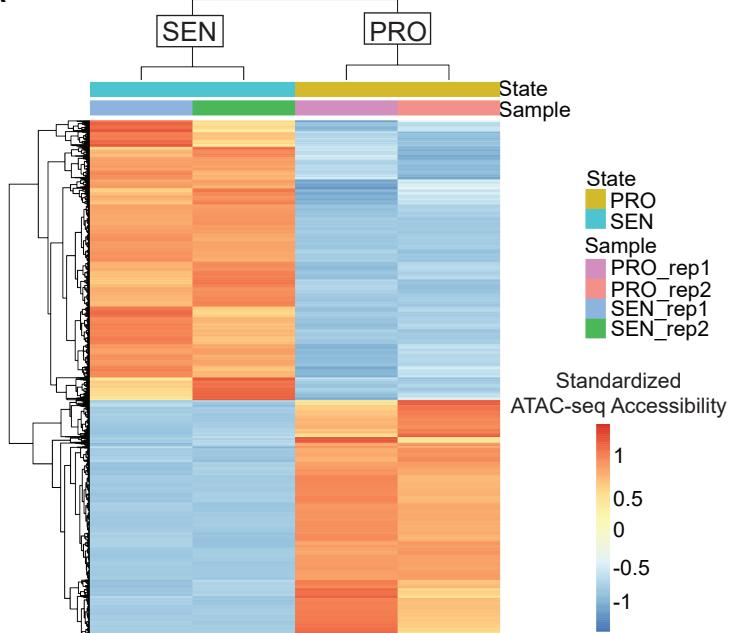
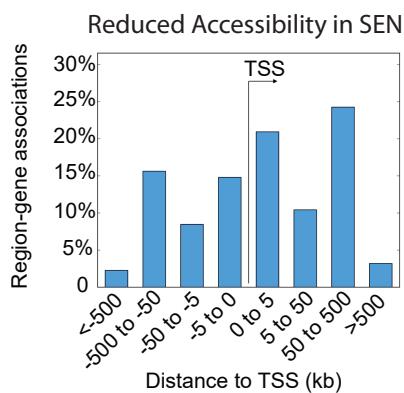


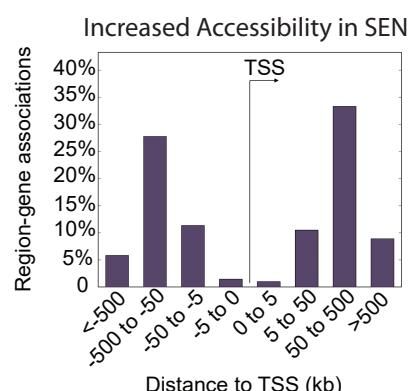
A



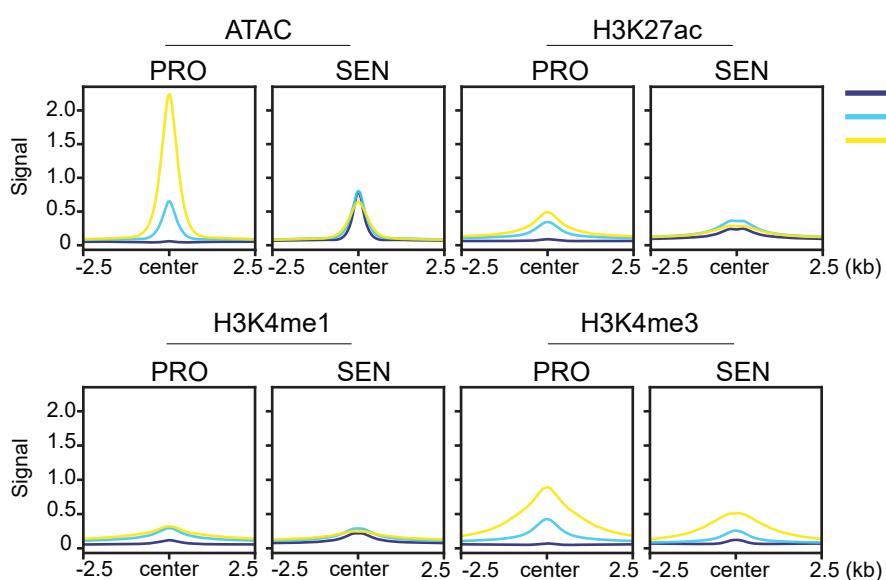
B



C



D



E

Increased Accessibility in SEN

- regulation of extent of cell growth
- regulation of axon extension
- androgen metabolic process
- regulation of hair follicle maturation
- cellular hormone metabolic process
- positive regulation of cytokine secretion
- epithelial to mesenchymal transition
- pericardium development
- peptide cross-linking
- positive regulation of p38MAPK cascade
- cardiac epithelial to mesenchymal transition
- renal vesicle formation
- positive regulation of epidermal growth factor-activated receptor activity
- fibroblast activation
- mammary gland duct morphogenesis
- regulation of astrocyte differentiation
- temperature homeostasis
- renal vesicle morphogenesis
- negative regulation of interleukin-1-mediated signaling pathway
- renal vesicle development
- negative regulation of collateral sprouting
- prostaglandin transport
- positive regulation of vascular endothelial growth factor receptor signaling pathway
- diterpenoid biosynthetic process
- negative regulation of interleukin-2 production

0 2 4 6 8 10
-log₁₀(p-value)

F

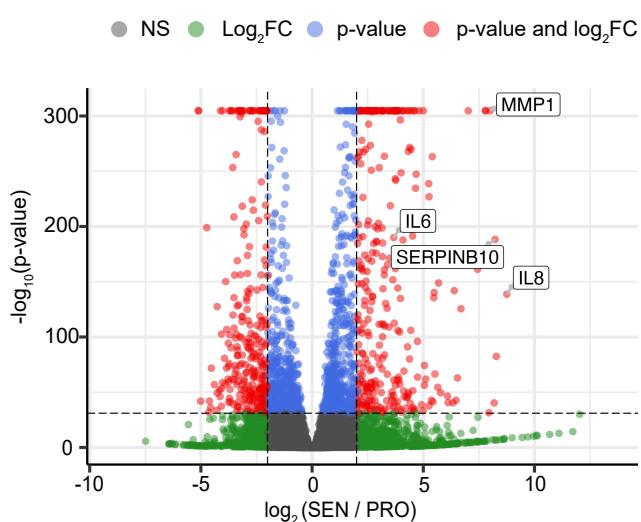
Reduced Accessibility in SEN

- termination of RNA polymerase II transcription
- chaperone-mediated protein folding
- mRNA 3'-end processing
- positive regulation of DNA-templated transcription, elongation
- cytoplasmic translation
- 'de novo' posttranslational protein folding
- positive regulation of mRNA catabolic process
- 'de novo' protein folding
- mismatch repair
- negative regulation of cyclin-dependent protein kinase activity
- negative regulation of cyclin-dependent protein serine/threonine kinase activity
- regulation of spindle organization
- regulation of mRNA 3'-end processing
- regulation of telomerase RNA localization to Cajal body
- regulation of nucleobase-containing compound transport
- positive regulation of telomerase RNA localization to Cajal body
- regulation of RNA export from nucleus

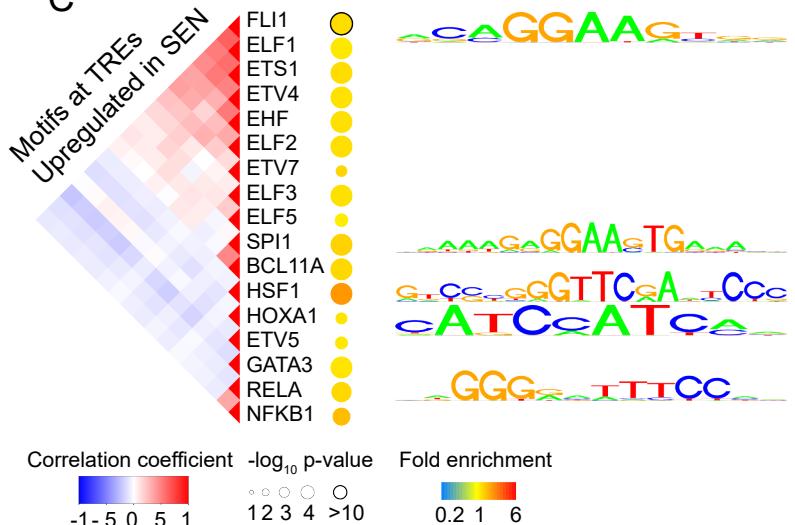
0 2 4 6 8 10
-log₁₀(p-value)

Figure 1. Chromatin accessibility is altered in senescence

A



C



B

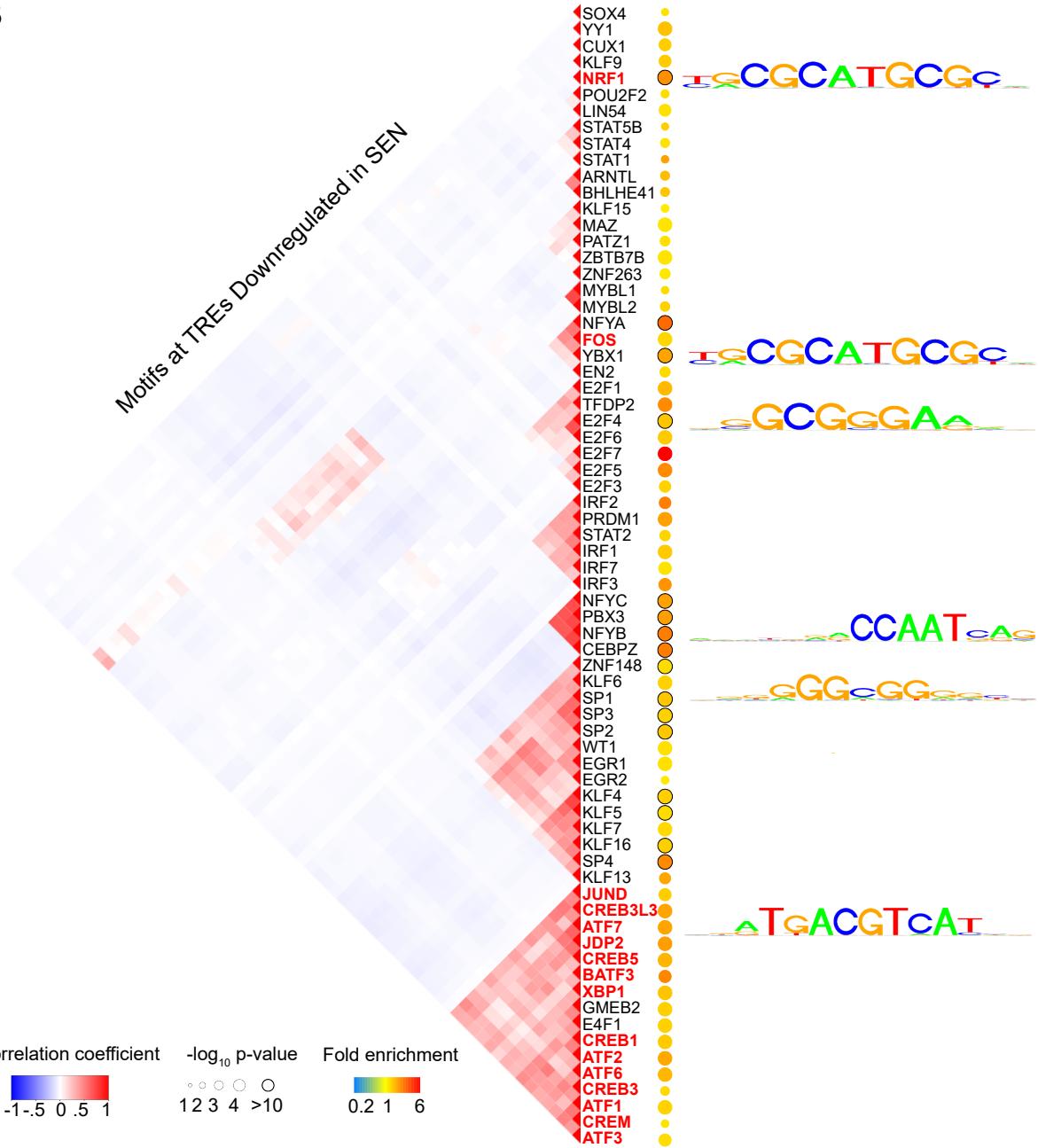


Figure 2. Nascent transcription is altered in senescence.

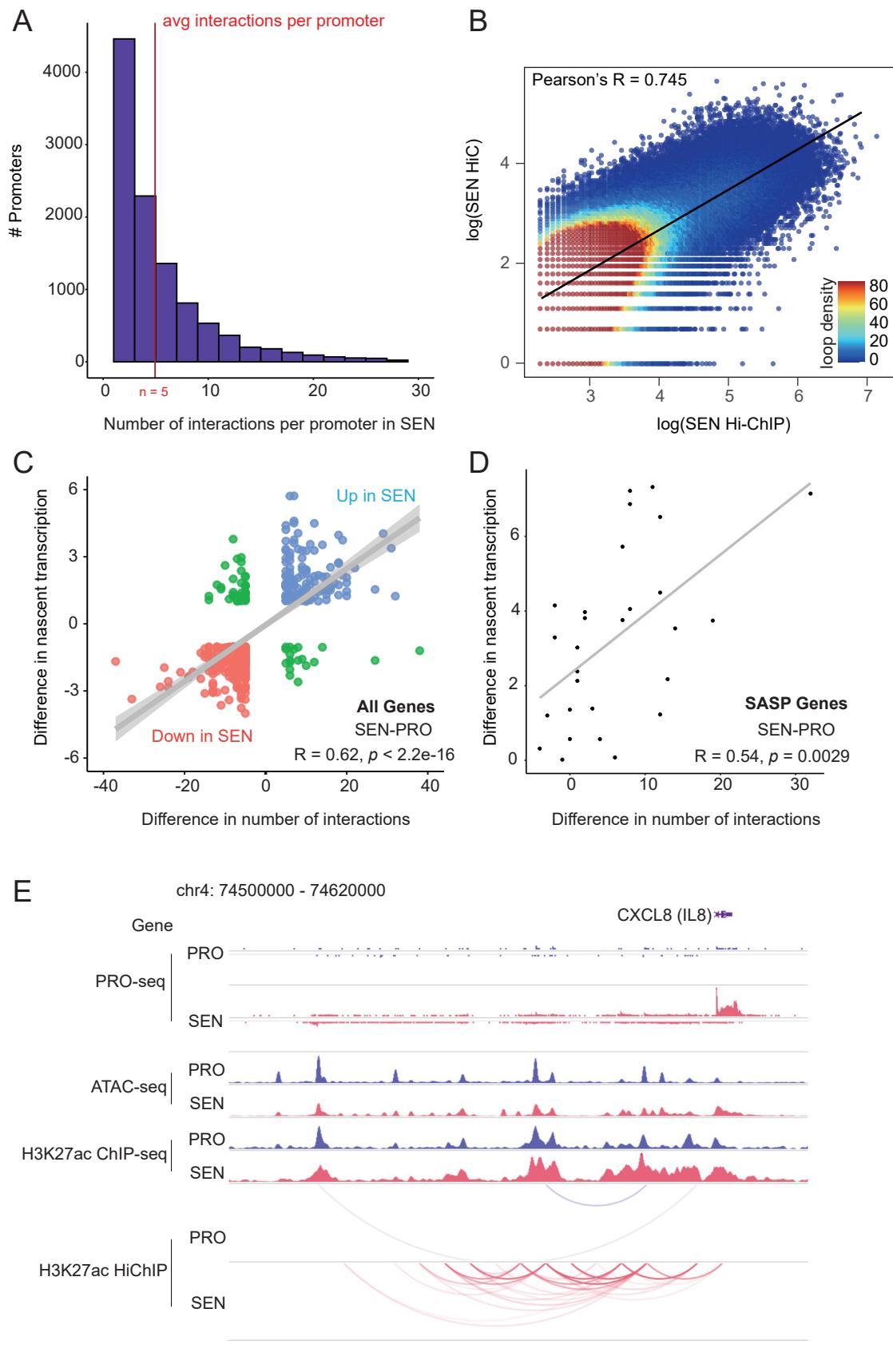


Figure 3. Multiple regulatory elements regulate gene expression.

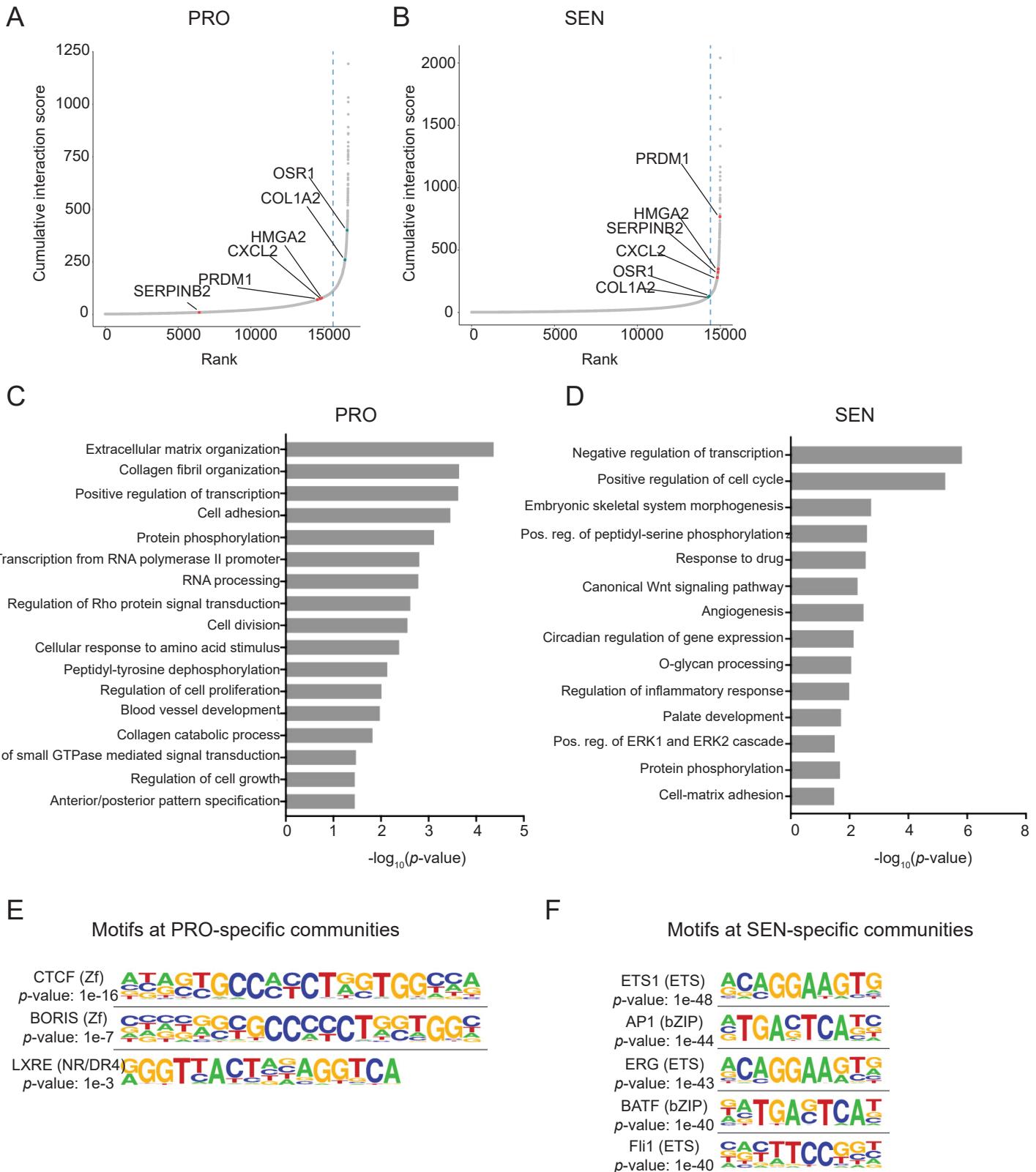


Figure 4. Hyperconnected enhancer hubs regulate state-specific genes.

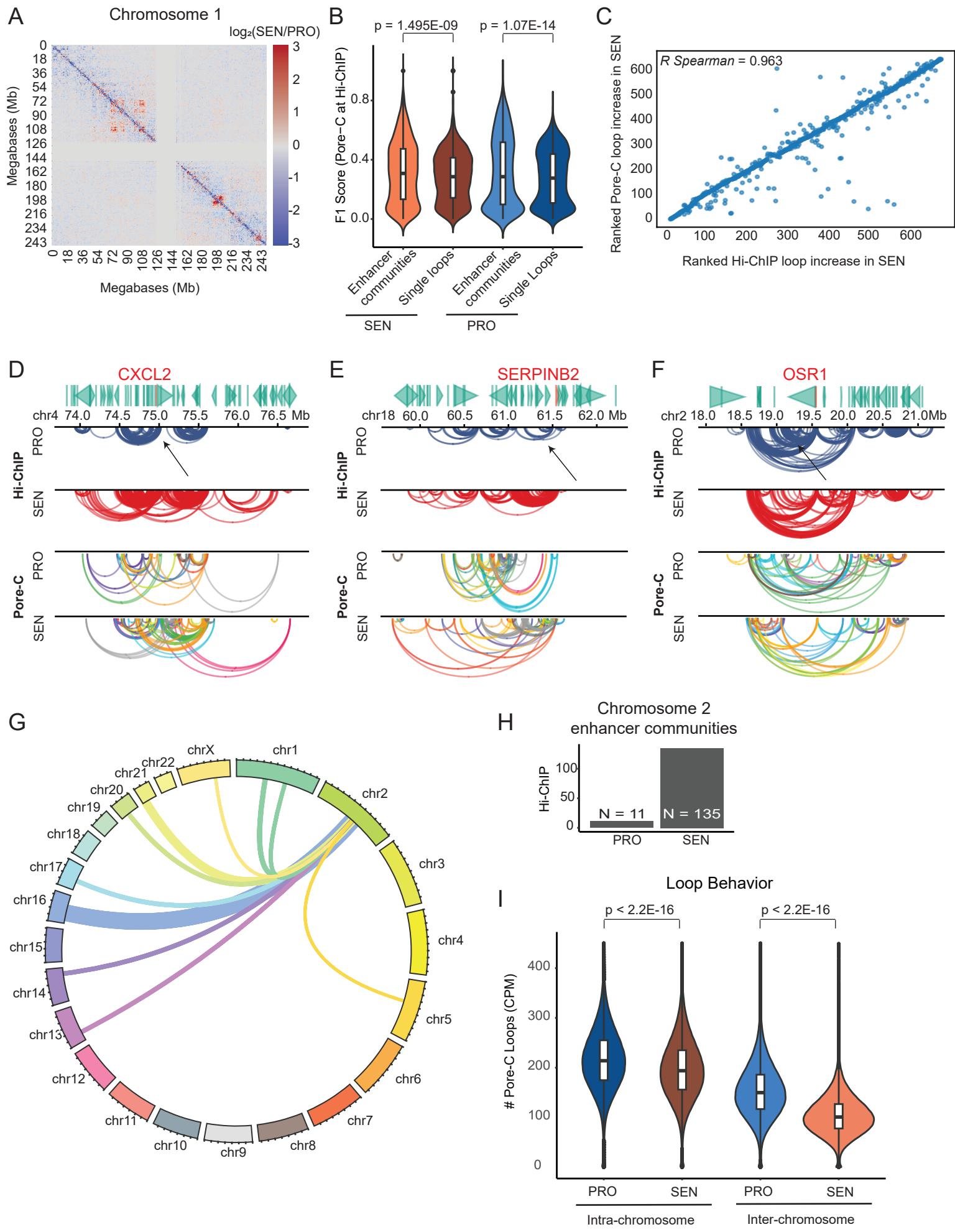


Figure 5. Pore-C captures enhancer communities in single cells

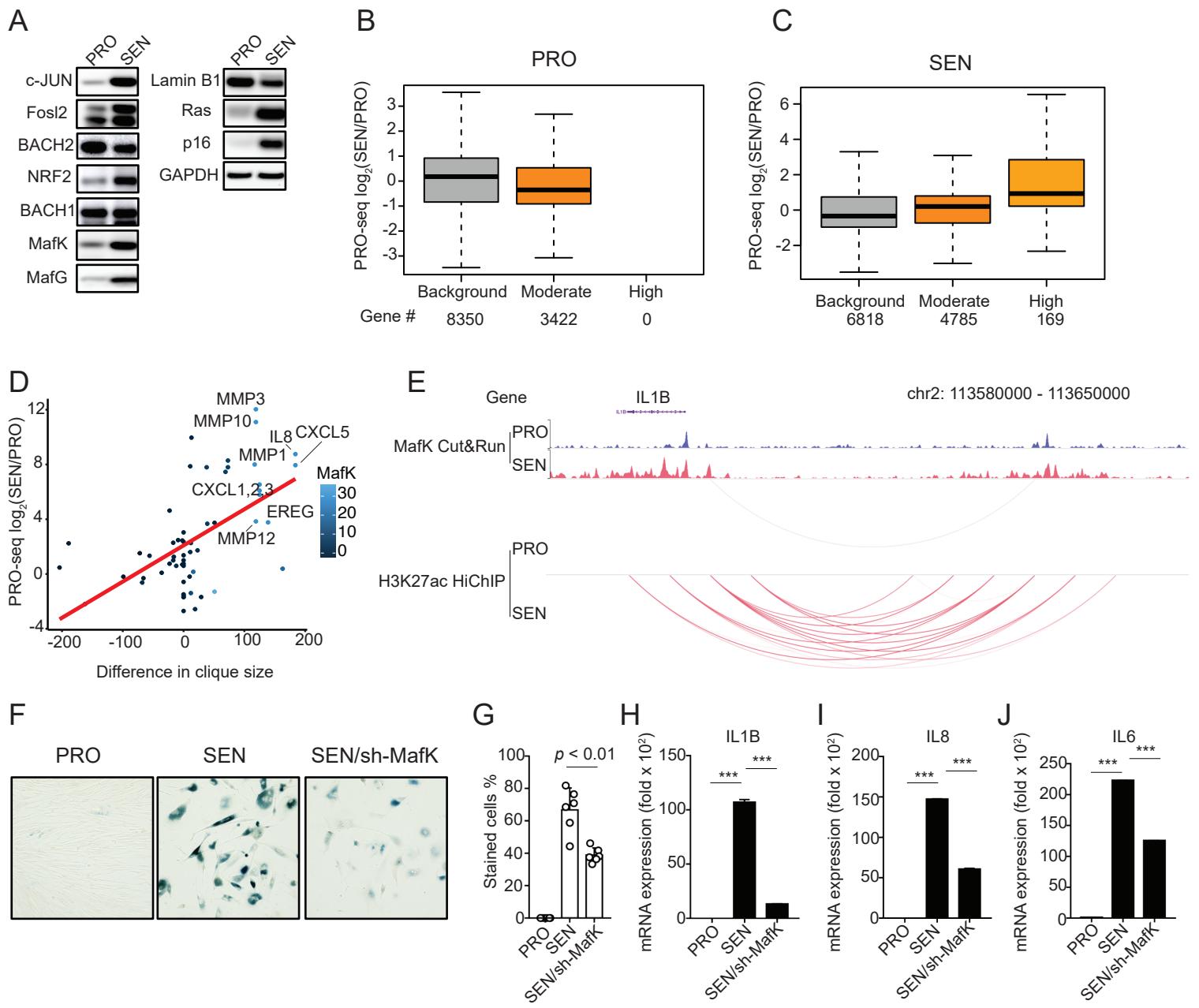


Figure 6. MafK regulates enhancer hubs and senescence.

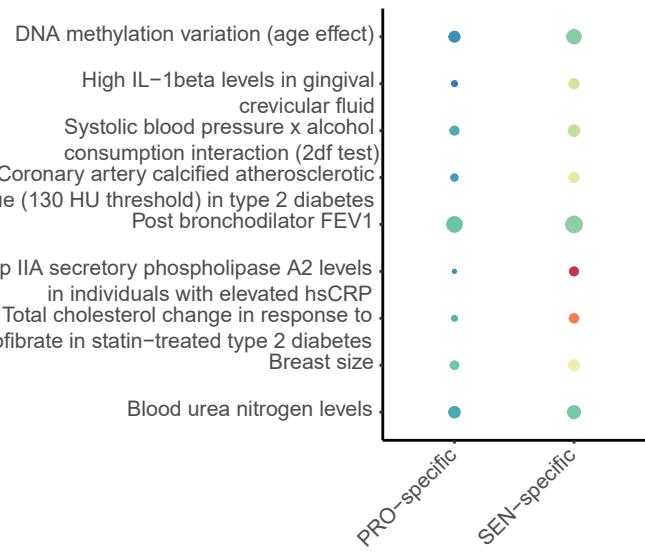
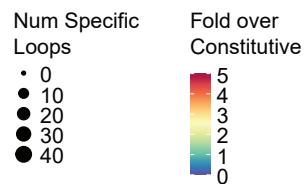
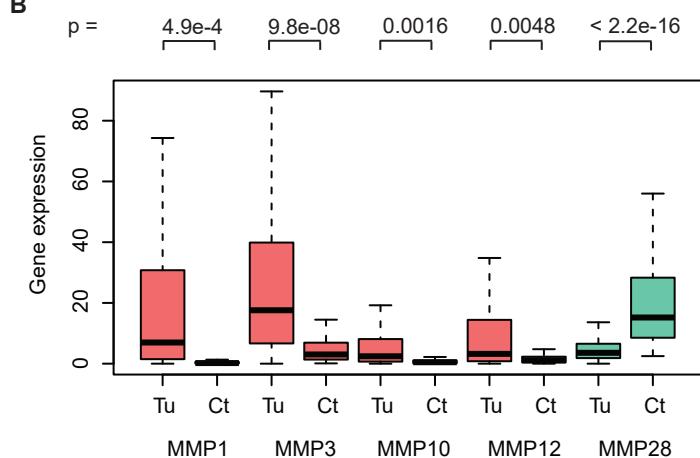
A**B**

Figure 7. Disease-associated traits in hyper-connected enhancer communities.

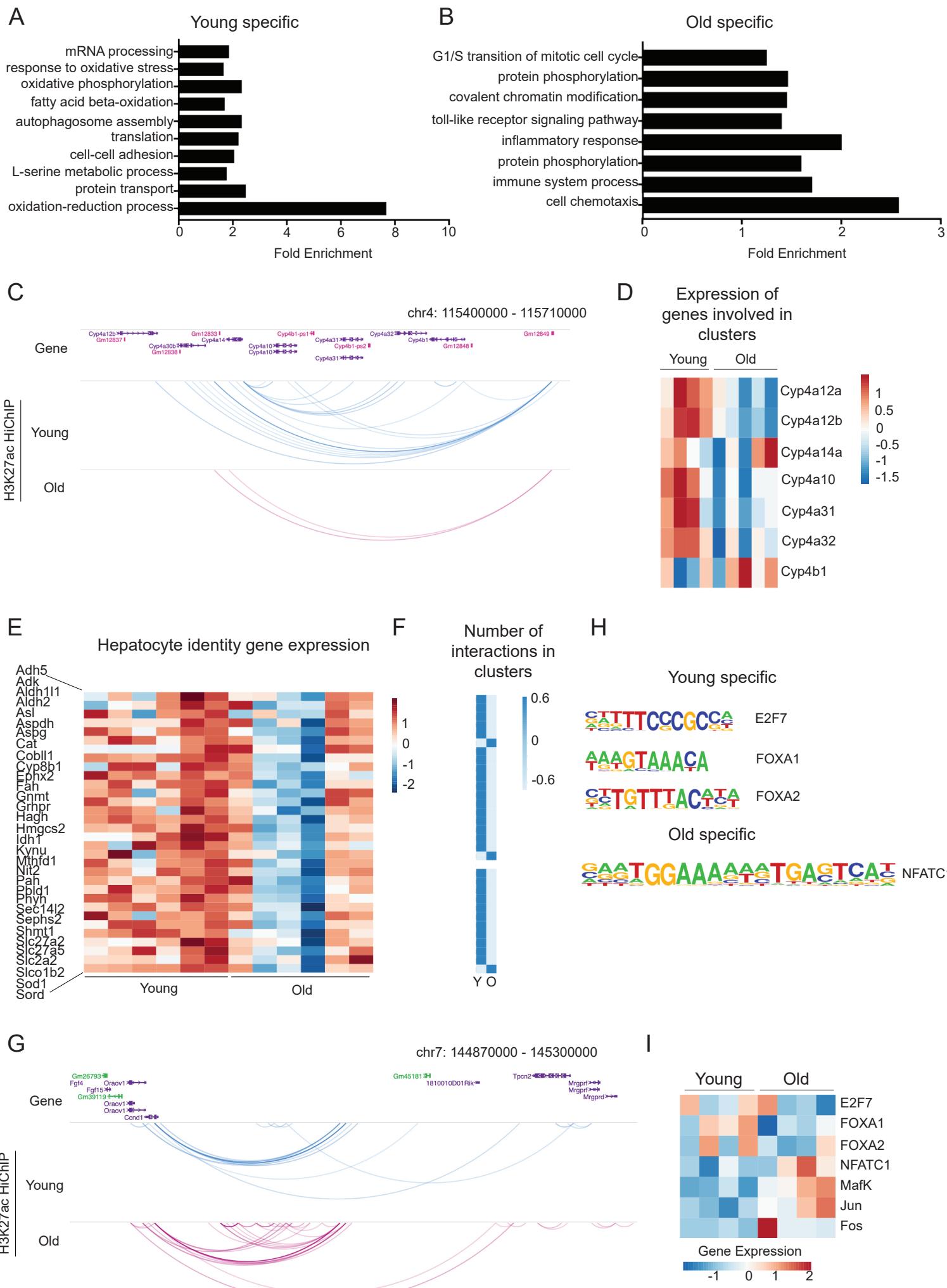


Figure 8. Enhancer hubs are dynamic during aging.