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Glucocorticoid receptor wields chromatin interactions and tunes transcription for podocyte cytoskeleton

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Objectives: Glucocorticoids (GCs) are the primary medication for podocytopathy. However, its effect on renal podocyte is not well understood. Glucocorticoid receptor (GR) is critical for understanding the role of GCs. 3D organization of the genome is necessary for understanding transcriptional regulation mediated by GR binding, but up to date there is no information about it in podocyte.

Methods: We captured and integrated GR binding map, transcriptome and transcription involved long range chromatin interactions to understand the role of GR in podocyte. In order to understand the GR binding profile in the genome in human podocyte, ChIP-seq assays were performed. The effect of elements activated by GR on transcription was investigated by RNA-seq. 3D interactome was captured by HiChIP with H3K27ac.

Results: First of all, genome wide occupancy of GR in podocyte was different from that in other studied human cell types. GR tended to bind directly at GRE in podocyte, probably functioned as pioneer factors. Secondly, GR prefers for autonomous binding and enriched at enhancers. Thirdly, exposure to GCs altered transcriptome in podocytes. With 3D interactome captured by HiChIP with H3K27ac, the regulatory link between GR sites and interacted target genes was significantly enhanced. Last of all, we found that ZBTB16 was a member of GR network that mediated its effect on podocyte cytoskeleton.

Conclusions: Collectively, our comprehensive analyses reveal specific features of GR in podocyte and identify a potential GR mediated regulatory network for podocyte cytoskeleton stabilization.