# Review of: "Tissue-Specific Control of Ribosomal RNA Synthesis Revealed by Transcription Factor Profiling"

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Potential competing interests: I had previously collaborated with one of the middle authors on this work.

Despite ribosomal RNA (rRNA) being the most abundant cellular RNA, the context-specific mechanisms that fine-tune RNA polymerase I transcription of the 47S rRNA genes (rDNA) in different cell types remain poorly understood. Antony et al provide a useful resource of an atlas of transcription factor (TF)-rDNA binding in mammalian hematopoiesis, generated to investigate TF roles in regulation of Pol I transcription. They used public ChIP-Seq datasets of human and mouse hematopoiesis to defines a set of distinct TF-rDNA binding patterns, and identified rDNA sites with binding of multiple TFs and families. In this manuscript, they have identified evolutionarily conserved as well as divergent patterns of rDNA occupancy for multiple critical hematopoietic TFs.

The mapping of ~2200 publicly available ChIP-Seq datasets for ~250 TFs and chromatin proteins to human and mouse rDNA appears to be robust demonstrating high-confidence patterns of rDNA occupancy. However, the mapping is customised to a single rDNA unit- the only known complete sequence of a single mouse and human rDNA unit. rDNA sequence variations and diversity remain a sequencing challenge and the rDNA loci remain “genomic black holes”. The TF-rDNA atlas presented here gives a solid, although perhaps not a complete picture of TF-rDNA biology.

The manuscript also demonstrates that the TF CEBPA, which is an important regulator of hematopoietic granulocyte differentiation, binds to active rDNA at a conserved site within the 18S transcribed region of rDNA located 5kb downstream of the transcription start site (TSS). Targeted degradation of CEBPA (C/EBP alpha) caused rapid reduction in Pol I occupancy across the transcribed region of rDNA. This was also associated with reduced rRNA synthesis measured by ‘47S-FISH-Flow,’ a sensitive assay to quantify nascent rRNA; as well as defective ribosome biogenesis. It is unclear how reduced CEBPA binding at a canonical site 5kb downstream of STT influences Pol I occupancy at the promoters. The authors propose looping or transient contact between CEBPA binding and rDNA promoters but this remains to be elucidates.

Overall, this is a useful resource with implications for understanding tissue-specific regulation of Pol I transcription and ribosome biogenesis. The data is well-presented, the results are robust and the methodologies are clearly described.