MicroRNAs as Biomarkers in Psoriasis

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Marianne B. Løvendorf defended her PhD thesis on September 26, 2014, entitled "MicroRNAs as Biomarkers in Psoriasis", at the University of Copenhagen. The thesis was supervised by Professor Lone Skov, Department of Dermato-Allergology, Gentofte Hospital, University of Copenhagen, Denmark, Mads A. Røpke, PhD, Medical Department, LEO Pharma A/S, Denmark and John R. Zibert, PhD, Scientific Affairs, LEO Pharma A/S, Denmark. Opponents and Member of the Evaluation Committee were Associate Professor Andor Pivarcsi, Center for Molecular Medicine, Karolinska Institutet, Sweden, Associate Professor Morten Lindow, Roche Innovation Center Copenhagen, and Professor Allan Randrup Thomsen, The Department of International Health, Immunology and Microbiology, The Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Psoriasis is a systemic inflammatory disease with cutaneous manifestations. Although several attempts have been made to identify systemic biomarkers for psoriasis there are still no specific biomarkers. It is highly relevant to identify systemic biomarker profiles in patients with psoriasis as these could aid in the prediction of disease progression or therapeutic response, altogether leading to improved patient management. MicroRNAs (miRNAs) are a class of small non-coding RNA molecules that modulate gene expression post-transcriptionally. MicroRNAs act primarily within the cell; however, recent evidence has shown the presence of miRNAs in cell-free environments including serum and plasma, where they have proved stable and resistant to degradation of RNAses.

Based on this, several groups have made an effort to explore whether miRNAs can be used as diagnostic and prognostic biomarkers for various diseases. Earlier studies on psoriasis-specific miRNA expression in skin were confined to frozen whole tissue extracts and thus, the established differences in global miRNA expression in psoriatic skin represent the average miRNA changes from a mixture of cells including keratinocytes, leucocytes, dendritic cells and endothelial cells. The overall aim of this PhD project was to elucidate miRNAs distribution and potential as biomarkers in psoriasis by investigating specific miRNA changes in skin and blood from patients with psoriasis.

In study I we aimed to investigate the influence of different preservation methods (formalin-fixed, paraffin-embedding, frozen and tissue-tek-embedding) of psoriatic skin on the global miRNA expression levels. Our findings demonstrated that miRNA detection in the skin is robust irrespective of preservation method [1].

In study II we aimed to investigate whether certain disease-related miRNAs could be specifically confined to the epidermis or to immune cells in the dermal inflammatory infiltrates including different T-cell subsets. We identified significant differences in miRNA expression between the epidermis and dermal inflammatory infiltrates of lesional psoriatic skin compared with non-lesional psoriatic skin including several novel miRNAs [2].

Fig. 1. Marianne B. Løvendorf (right) defended her thesis on "MicroRNAs as Biomarkers in Psoriasis". Supervisor was Lone Skov (middle) and Opponent Andor Pivarcsi (left).

In study III we aimed to analyse the miRNA expression in different blood compartments from patients with psoriasis and healthy controls to explore miRNAs potential as blood biomarkers for psoriasis. We identified several deregulated miRNAs in whole blood, plasma and peripheral blood mononuclear cells (PBMCs) from patients with psoriasis among those in PBMCs, miR-143 and miR-223 which may serve as biomarkers for psoriasis activity [3].

In conclusion, our results add to the evidence that psoriatic lesions indeed are associated with an altered epidermal and

dermal miRNA expression profile. In addition, similar changes in the miRNA expression in blood and skin from patients with psoriasis may contribute to the pathogenesis of psoriasis and thereby potentially serve as novel biomarkers for psoriasis.

Literature

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