Targeting epigenetics to treat psoriasis

Applicant

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Abstract

Psoriasis is a frequent auto-inflammatory skin disease characterized by keratinocyte hyperproliferation and massive infiltration of immune cells. Whereas cytokines such as IL-36 and IL-17A represent key drivers of psoriasis, little is known about the contribution of epigenetic regulators to this disease. In previous experiments, we identified RING1B and EZH2, catalytic components of polycomb repressor complexes (PRCs), as key mediators of pro-psoriatic cytokine action in keratinocytes. Surprisingly, whereas PRCs are mostly known to suppress gene expression via histone modifications, we observed that RING1B and EZH2 activate pro-inflammatory gene expression. This project will therefore reveal the determinants that control gene repressor versus activator functions of both proteins and investigate their role in psoriasis using state-of-the-art molecular tools and faithful preclinical mouse models. Based on these results we will investigate if pharmaceutical inhibition of EZH2 or RING1B constitutes an attractive new therapy approach for the treatment of psoriasis.