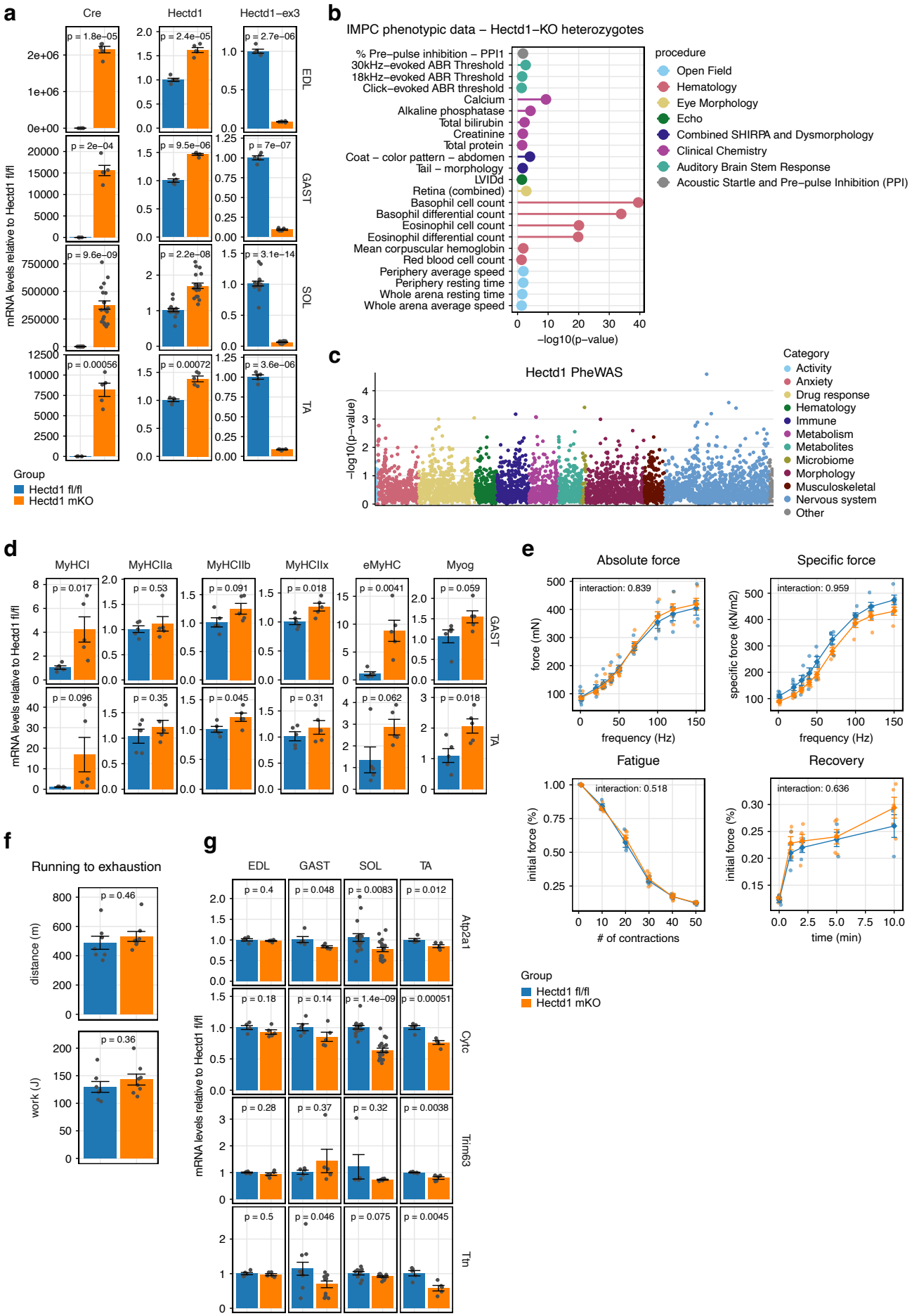
a
Cre
Hectd1
Hectd1−ex3
EDL
GAST
SOL
TA
mRNA levels relative to Hectd1 fl/fl
Group
Hectd1 fl/fl
Hectd1 mKO
b
IMPC phenotypic data – Hectd1−KO heterozygotes
% Pre−pulse inhibition − PPI1
30kHz−evoked ABR Threshold
18kHz−evoked ABR Threshold
Click−evoked ABR threshold
Calcium
Alkaline phosphatase
Total bilirubin
Creatinine
Total protein
Coat − color pattern − abdomen
Tail − morphology
LVIDd
Retina (combined)
Basophil cell count
Basophil differential count
Eosinophil cell count
Eosinophil differential count
Mean corpuscular hemoglobin
Red blood cell count
Periphery average speed
Periphery resting time
Whole arena resting time
Whole arena average speed
−log10(p−value)
procedure
Open Field
Hematology
Eye Morphology
Echo
Combined SHIRPA and Dysmorphology
Clinical Chemistry
Auditory Brain Stem Response
Acoustic Startle and Pre−pulse Inhibition (PPI)
c
Hectd1 PheWAS
−log10(p−value)
Category
Activity
Anxiety
Drug response
Hematology
Immune
Metabolism
Metabolites
Microbiome
Morphology
Musculoskeletal
Nervous system
Other
d
MyHCI
MyHCIIa
MyHCIIb
MyHCIIx
eMyHC
Myog
GAST
TA
mRNA levels relative to Hectd1 fl/fl
e
Absolute force
Specific force
Fatigue
Recovery
interaction: 0.839
interaction: 0.959
interaction: 0.518
interaction: 0.636
force (mN)
specific force (kN/m2)
frequency (Hz)
initial force (%)
# of contractions
time (min)
Group
Hectd1 fl/fl
Hectd1 mKO
f
Running to exhaustion
distance (m)
work (J)
g
EDL
GAST
SOL
TA
Atp2a1
Cytc
Trim63
Ttn
mRNA levels relative to Hectd1 fl/fl

Supplementary Fig. 4.

a, Gene expression of HSA-Cre, Hectd1 exon 22/23 and Hectd1 deleted exon 3 in different skeletal muscle beds assessed by RT-qPCR (n = 5-19). **b**, IMPC phenotypic data for whole-body Hectd1 KO heterozygous animals. **c**, Inferred possible phenotypes of Hectd1 in various tissues from phenome-wide association studies from BXD mouse population dataset. **d**, Gene expression analysis of skeletal muscle myosin heavy chain (MyHC) isoforms and Myogenin in the GAST and TA muscle of control and Hectd1 mKO mice assessed by RT-qPCR (n = 5). **e**, Ex vivo analysis of the EDL fatigue, recovery, and contractile force in control and Hectd1 mKO mice (n = 4-5). **f**, Total distance and work achieved by the 4-month-old male control and Hectd1 mKO mice during treadmill running to exhaustion protocol (n = 7-8). **g**, Expression analysis of skeletal muscle genes representative of calcium handling, bioenergetics, protein turnover and muscle structure in the EDL, GAST, SOL and TA muscle of control and Hectd1 mKO mice assessed by RT-qPCR (n = 5-19). All data are represented as mean ± SD. Data in a, d, f, g, were analyzed by Student's t-test. Data in e were analyzed by repeated measures ANOVA, interaction between either frequency, time or number of contractions and genotype is indicated on the graph. IMPC – International Mouse Phenotyping Consortium, EDL - extensor digitorum longus, GAST – gastrocnemius, SOL – soleus, TA – tibialis anterior.