



## Project Monitoring

<b>PROJECT TITLE</b>	Tackling trypanosomiasis cardiomyopathy with microRNAs and tridimensional (3D) cell models
<b>ACRONYM</b>	MiT3D
<b>CONTRACT no.</b>	EXPL/CVT-CVT/0175/2021
<b>BRIEF DESCRIPTION</b>	<p>Background: Chagas disease (CHD), also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite <i>Trypanosoma cruzi</i>. Declared by the World Health Organization as neglected zoonotic disease (NZD), CHD constitute a serious threat to social and economic development of endangerous populations, with increasing health comorbidities and high number of premature deaths, mainly occurring in economically disadvantages areas. Wild and domestic animals, such as pig, cattle, horse, cats and dogs, my be infeced by <i>T. cruzi</i> and act as reservoir for human populations. Cardiomyopathy is one of the most serious consequences of <i>T. cruzi</i> infection and is characterized by progressive infiltration of inflammatory leukocytes in the heart tissue, leading to myocardial necrosis and formation of fibrotic scar tissue, that results in permanent heart damage and may lead to death. However, very litle is known on CHD chronic phase onset on animals of economic value and epidemiological interest for <i>T. cruzi</i> control, such as pig, cattle and horse. With no vaccine available, limited therapeutic options and actual CHD expansion, crossing boundaries to non-endemic areas, the urge to develop new approaches to control and cure CHD constitutes an emerging global health challenge.</p> <p>As in most infections, it is the interaction of parasite with the host immune system that constitutes a decisive point in defining the disease outcome. Consequently, trypanosomatids have evolved strategies to persist and disperse inside the host by subverting and exhausting host immune defences. Therefore, explore parasite-host communication may reveal to be key in restrain parasite dissemination in the host. In recent years, microRNAs (miRNAs) which are a class of non-coding RNAs that play important roles in normal regulation of gene expression have attracted the attention of the scientific community, as potential host-parasite communication regulators influencing host immune response and having a possible effect on disease.</p> <p>The use of state-of-the-art tridimensional (3D) cell cultures to addresses host-parasite interactions, constitutes a groundbreaking and innovative approach, as it mimics the <i>in vivo</i> tissue microenvironment with an intricate cell-to-cell and cell-to-matrix interactions, generating a dynamic and complex network of nutrients transport, waste removal, and cell signalling pathways, allowing a detailed analysis of cell's behaviour. At the same time, 3D cell models allow increasing in data quality and reduction of animal experimentation. Thus, 3D cell models constitute valuable tool to be used to unreval parasite-host interactions.</p>
<b>OBJECTIVES</b>	The present proposal aims to apply tridimensional (3D) cardiac models of several <i>T. cruzi</i> hosts of veterinary importance, to address the role of



	<p>microRNAs in the disease progression and establishment of cardiomyopathies derived by <i>T. cruzi</i> infection.</p>
<b>IMPLEMENTATION</b>	<p>Innovation and expectations: miT3D constitutes a breakthrough on traditional approaches, as it takes advantage of 3D-cell models of cardiac tissue, which can mimic the <i>in vivo</i> cellular microenvironment, allied with cutting-edge molecular and cellular techniques to address the role of miRNA dynamics in <i>T. cruzi</i> related cardiomyopathy. This constitutes a pioneering, innovative and exploratory approach to animal trypanosomiasis health issues and can be extended to other infectious diseases and even to diseases whose resolution are depending on the proper activation of the immune system, such as cancer or autoimmune diseases.</p>
<b>FUNDING AGENCY</b>	FCT
<b>DURATION</b>	02/01/2023 – 01/01/2025
<b>INSTITUTIONS   RESEARCH TEAM</b>	NOVA-IHMT-GHTM: Armanda Rodrigues (PI)
<b>URL</b>	<a href="http://mit3d.ihmt.unl.pt/">http://mit3d.ihmt.unl.pt/</a>
<b>SUSTAINABLE DEVELOPMENT GOALS</b>	1, 3 and 10
<b>PUBLICATIONS</b>	<p>Durães-Oliveira, J.; Palma-Marques, J.; Moreno, C.; Rodrigues, A.; Monteiro, M.; Alexandre-Pires, G.; da Fonseca, I.P.; Santos-Gomes, G. Chagas Disease: A Silent Threat for Dogs and Humans. <i>Int. J. Mol. Sci.</i> <b>2024</b>, <i>25</i>, 3840. <a href="https://doi.org/10.3390/ijms25073840">https://doi.org/10.3390/ijms25073840</a></p>
<b>THESES</b>	<p>"Animal trypanosomiasis: effect of <i>Trypanosoma cruzi</i> infection on cardiac tissue in three-dimensional (3D) cellular models". Master in Biomedical Sciences. IHMT-UNL. Supervised by Dr. Armanda Rodrigues. Ongoing.</p> <p>"Explore the role of microRNA in the context of <i>Trypanosoma cruzi</i> infection in cardiac tissue". Master in Tropical Health. IHMT-UNL. Supervised by Dr. Armanda Rodrigues. Ongoing.</p>
<b>OTHER OUTREACH ACTIVITIES</b>	<p>Poster presentation:</p> <p>Armanda Viana Rodrigues; Meunier, Mafalda; Aleska Silva; Victória Tavares; Alexandre-Pires, Graça; Cláudia Jassica Gonçalves Moreno ; Isabel Pereira da Fonseca; Gabriela Santos-Gomes. "Tackling Chagas disease cardiomyopathies: are <i>Trypanosoma cruzi</i> extracellular vesicles the key?". XLIX Annual Meeting of the Portuguese Society for Immunology, 2024.</p> <p>Armanda Viana Rodrigues ; Meunier, Mafalda; Durães-Oliveira, João; Aleska Silva; Cláudia Jassica Gonçalves Moreno ; Victória Tavares; Joana Palma-Marques; et al. Corresponding author: Armanda Viana Rodrigues. "Immunomodulatory effect of extracellular vesicles from <i>Trypanosoma cruzi</i>: an example of parasite-host co-evolution". International meeting of Portuguese Association for Evolutionary Biology (ENBE), 2023.</p>



	<p>Rodrigues, Armanda; Cláudia Jassica Gonçalves Moreno ; Meunier, Mafalda; Marta Monteiro; Victória Tavares; Aleska Silva; Alexandre-Pires, Graça; Isabel Pereira-da-Fonseca; Gabriela Santos-Gomes. "One Health approach to tackle Chagas disease: Cardiac explant culture". 2nd Egas Moniz One Health Symposium, 2023.</p> <p>Oral presentation:</p> <p>Rodrigues A, Meunier M, Tavares V, Silva A, Moreno C, Monteiro M, Alexandre-Pires G, Pereira-da-Fonseca I, Santos-Gomes G. Chagas Disease: new insights into cardiomyopathies. Oral presentation on the online and live international webinar Changing the game in the battle against Tripanossomatids. Lisbon, 10 January 2024.</p>
<b>EQUIPMENT</b>	N/A
<b>PATENTS</b>	N/A
<b>SOCIAL IMPACT</b>	