Human monocyte-derived dendritic cells exposed to hyperthermia show a distinct gene expression profile and selective upregulation of *IGFBP6*

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Keywords: apoptosis, B cells, chemotaxis, dendritic cells, hyperthermia, Immunology and Microbiology Section, Immune response, Immunity

Received: *April 16, 2017* ***Accepted***: *May 12, 2017* ***Published***: *June 01, 2017*

ABSTRACT

Fever plays a role in activating innate immunity while its relevance in activating adaptive immunity is less clear. Even brief exposure to elevated temperatures significantly impacts on the immunostimulatory capacity of dendritic cells (DCs), but the consequences on immune response remain unclear. To address this issue, we analyzed the gene expression profiles of normal human monocyte-derived DCs from nine healthy adults subjected either to fever-like thermal conditions (39°C) or to normal temperature (37°C) for 180 minutes. Exposure of DCs to 39°C caused upregulation of 43 genes and downregulation of 24 genes. Functionally, the up/downregulated genes are involved in post-translational modification, protein folding, cell death and survival, and cellular movement. Notably, when compared to monocytes, DCs differentially upregulated transcription of the secreted protein IGFBP-6, not previously known to be specifically linked to hyperthermia. Exposure of DCs to 39°C induced apoptosis/necrosis and resulted in accumulation of IGFBP-6 in the conditioned medium at 48 h. IGFBP-6 may have a functional role in the hyperthermic response as it induced chemotaxis of monocytes and T lymphocytes, but not of B lymphocytes. Thus, temperature regulates complex biological DC functions that most likely contribute to their ability to induce an efficient adaptive immune response.

INTRODUCTION

The effect of heat on cells can vary from survival and adaptation to apoptosis and, in extreme conditions, to necrosis [1-3]. These effects are either a direct consequence of heat itself on cellular components (*e.g.* denaturation of proteins) or a secondary effect mediated by cellular adaptive mechanisms such as the expression of