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High glucose concentrations impair the processing and presentation of Mycobacterium tuberculosis antigens in vitro

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Type 2 diabetes is an established risk factor for tuberculosis, but the underlying mechanisms are largely unknown. We established an in vitro model to analyze the effect of high glucose concentrations in antigen processing and presentation in antigen-presenting cells. Human monocyte-derived macrophages (MDMs) were exposed to high (11 mM and 30 mM) and low (5.5 mM) glucose concentrations and infected with Mycobacterium tuberculosis (Mtb). Flow cytometry was used to analyze the effect of high glucose concentrations in histocompatibility complex (MHC) class II molecules (HLA-DR) and co-stimulatory molecules (CD80 and CD86), indispensable for an adequate antigenic presentation and CD4+ T cell activation. HLA-DR and CD86 were significantly decreased by high glucose concentrations compared with low glucose concentrations. Confocal microscopy was used to detect Rab 5 and Lamp-1, proteins involved in the kinetics of antigen processing as early markers, and Rab 7 and cathepsin D as late markers. We observed a delay in the dynamics of the acquisition of Rab 7 and cathepsin D in high glucose concentrations. Moreover, the kinetics of the formation M. tuberculosis peptide–MHC II complexes in MDMs was decreased under high glucose concentrations, reducing their capacity for T cell activation. These findings suggest that high glucose concentrations directly affect antigenic processing, and therefore antigenic presentation.

Biography

Guadalupe Monroy is a medical who still learning. Since she was a medical student she had interest in clinical research, in her formation did some internships in a few laboratories, when she finished medical career, she did a master degree in the Nacional Institute of Respiratory Disease, there she realized the impact of diabetes in the infective diseases, and she did the research of this abstract, now she is doing the cardiology residence, and diabetes still been a topic of relevance in her formation.