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Effects of melittin on gene expression in a dendritic cell/Hodgkin lymphoma co-culture model

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Objectives: Hodgkin lymphoma (HL) is a rare neoplasia characterized by abnormal B lymphocytes and an increased risk of secondary malignancies. The currently available treatment options for refractory cases are limited and highlight the need for novel therapies. Melittin (MEL), a component found in bee venom, kills HL cells at concentrations that are not toxic for normal cells. We analyzed effects of MEL on gene expression in dendritic cells (DC) after co-culture with HL cells.
Methods: DC were diferentiated from peripheral blood mononuclear cells after CD14-selcetion or plastic adherence using standard protocols. Transwell-assays were used for co-culture of HL cells (upper compartment of the transwell system) with DC (lower compartment). During co-culture, MEL was present or absent. After 24 hours, transwells with HL cells were removed, DC were matured and RNA was isolated. Gene expression was analyzed by RNAseq. DC cultured without HL cells served as control. Differential gene expression analysis was conducted and the results were compared to public datasets from different cell populations.
Results: After MEL treatment, several genes were differentially expressed in DC. MEL induced proinflammator signaling cascades in DC involving MAPK, TNF and TLR pathways. Furthermore, the culture of immature DC in the presence of HL cells had a strong impact on gene expression in mature DC.
Conclusions: Our data suggest that MEL has immune-modulatory activities by effecting the gene expression profile of DC. This observation might contribute to a better understanding of the mechanisms underlying the anti-tumor properties of melittin and its potential therapeutic applications.
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