Molecular epidemiology of brucellosis in northern Tanzania (Brucella)

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Abstract

Brucellosis is one of the most widespread zoonotic diseases and is identified as one of the highest priority animal diseases in Africa. Sub-Saharan Africa has the world's fastest growing human population and highly dynamic societies undergoing rapid urbanization. Changes in connections between urban and rural populations and the supply of animal products into urban areas could significantly shift patterns of exposure to brucellosis. Effective brucellosis control requires integrated combinations of control measures, but targeted vaccination is a key tool in reducing prevalence of disease in livestock populations. However, to develop plans for the optimal use of existing vaccines we need to understand which host species are infected by which *Brucella* species, and which routes are most important in transmitting brucellosis to humans in different settings. This project will generate data, and tools, provide training, and establish and enhance partnerships necessary for the development of a brucellosis control program for Tanzania. The development of diagnostic capacity in Tanzanian research laboratories needed for species-level diagnosis of *Brucella* will enable detection and identification of the *Brucella* species present in different livestock and human populations. These data will enable identification of the ruminant species acting as sources of human infection and the *Brucella* species responsible for human disease, providing the first systematic evidence-base to guide which brucellosis vaccine is best used in different animal populations. Our team includes policy-makers in Tanzanian government who will help ensure that research findings are made directly available to those who need to know most (including vaccine producers). The project will provide the evidence-base identified by the Tanzanian government that is needed to formulate national brucellosis control policy and place Tanzania on the roadmap for progressive control of this high priority disease.

Summary

This project will develop the evidence-base to inform the use of *Brucella* vaccines in sub-Saharan Africa and build capacity in Tanzanian laboratories to generate critical *Brucella* typing data. The research will be conducted hand-in-hand with Tanzanian government scientists charged with formulating national policies for the control of brucellosis. Brucellosis is a disease caused by a number of species of bacteria collectively called *Brucella*. Brucellosis is one of most widespread human diseases acquired from animals, and is one of the highest priority animal diseases in Africa. Brucellosis infects many animal species, including key livestock species - cattle, sheep, and goats - and most human infections are acquired through direct contact with livestock or via indirect transmission through untreated milk products. Brucellosis has wide-ranging impacts that include animal losses due to abortion, lost milk production, killing of infected animals, and human illness causing reduced work capacity. One third of the human population of sub-Saharan Africa lives and works closely with livestock. Areas with both high livestock populations and demand for livestock products offer the greatest opportunity for livestock to serve as a pathway out of poverty. Tanzania

has been identified as a hotspot for endemic zoonoses burden, poverty burden and reliance on livestock. Sub-Saharan Africa also has the worlds fastest growing human population and highly dynamic societies undergoing rapid urbanization. Changes in connections between urban and rural populations and the supply of animal products into urban areas could lead to significant shifts in patterns of exposure to zoonotic diseases such as brucellosis. Control programmes implemented previously demonstrate that the use of existing tools for brucellosis control can markedly improve the livelihoods of the poor communities that are most affected by brucellosis. However important gaps remain in our understanding of the epidemiology of brucellosis in sub-Saharan Africa. To develop practical plans for brucellosis control it is crucial to understand which host species are infected by which *Brucella* species, and which routes are most important in transmitting brucellosis to humans in rural environments, towns and rapidly expanding cities. This project will generate data, and tools, provide training, and establish and enhance national and trans-national partnerships critical to the development and implementation of a brucellosis control program for Tanzania. The development of diagnostic capacity in Tanzanian research laboratories necessary for species-level diagnosis of *Brucella* will enable detection of animal infections and - crucially - the identification and characterisation of the *Brucella* species present in different livestock and human populations. These data will be critical for identifying the ruminant species that act as sources of human infection and the *Brucella* species most responsible for human disease in rural and urban environments of northern Tanzania. This project will provide the first large systematic evidence base to guide which vaccine is best used in which different animal population. In the short term, this project will build significant laboratory diagnostic capacity and expertise in Tanzania and strengthen academic links between UK and Tanzanian laboratories working on brucellosis. Our team includes policy-makers in Tanzanian government and will help ensure that research findings are made directly available to those who need to know most (including vaccine producers). The project will provide the evidence-base specifically identified by the Tanzanian government to formulate national brucellosis control policy and place Tanzania on the roadmap for progressive control of this high priority disease.

Impact Summary

The outputs of this project will fill key data gaps that currently hinder the development and implementation of a national brucellosis control policy in Tanzania. The project will deliver impact over a range of time-scales. The ultimate long-term beneficiaries of brucellosis control are livestock keepers and their families, milk consumers, butchers, abattoir and slaughterhouse workers, and veterinary professionals. In sub-Saharan African, endemic zoonoses are responsible for a considerable burden of human illness, mortality, and reduction in livestock productivity. There is a strong association between poverty, livestock keeping and zoonoses. Areas with both high livestock populations and rising demand for livestock products therefore offer the greatest opportunity for livestock to serve as a pathway out of poverty, making Sub-Saharan Africa, and Tanzania in particular, a prime beneficiary of improvements in the control of zoonotic diseases. Brucellosis can be effectively controlled to reduce the burden of disease in both humans and animals through the application of a range of existing control approaches. When costs are distributed between health and veterinary sectors in proportion to the benefits accruing, livestock vaccination has been shown to be a highly cost-effective veterinary intervention. However, it is key to cost-effective control to ensure that the right interventions are targeted at the most appropriate control-points. In the case

of brucellosis, which can be caused by a number of distinct pathogen species, identification of the pathogens and hosts that are most important in disease transmission is crucial, but this is largely unknown. Vaccines currently exist for a number of *Brucella* species, and this project will provide the first large-scale systematically compiled evidence-base to guide which vaccine should be used in which host population. In the long-term we believe that the provision of operational information on what vaccine to use in whichpopulations will help persuade organizations such as GALVmed to distribute and deploy vaccines in the future. Our team has been developed specifically to engage policy-makers in the research, and researchers in the policy from the outset, and we present an analysis of the pathway to this long-term impact in 'Pathways to Impact'. In the medium-term the project will strengthen academic links between UK and Tanzanian partner institutions working on brucellosis through the development of 4 primary partnerships. 1 - between KCMC in Tanzania and the AHVLA in the UK and 2 - between TVI/TVLA and the AHVLA to establish and maintain resilient diagnostic capacity at these Tanzanian institutions. 3 - between NMAIST and UG by training a future independent Tanzanian scientist, embedded within a supportive network of international experts, enabling the seeding of future research activities between these organizations. 4 -adding a new dimension to an existing relationship between MoLFD/TVI and UG, strengthening policy-forming units and enabling ministry officials charged with developing national disease control policy to access a nucleus of experts with a proven track record of translating one-health research into policy. In the short-term, this project will build significant epidemiological and diagnostic capacity and expertise at research institutions in Tanzania, and provide individual training to a Tanzanian research scientist that will include opportunities to train at the AHVLA and take new skills and knowledge back to Tanzania to set up capacity in situ with ongoing financial and academic support from the UK and Tanzanian research consortium. Most importantly, this project will build sustainable laboratory capacity to provide the higher resolution, species-specific diagnostic testing necessary for the most effective use of available vaccines to ultimately reduce disease burden.