

Description of Additional Supplementary Files

Supplementary Data 1: iBAQ of biological replicates across tissues and domains, related to Supplementary Fig. 1.

Supplementary Data 2: HOIP interactions identified by differential analysis, related to Fig. 1.

Supplementary Data 3: HOIP interaction partners were enriched in biological process terms, related to Supplementary Fig. 2.

- a) Total biological process list for HOIP interactors across tissues.
- b) Manual selected biological process list related to Supplementary Fig. 2a.

Supplementary Data 4: Tissue-shared and tissue-specific HOIP PPIs, related to Fig. 2.

- a) Statistical result for tissue-specific and tissue-shared interactors across nine tissues.
- b) Total HOIP-interacting proteins list for tissue-specific and tissue-shared interactors across nine tissues.
- c) Tissue-shared HOIP interaction partners were enriched in biological process terms refer to Fig. 2c.
- d) Intra tissue-shared HOIP interaction partners curated from STRING database refer to Fig. 2c.
- e) Tissue-specific HOIP interaction partners were enriched in biological process terms refer to Fig. 2e.
- f) Intra tissue-specific HOIP interaction partners curated from STRING database refer to Fig. 2e.
- g) Enriched proteins in genetic diseases across tissues.

Supplementary Data 5: HOIP domains mediated PPIs

- a) Biological process list for all HOIP interaction partners identification of different domains, related to Supplementary Fig. 3a.
- b) Manual selected representative biological processes, related to Fig. 3a.
- c) Manual selected biological process list of domain-specific HOIP PPIs, related to Supplementary Fig. 4a.
- d) GO terms specifically enriched in manual selected tissues and domains.

Supplementary Data 6: HOIP PPIs in lungs from LPS-induced sepsis models, related to Supplementary Fig. 5.

- a) Total HOIP-interacting proteins list in lungs from LPS-induced sepsis models.
- b) Manual selected biological process list of LPS-specific HOIP PPIs, related to Supplementary Fig. 5d.
- c) Total HOIP-PUB interacting proteins list in lungs from LPS-induced sepsis models, related to Supplementary Fig. 5d.
- d) Total HOIP-NZF interacting proteins list in lungs from LPS-induced sepsis models, related to Supplementary Fig. 5d.
- e) Total HOIP-UBA interacting proteins list in lungs from LPS-induced sepsis models, related to Supplementary Fig. 5d.
- f) Total HOIP-RBR interacting proteins list in lungs from LPS-induced sepsis models, related to Supplementary Fig. 5d.

Supplementary Data 7: HOIP PPIs involved in the Kinase, TF, E3 and DUBs, related to Supplementary Fig. 3.

- a) Statistical result of HOIP PPIs involved in indicated protein classes, related to Supplementary Fig. 6a
- b) Gene list of HOIP PPIs involved in indicated protein classes
- c) The list of kinases interacting with HOIP across tissues and domains, related to Supplementary Fig. 6c

Supplementary Data 8: oligonucleotides.