The STAT3 Target METTL8 is a novel epigenetic factor Regulating ESC Differentiation

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Abstract

The capacity of embryonic stem cells (ESCs) to differentiate into all lineages of mature organism is precisely regulated by cellular signaling factors. STAT3 is a crucial transcription factor that plays a central role in maintaining ESC identity. However, the underlying mechanism by which STAT3 directs differentiation is still not completely understood. Here, we show that STAT3 positively regulates gene expression of methyltransferase-like protein 8 (Mettl8) in mouse ESCs. We found that METTL8 is dispensable for pluripotency but affects ESC differentiation. Subsequently, we discovered that METTL8 interacts with Mapkbp1's mRNA, which is an intermediate factor in c-Jun N-terminal kinase (JNK) signaling, and inhibits the translation of the mRNA. Thereby, METTL8 prohibits the activation of JNK signaling and enhances the differentiation of mouse ESCs. Collectively, our study uncovers a STAT3 target, Mettl8, which regulates mouse ESC differentiation via JNK signaling.