Quantitative proteomics reveals differential effects of ZMPSTE24 and LMNA knockdown on human fibroblasts.

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The nuclear lamina physically supports the cell nucleus and has a central role in gene regulation. Mutations in the *LMNA* gene, which encodes A-type lamins, cause a spectrum of tissue-specific and systemic diseases collectively called laminopathies. To elucidate the molecular mechanisms underlying this phenotypic diversity, we set out to identify changes in the proteome upon specific lamin perturbations. More specifically, mature lamin A was reduced or farnesylated prelamin A was enriched by knockdown of *LMNA* or *ZMPSTE24*, respectively, in human dermal fibroblasts. To quantitatively compare protein composition, we made use of SILAC-based shotgun proteomics. Gene Ontology analysis of the most significant hits revealed that the largest fraction of the differentially produced proteins in LMNA depleted cells were cytoskeletal proteins, more specifically those involved in actin cytoskeleton organization (e.g. ARPC4, FSCN1 and TPM1). *ZMPSTE24* knockdown on the other hand, mainly altered the levels of mitochondrial proteins such as TOMM70A, CYC1 and ATP5H. The top hits were validated by western blot and a comparison at the transcriptome level showed that some changes were due to differential gene expression whereas others were not.