 communities in Loja, Ecuador from 2004 to 2018. a strong signal of structuring (F_{ST} = 0.225, P-value = 0.001) was detected by our hierarchical analysis of molecular variance (AMOVA), which attributed most of the variation to regions (17.21 %) and individuals within populations (77.50%) as compared to populations within regions (domicile vs sylvatic populations – 5.29%). Interestingly, populations pairwise F_{ST} comparisons showed similar patterns of structure. After that, we identified 13 genomic clusters among samples using discriminant analysis of principal components (DAPC). Additionally, we explored phylogenetic relationship using a neighbour-joining tree of pairwise genetic distance from samples allele counts which clustered them by region, similarly to pairwise F_{ST} comparisons and DAPC results. Once genomic differentiation pattern was stablished, we tested isolation-by-distance (IBD) as null hypothesis using mantel test and correlograms which drew a significant correlation (mantel r = 0.55, P-value = 0.001). Finally, we tested the usability of our 2,552 SNPs to detect *loci* more differentiated than the expected of neutral *loci* and found 157 candidate F_{ST}-outlier

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