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A proteomic analysis of skeletal muscle in HspB1 knock-out mouse

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BACKGROUND

Hsp27 is a member of the small heat shock proteins (sHsp, 12-43 kDa) family

There is increasing evidence to substantiate Hsp27 as biomarker in many disease states including renal injury, cancer, cardiovascular disease, and neuro-degenerative disease. Abundance of Hsp27 is the highest in skeletal muscle (Neufer et Benjamin 1996) indicating a crucial role for muscle physiology.



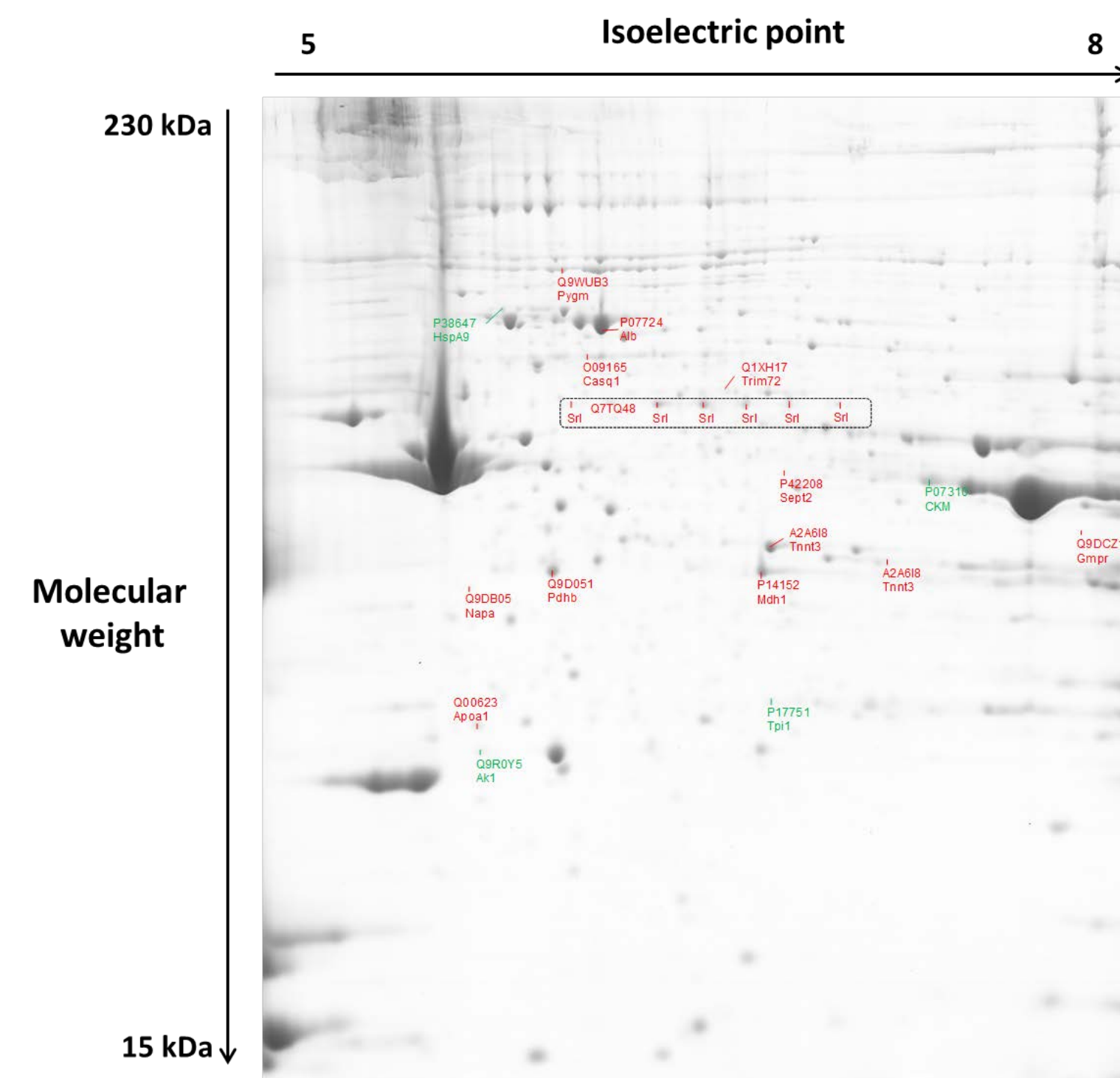
→ *HspB1-null mouse* to address the role of *Hsp27* in muscle development, physiology and structure

- viable, fertile, no apparent morphological nor anatomical alterations
- abnormalities in the myofibrillar structure and muscle ultrastructure

AIM AND STRATEGY

Comparative proteomics

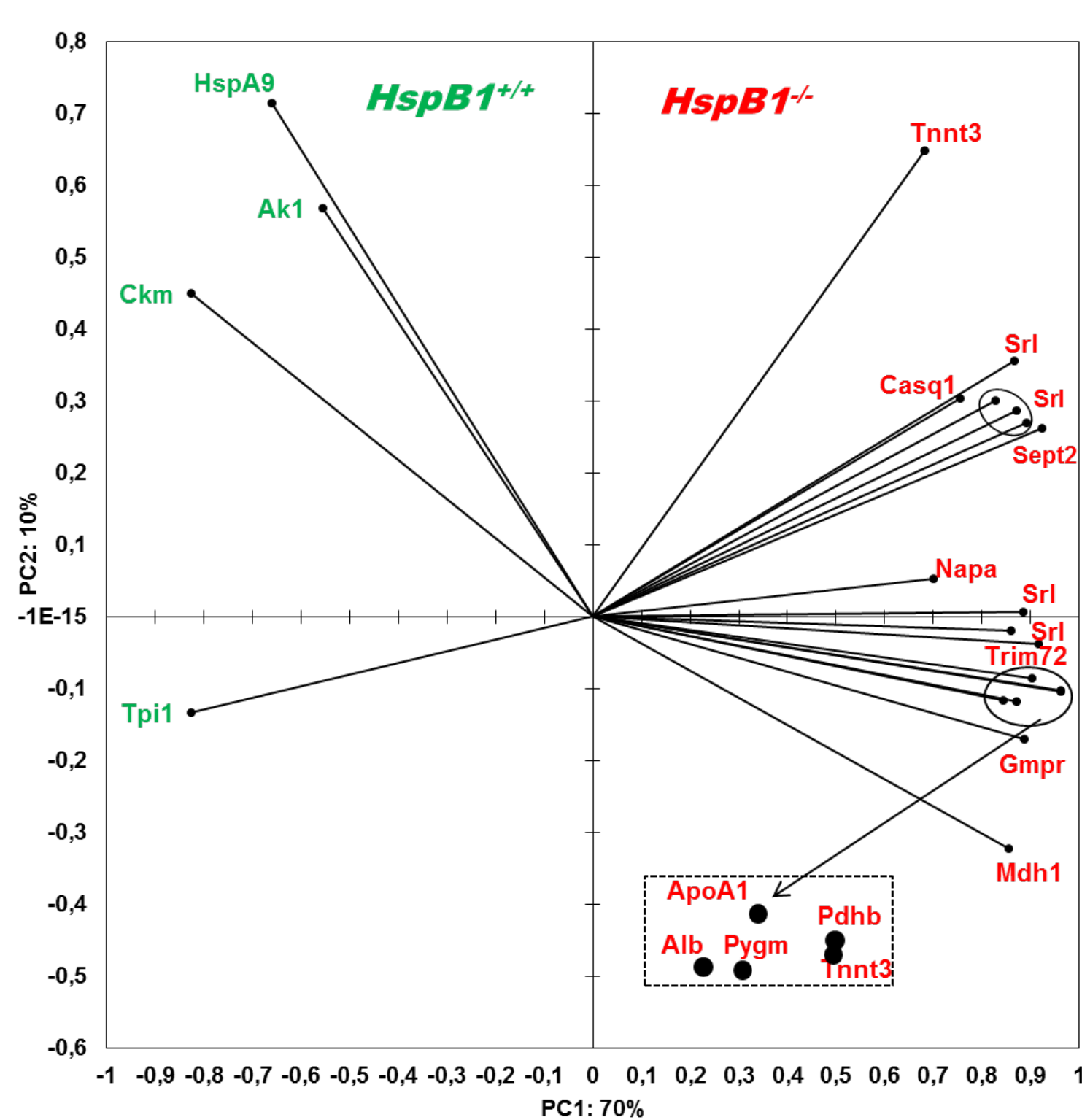
The aim was to analyse the impact of *HspB1* invalidation on the proteomic profile of the m. *Tibialis anterior*.



N=5 mice per group (Ko vs controls)
12 weeks postnatal
2DE (pH range 5-8)
Mass Spectrometry LC-MS/MS
Thermo Proteome Discoverer v1.2
Mascot analysis

464 protein spots

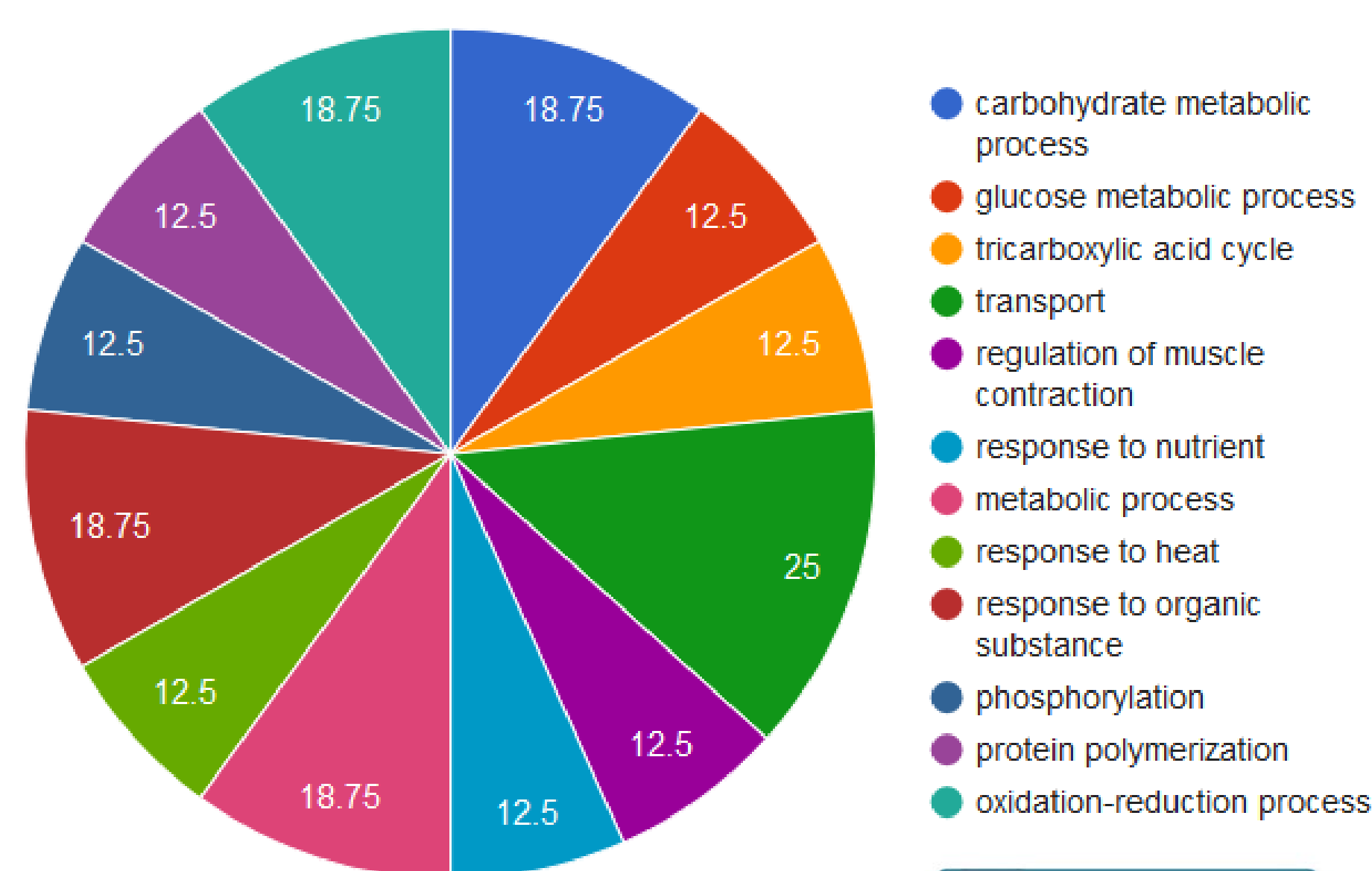
Differential proteins



35 spots with significant differences
16 proteins with different Uniprot ID
18 up- and 4 down-regulated spots
6 isoforms of sarcalumenin

Protein functions

Percentage of annotation frequency by GO on the ontology group (%)



RESULTS

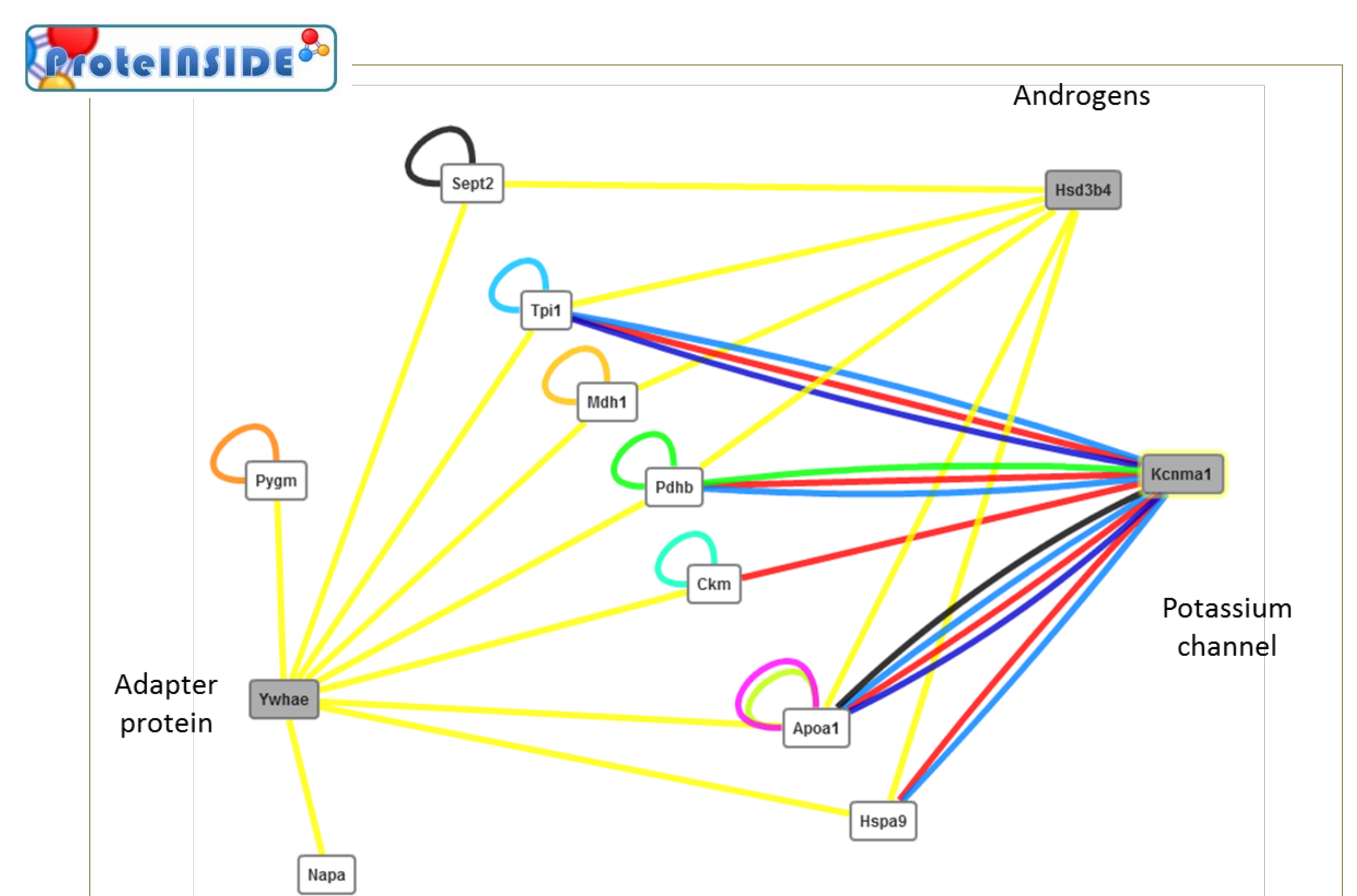
HspB1-null mouse

Validation (Western-blot)

	HspB1-null	WT	SEM	Signification
Pygm	61072	64897	4897	NS
Casq1	107586	103184	5015	NS
HspA9	20946	40914	3583	**
HspA8	233744	404037	32292	**
Park7	328440	383780	17540	*
Mdh1	93353	161232	23589	t
Srl	18690	17144	489	t
Alb	955617	975046	20705	NS
Ar	611888	1001119	75910	**

Molecular networks

603 interactions (PPI) detected outside the dataset for 415 proteins including 14 of the differential proteins



3 proteins highly connected to 9 differential proteins based on curated experimental interactions

CONCLUSION The invalidation of *HspB1* was associated to changes in proteins involved in muscle energy metabolism, calcium metabolism, apoptosis and Hsp status. The information gained by this study will be helpful to predict the side-effect consequences of Hsp27 depletion in muscle development and in cancer or inflammatory pathologies linked to sHsps.