

Supplementary File S1. Some clinical, hematological, serum biochemical and echocardiographic parameters (mean $\pm$ SEM) in dogs with different stages of CHF (ACVIM Consensus Guidelines, Keene et al., 2019).

Parameter.	Stage A (n = 8)	Stage B2 (n = 8)	Stage C (n = 8)	Stage D (n = 8)
Clinical parameters				
PR /min	119 $\pm$ 31 ^a	128 $\pm$ 23 ^{ab}	156 $\pm$ 18 ^{abc}	191 $\pm$ 72 ^{c***#}
BR /min	18 $\pm$ 10 ^a	19 $\pm$ 6 ^{b**}	68 $\pm$ 14 ^{b***}	63 $\pm$ 19 ^{b**}
Hemobiochemical parameters				
Hct %	43.8 $\pm$ 3.2 ^{ab}	48.8 $\pm$ 5.3 ^a	43.6 $\pm$ 9.2 ^{ab}	37.6 $\pm$ 7 ^{b***}
CRP μ g/mL	2,1 $\pm$ 3,2 ^a	4,3 $\pm$ 4,2 ^a	10,1 $\pm$ 4,5 ^{ab}	37,8 $\pm$ 13,9 ^{b**}
cTnI ng/mL	0.03 $\pm$ 0.04 ^a	0.03 $\pm$ 0.04 ^a	1.80 $\pm$ 1.39 ^{b*}	7.09 $\pm$ 12.2 ^{b*}
BUN mg/dL	14.1 $\pm$ 4.3 ^a	15.1 $\pm$ 6.1 ^a	22.3 $\pm$ 15.5 ^a	34.5 $\pm$ 24.2 ^a
Cr mg/dL	0.8 $\pm$ 0.2 ^a	0.8 $\pm$ 0.07 ^a	0.91 $\pm$ 0.3 ^a	1 $\pm$ 0.25 ^a
Echocardiographic parameters				
LA/Ao	1.1 $\pm$ 0.1 ^a	1.6 $\pm$ 0.1 ^b	2.2 $\pm$ 0.5 ^{b***}	2.3 $\pm$ 0.5 ^{bc***}
LVIDDn	1.5 $\pm$ 0.2 ^a	1.8 $\pm$ 0.2 ^{ab}	2.3 $\pm$ 0.3 ^{bc}	3.0 $\pm$ 0.4 ^{d***#}
FS %	32.2 $\pm$ 6.0 ^a	35.0 $\pm$ 5.2 ^a	29.5 $\pm$ 9.0 ^a	26.7 $\pm$ 14.6 ^a
MV E/A ratio	1.5 $\pm$ 0.4 ^a	2.0 $\pm$ 0.4 ^{b*}	2.2 $\pm$ 0.6 ^{b*}	3.8 $\pm$ 1.4 ^{b**}
Medication				
Pimobendan	0/8	8/8	8/8	8/8
Enalapril/Ramipril	0/8	0/8	8/8	8/8
Furosemide	0/8	0/8	8/8	4/8
Hydrochlorothiazide	0/8	0/8	0/8	8/8
Spironolactone	0/8	0/8	0/8	5/8
Torasemide	0/8	0/8	0/8	4/8
Antiarrhythmic +	0/8	0/8	0/8	4/8

* P < 0.05 ** P < 0.01 *** P < 0.001

Compared to stage B2

PR- Pulse Rate, **BR**- Breath Rate, **Hct**- Hematocrit, **CRP**- Serum C-reactive protein, **BUN**- Blood urea nitrogen, **Cr**- Creatinine, **LA/Ao**- aorta to left atrium ratio, **LVIDDn**, normalized left

ventricular internal dimension in diastole, **FS**- fractional shortening, **MV E/A** – Mitral valve E and A velocity

+ Digoxin (0.005 – 0.008 mg/kg, q12 hr, PO) and/or diltiazem (0.5-1 mg/kg, q8-12hr, PO).

Supplementary File S2. Pre- and post-treatment results of some clinical, hematological, serum biochemical and echocardiographic parameters (mean $\pm$ SEM) in dogs with CHF in stage C (ACVIM Consensus Guidelines, Keene et al., 2019).

Parameter.	Pre-treatment (n = 8)	Post-treatment ^Ψ (n = 8)
Clinical parameters		
PR /min	156 $\pm$ 18 ^{abc}	144 $\pm$ 16 ^{**}
BR /min	68 $\pm$ 14 ^{b***}	28 $\pm$ 14 ^{***}
Hemobiochemical parameters		
Hct %	43.6 $\pm$ 9.2 ^{ab}	42.6 $\pm$ 6.5
CRP μ g/mL	10,1 $\pm$ 4,5 ^{ab}	3,3 $\pm$ 2,2 ^{***}
cTnI ng/mL	1.80 $\pm$ 1.39 ^{b*}	1.10 $\pm$ 0.91
BUN mg/dL	22.3 $\pm$ 15.5 ^a	30.7 $\pm$ 26.0
Cr mg/dL	0.91 $\pm$ 0.3 ^a	0.84 $\pm$ 0.33
Echocardiographic parameters		
LA/Ao	2.2 $\pm$ 0.5 ^{b***}	1.9 $\pm$ 0.4
LVIDDn	2.3 $\pm$ 0.3 ^{bc}	2.0 $\pm$ 0.2
FS %	29.5 $\pm$ 9.0 ^a	33.4 $\pm$ 8.2
MV E/A ratio	2.2 $\pm$ 0.6 ^{b*}	1.9 $\pm$ 0.6
Medication		
Pimobendan	8/8	8/8
Enalapril/Ramipril	8/8	8/8
Furosemide	8/8	8/8
Hydrochlorothiazide	0/8	3/8 ^ε
Spironolactone	0/8	3/8 ^ε
Torsemide	0/8	0/8
Antiarrhythmic +	0/8	2/8 ^ε

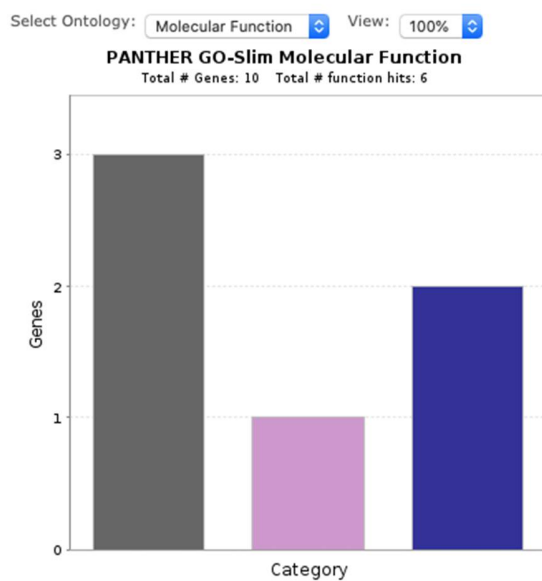
* P < 0.05 ** P < 0.01 *** P < 0.001

^Ψ compared to stage C before treatment ^ε added according to requirement of the dogs based on the cardiac observations (radiography, ECG, and echocardiography) during re-examinations, two weeks later from initial treatments.

PR- Pulse Rate, **BR**- Breath Rate, **Hct**- Hematocrit, **CRP**- Serum C-reactive protein, **BUN**- Blood urea nitrogen, **Cr**- Creatinine, **LA/Ao**- aorta to left atrium ratio, **LVIDDn**, normalized left ventricular internal dimension in diastole, **FS**- fractional shortening, **MV E/A** – Mitral valve E and A velocity

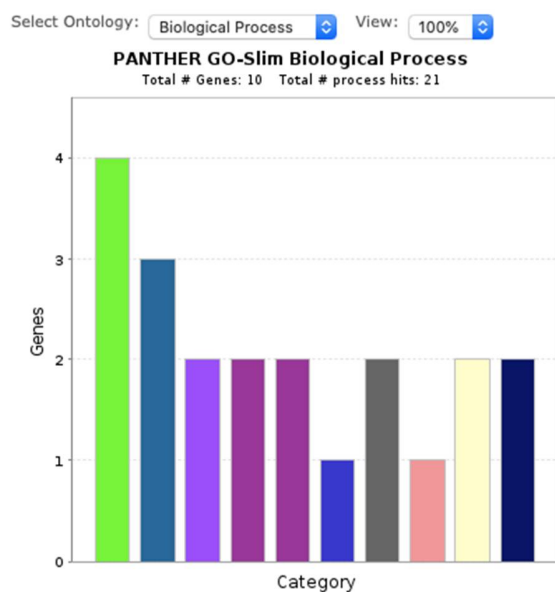
+ Digoxin (0.005 – 0.008 mg/kg, q12 hr, PO) and/or diltiazem (0.5-1 mg/kg, q8-12hr, PO).

Supplementary File S3. Molecular and biological functions, cellular component, protein class and pathway analysis of the proteins showing statistically significant fold-changes in dogs with CHF compared to those of healthy controls.



Click to get gene list for a category:

- [binding \(GO:0005488\)](#)
- [catalytic activity \(GO:0003824\)](#)
- [molecular function regulator \(GO:0098772\)](#)



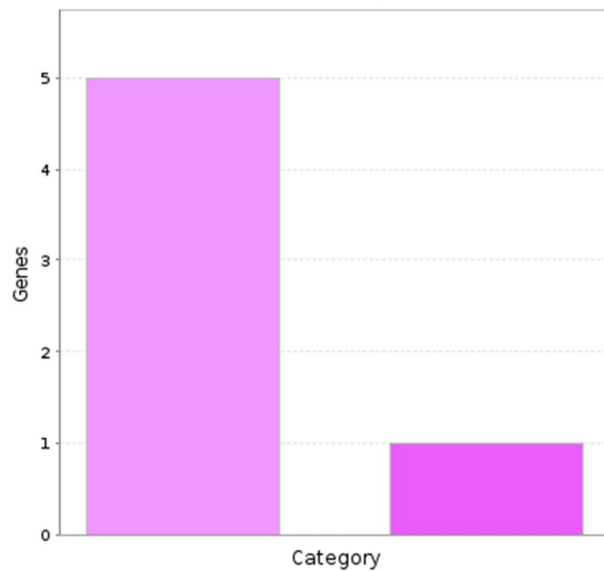
Click to get gene list for a category:

- [biological regulation \(GO:0065007\)](#)
- [cellular process \(GO:0009987\)](#)
- [immune system process \(GO:0002376\)](#)
- [interspecies interaction between organisms \(GO:0044419\)](#)
- [localization \(GO:0051179\)](#)
- [locomotion \(GO:0040011\)](#)
- [metabolic process \(GO:0008152\)](#)
- [multicellular organismal process \(GO:0032501\)](#)
- [response to stimulus \(GO:0050896\)](#)
- [signaling \(GO:0023052\)](#)

Select Ontology: Cellular Component View: 100%

PANTHER GO-Slim Cellular Component

Total # Genes: 10 Total # component hits: 6



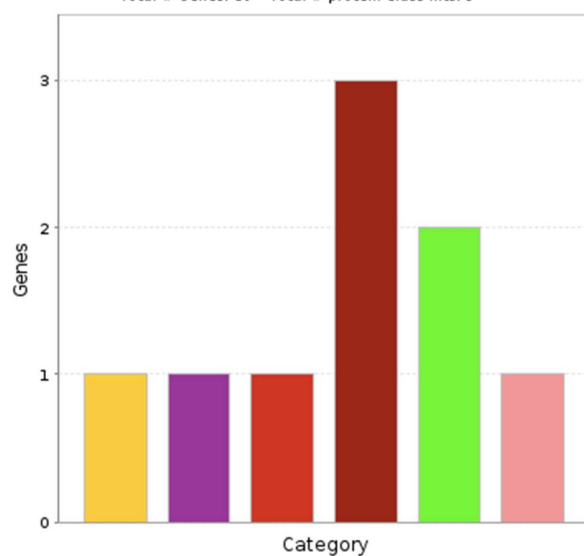
Click to get gene list for a category:

- [cellular anatomical entity \(GO:0110165\)](#)
- [intracellular \(GO:0005622\)](#)

Select Ontology: Protein Class View: 100%

PANTHER Protein Class

Total # Genes: 10 Total # protein class hits: 9



Click to get gene list for a category:

- [cytoskeletal protein \(PC00085\)](#)
- [intercellular signal molecule \(PC00207\)](#)
- [metabolite interconversion enzyme \(PC00262\)](#)
- [protein-binding activity modulator \(PC00095\)](#)
- [transfer/carrier protein \(PC00219\)](#)
- [transmembrane signal receptor \(PC00197\)](#)