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[Transcriptional networks of murine diabetic peripheral neuropathy and nephropathy: common and distinct gene expression patterns.](#)

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**Abstract**

**AIMS/HYPOTHESIS:** Diabetic peripheral neuropathy (DPN) and diabetic nephropathy (DN) are two common microvascular complications of type 1 and type 2 diabetes mellitus that are associated with a high degree of morbidity. In this study, using a variety of systems biology approaches, our aim was to identify common and distinct mechanisms underlying the pathogenesis of these two complications. **METHODS:** Our previously published transcriptomic datasets of peripheral nerve and kidney tissue, derived from murine models of type 1 diabetes (streptozotocin-injected mice) and type 2 diabetes (BKS-db/db mice) and their respective controls, were collected and processed using a unified analysis pipeline so that comparisons could be made. In addition to looking at genes and pathways dysregulated in individual datasets, pairwise comparisons across diabetes type and tissue type were performed at both gene and transcriptional network levels to complete our proposed objective. **RESULTS:** Gene-level analysis identified exceptionally high levels of concordant gene expression in DN (94% of 2,433 genes), but not in DPN (54% of 1,558 genes), between type 1 diabetes and type 2 diabetes. These results suggest that common pathogenic mechanisms exist in DN across diabetes type, while in DPN the mechanisms are more distinct. When these dysregulated genes were examined at the transcriptional network level, we found that the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway was significantly dysregulated in both complications, irrespective of diabetes type. **CONCLUSIONS/INTERPRETATION:** Using a systems biology approach, our findings suggest that common pathogenic mechanisms exist in DN across diabetes

type, while in DPN the mechanisms are more distinct. We also found that JAK-STAT signalling is commonly dysregulated among all datasets. Using such approaches, further investigation is warranted to determine whether the same changes are observed in patients with diabetic complications.

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