

### Supplementary Material

**Table S1:** Gene variants of preclinical carriers and HOCM patients including mutation type, sex and age of the individuals.

Gene	Mutation	Type, class	Age	Sex
<b>Preclinical Carriers</b>				
MYH7	c.1727A>G p.His576Arg	missense, class 4	34	F
MYH7	c.1207C>T p.Arg403Trp	missense, class 5	35	F
MYH7	c.1816G>A p.Val606Met	missense, class 4/5	30	M
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	58	F
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	36	F
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	21	M
MYH7	c.1207C>T p.Arg403Trp	missense, class 5	21	F
MYH7	c.1207C>T p.Arg403Trp	missense, class 5	65	F
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	44	F
MYH7	c.5135G>A p.Arg1712Gln	missense, class 4	45	F
MYH7	c.5135G>A p.Arg1712Gln	missense, class 4	33	M
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	18	F
MYH7	c.4130C>T p.Thr1377Met	missense, class 4	31	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	60	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	28	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	30	F

MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	22	M
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	34	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	60	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	24	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	56	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	26	M
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	43	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	31	F
MYBPC3	c.897delG p.Lys301fs	frameshift, class 4/5	41	F
TNNT2	c.304C>T p.Arg102Trp	missense, class 5	59	F
TNNT2	c.304C>T p.Arg102Trp	missense, class 5	58	F
TNNT2	c.856C>T p.Arg286Cys	missense	48	F
TNNT2	c.430C>T p.Arg144Trp	missense, class 4/5	40	F
TNNT2	c.853C>T p.Arg285Cys	missense	32	M
TNNI3	c.497C>T p.Ser166Phe	missense, class 4/5	22	M
<b>HOCM patients</b>				
MYH7	p.Gln895His	missense	66	M
MYBPC3			54	F
MYBPC3	c.2373dup p.Trp792ValfsX41	frameshift, class 5	18	M
MYBPC3	c.2827C>T p.Arg943*	frameshift, class 5	54	F
TNNT2	c.853C>T	missense	43	M

	p.Arg285Cys			
<i>TNNT2</i>	c.304C>T p.Arg102Trp	missense, class 5	27	M
<i>TNNT2</i>	c.856C>T p.Arg286Cys	missense	53	M
<i>TNNT2</i>	c.835C>T p.Gln279*	truncation, class 4/5	54	M
<i>MYL2</i>	c.401A>C p.Glu134Ala	missense, class 3/4	57	F
Sarcomere mutation negative			64	M
Sarcomere mutation negative			52	M
Sarcomere mutation negative			68	F
Sarcomere mutation negative			46	M
Sarcomere mutation negative			47	M

**Table S2:** Metabolite identifications and functional classes of the top 30 metabolites of all three group-wise comparisons<sup>1</sup>.

Metabolite	Possible identifications	Functional class	p value MEE	padj_BH MEE	p value MVO <sub>2</sub>	padj_BH MVO <sub>2</sub>
Metabolite 1	19-Hydroxyandrost-4-ene-3,17-dione; 19-Oxotestosterone; 7a-Hydroxyandrost-4-ene-3,17-dione; 11b-Hydroxyandrost-4-ene-3,17-dione; 16a-Hydroxyandrost-4-ene-3,17-dione; 4-Methoxy-17beta-estradiol; 2-Hydroxyestradiol-3-methyl ether	Lipids and lipid-like molecules				
Metabolite 2	p-Ethylacetophenone; Anethole	Benzenoids				
Metabolite 3	Ceramide (d18:1/18:0); Cer(d18:0/18:1(11Z)); Cer(d18:0/18:1(9Z)); N-Stearoylsphingosine	Lipids and lipid-like molecules	<b>0.0203</b>	0.9617		
Metabolite 4	Alanyl-Glutamine; Alanyl-Gamma-glutamate; Glutaminyl-Alanine; Gamma-glutamyl-Alanine; N-a-Acetylcitrulline	Organic acids and derivatives	<b>0.0226</b>	0.9617	<b>0.0039</b>	0.2924
Metabolite 5	11-peroxy-5Z,8Z,12E,14Z-eicosatetraenoate; 9-peroxy-5Z,7E,11Z,14Z-eicosatetraenoate	Lipids and lipid-like molecules			<b>0.0010</b>	0.2875
Metabolite 6	5-HEPE; Leukotriene A4; 12-HEPE; 14,15-EpETE; 15-HEPE; 15-KETE; 17,18-EpETE; 5-KETE; 11R-HEPE; 18R-HEPE; 9-HEPE	Lipids and lipid-like molecules			<b>0.0010</b>	0.2875

Metabolite 7	Prostaglandin E3; Prostaglandin D3; 15-Keto-prostaglandin E2; Resolvin E1; 12-Oxo-20-hydroxy-leukotriene B4; 15-Epi-lipoxin B5; 15-Oxo-lipoxin A4; 20-oxo-leukotriene B4; PGH3; 5,12,18R-TriHEPE; 8-iso-15-keto-PGE2	Lipids and lipid-like molecules
Metabolite 8	4-Hydroxy-5-(3',5'-dihydroxyphenyl)-valeric acid-O-methyl-O-glucuronide; 4-Hydroxy-5-(3',4'-dihydroxyphenyl)-valeric acid-O-methyl-O-glucuronide	Organic oxygen compounds
Metabolite 9	Tryptophyl-Serine; Serinyl-Tryptophan	Organic acids and derivatives
Metabolite 10	O-6-deoxy-a-L-galactopyranosyl-(1->2)-O-b-D-galactopyranosyl-(1->4)-2-(acetylamino)-1,5-anhydro-2-deoxy-D-arabino-Hex-1-enitol; O-6-deoxy-a-L-galactopyranosyl-(1->2)-O-b-D-galactopyranosyl-(1->3)-2-(acetylamino)-1,5-anhydro-2-deoxy-D-arabino-Hex-1-enitol	Organic oxygen compounds
Metabolite 11	Alanyl-Leucine; Isoleucyl-Alanine; Leucyl-Alanine; Alanyl-Isoleucine	Organic acids and derivatives
Metabolite 12	Tyrosyl-Glutamate; Glutamyl-Tyrosine	Organic acids and derivatives
Metabolite 13	Glutamyl-Alanine; Alanyl-Glutamate	Organic acids and derivatives
Metabolite 14	sn-glycero-3-Phosphoethanolamine; Glycerylphosphorylethanolamine	Lipids and lipid-like molecules

Metabolite 15	S-Acetyldihydrolipoamide; S-Acetyldihydrolipoamide-E	Lipids and lipid-like molecules		
Metabolite 16	Medroxyprogesterone; 17-HDoHE; 19(20)-EpDPE; 16(17)-EpDPE; 10-HDoHE; 11-HDoHE; 16-HDoHE; 20-HDoHE; 4-HDoHE; 7-HDoHE; 8-HDoHE; 4-Hydroxy-all-trans-retinyl acetate	Lipids and lipid-like molecules	0.0009	0.2875
Metabolite 17	Aspartyl-Glutamate; Glutamyl-Aspartate	Organic acids and derivatives		
Metabolite 18	MG(0:0/20:3(5Z,8Z,11Z)/0:0); MG(0:0/20:3(8Z,11Z,14Z)/0:0); MG(20:3(11Z,14Z,17Z)/0:0/0:0); MG(20:3(5Z,8Z,11Z)/0:0/0:0); MG(20:3(8Z,11Z,14Z)/0:0/0:0); MG(0:0/20:3(11Z,14Z,17Z)/0:0)	Lipids and lipid-like molecules	0.0012	0.9617
Metabolite 19	Hydroxypropyl-Valine; Valyl-Hydroxyproline	Organic acids and derivatives		
Metabolite 20	Asparaginyl-Tryptophan; Histidiny-Tyrosine; Tryptophyl-Asparagine; Tyrosyl-Histidine	Organic acids and derivatives		
Metabolite 21	Asymmetric dimethylarginine; Symmetric dimethylarginine	Organic acids and derivatives	0.0045	0.2924
Metabolite 22	Estriol; 2-Hydroxyestradiol; 16b-Hydroxyestradiol; 17-Epiestriol; 16,17-Epiestriol; 4-Hydroxyestradiol; 2-Polyprenyl-	Lipids and lipid-like molecules	0.0014	0.2875

3-methyl-6-methoxy-1,4-benzoquinone; 4-hydroxystradiol

Metabolite 23	Alpha-CEHC; Monoethylhexyl phthalic acid	Organoheterocyclic compounds	<b>&lt;0.0001</b>	0.1720
Metabolite 24	Asparaginy-Lysine; Lysyl-Asparagine	Organic acids and derivatives		
Metabolite 25	Tetracosahexaenoic acid; Tetracosahexaenoic acid, n-3	Lipids and lipid-like molecules	<b>0.0043</b>	0.2924
Metabolite 26	3'-Hydroxy-e,e-caroten-3-one; 3-Hydroxy-b,e-caroten-3'-one	Lipids and lipid-like molecules	<b>0.0076</b>	0.3950
Metabolite 27	15-Keto-13,14-dihydroprostaglandin A2; Prostaglandin J2; Prostaglandin A2; 12-Keto-leukotriene B4; Prostaglandin B2; Delta-12-Prostaglandin J2; Leukotriene B5; 5-Oxo-6-trans-leukotriene B4; 7'-Carboxy-gamma-chromanol; 15d PGD2; bicyclo-PGE2; Prostaglandin-c2	Lipids and lipid-like molecules	<b>0.0190</b>	0.5463
Metabolite 28	DG(16:0/15:0/0:0); DG(15:0/0:0/16:0); DG(15:0/16:0/0:0)	Lipids and lipid-like molecules		
Metabolite 29	Lysyl-Glutamine; Lysyl-Gamma-glutamate; Gamma-glutamyl-Lysine; Glutaminy-Lysine	Organic acids and derivatives	<b>0.0107</b>	0.9617
Metabolite 30	DG(15:0/14:0/0:0); DG(14:0/0:0/15:0); DG(14:0/15:0/0:0)	Lipids and lipid-like molecules	<b>0.0117</b>	0.4829

Metabolite 31	Cysteinyl-Leucine; Isoleucyl-Cysteine; Leucyl-Cysteine; Cysteinyl-Isoleucine	Organic acids and derivatives		
Metabolite 32	Tyrosyl-Glutamine; Tyrosyl-Gamma-glutamate; gln-tyr; Glutaminyl-Tyrosine	Organic acids and derivatives		
Metabolite 33	N-Acetyl-a-neuraminic acid; N-Acetylneuraminic acid	Organic oxygen compounds		
Metabolite 34	MG(20:5(5Z,8Z,11Z,14Z,17Z)/0:0/0:0); 9'-Carboxy-gamma-chromanol; MG(0:0/20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	Lipids and lipid-like molecules	<b>0.0110</b>	0.9617
Metabolite 35	5-(3',4',5'-trihydroxyphenyl)-gamma-valerolactone-O-methyl-5'-O-glucuronide; 5-(3',4',5'-trihydroxyphenyl)-gamma-valerolactone-O-methyl-4'-O-glucuronide	Organic oxygen compounds	<b>0.0200</b>	0.9617
Metabolite 36	Tyrosyl-Cysteine; Cysteinyl-Tyrosine	Organic acids and derivatives		
Metabolite 37	5-Hydroxyindoleacetaldehyde; Indoleacetic acid			
Metabolite 38	Histidiny-Threonine; Threoninyl-Histidine; 2-(3-Carboxy-3-aminopropyl)-L-histidine	Organic acids and derivatives		
Metabolite 39	DG(14:1(9Z)/20:0/0:0); DG(16:0/18:1(11Z)/0:0); DG(16:0/18:1(9Z)/0:0); DG(16:1(9Z)/18:0/0:0); DG(18:0/16:1(9Z)/0:0); DG(18:1(11Z)/16:0/0:0); DG(18:1(9Z)/16:0/0:0); DG(20:0/14:1(9Z)/0:0); DG(20:1(11Z)/14:0/0:0); DG(14:0/0:0/20:1n9);	Lipids and lipid-like molecules		

	DG(16:0/0:0/18:1n7); DG(16:0/0:0/18:1n9); DG(18:0/0:0/16:1n7); DG(20:0/0:0/14:1n5); DG(14:0/20:1(11Z)/0:0)			
Metabolite 40	Chenodeoxycholic acid 3-sulfate; Ursodeoxycholic acid 3-sulfate; Chenodeoxycholic acid sulfate	Lipids and lipid-like molecules		
Metabolite 41	MG(0:0/18:3(6Z,9Z,12Z)/0:0); MG(0:0/18:3(9Z,12Z,15Z)/0:0); MG(18:3(6Z,9Z,12Z)/0:0/0:0); MG(18:3(9Z,12Z,15Z)/0:0/0:0)	Lipids and lipid-like molecules	<b>0.0012</b>	0.9617
1,3,5-Trimethoxybenzene		Benzenoids		
2-Pyrrolidinone		Organoheterocyclic compounds		
3-Polyprenyl-4,5-dihydroxybenzoate		Benzenoids	<b>0.0042</b>	0.2924
3,4-Methylenesebacic acid		Lipids and lipid-like molecules		
5-(methylthio)-2,3-Dioxopentyl phosphate		Organic acids and derivatives	<b>0.0013</b>	0.9617
5b-Cyprinol sulfate		Lipids and lipid-like molecules		
6-Carboxy-5,6,7,8-tetrahydropterin		Organoheterocyclic compounds		

6-Dimethylaminopurine	Organoheterocyclic compounds		
7-Hydroxy-6-methyl-8-ribityl lumazine	Organoheterocyclic compounds		
7a,12a-Dihydroxy-3-oxo-4-cholenoic acid	Lipids and lipid-like molecules	0.0003	0.1957
8-[(Aminomethyl)sulfanyl]-6-sulfanyloctanoic acid	Lipids and lipid-like molecules		
9'-Carboxy-gamma-tocotrienol	Lipids and lipid-like molecules	0.0486	0.6320
11beta,20-Dihydroxy-3-oxopregn-4-en-21-oic acid	Lipids and lipid-like molecules	0.0086	0.4078
13'-Hydroxy-alpha-tocotrienol	Lipids and lipid-like molecules		
19,20-DiHDPA	Lipids and lipid-like molecules		
Cinnavalinate	Organoheterocyclic compounds		
Cytidine 2',3'-cyclic phosphate	Organic acids and derivatives		

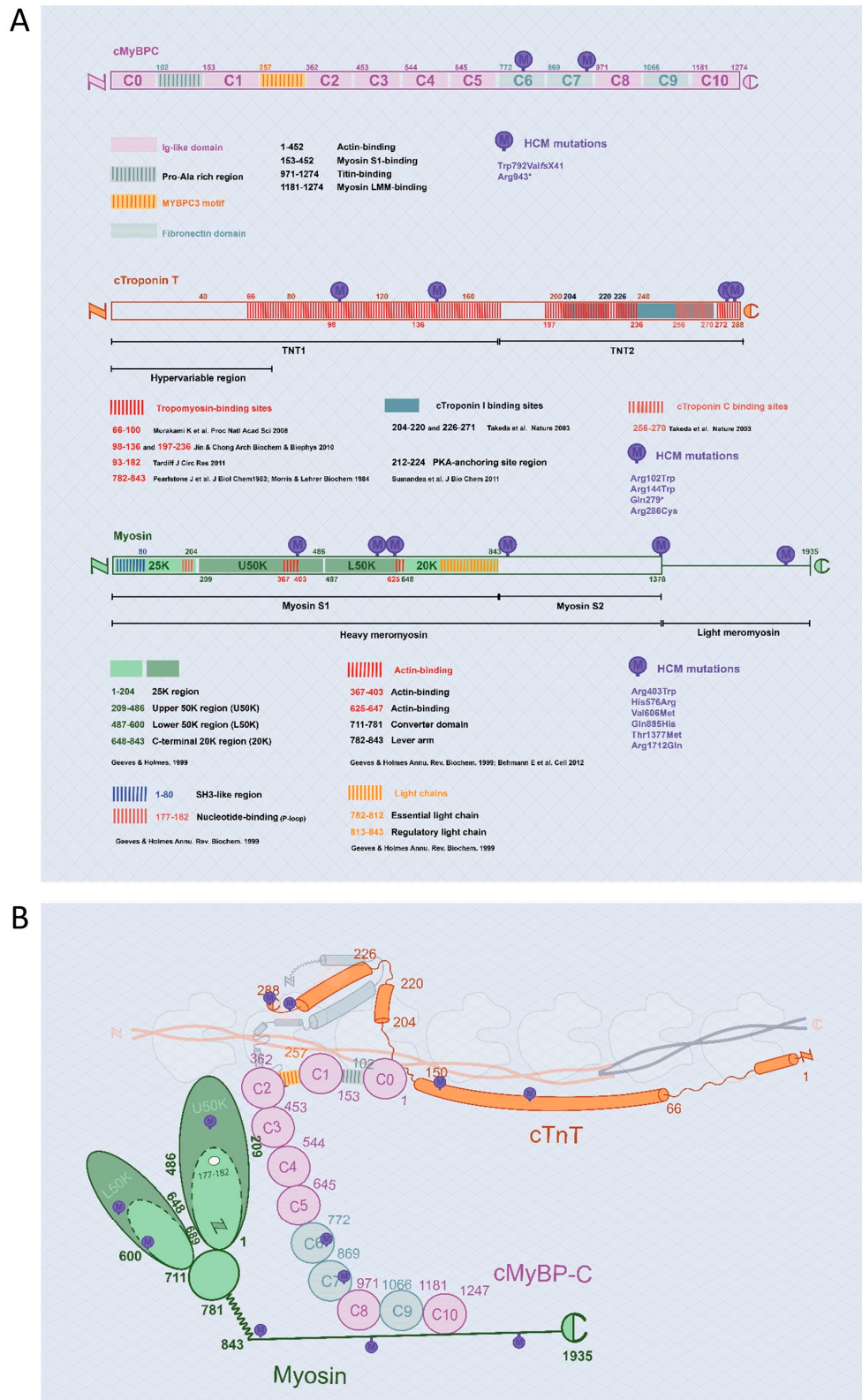
dADP	Nucleosides, nucleotides and analogues	0.0459	0.9617
Dimethyl sulfone	Organosulfur compounds		
Dityrosine	Organic acids and derivatives	0.0208	0.9617
Epinephrine glucuronide	Organic oxygen compounds		
Equol	Phenylpropanoids and polyketides		
Gamma Glutamylglutamic acid	Organic acids and derivatives	0.0447	0.9617
Glutarylcarntine	Lipids and lipid-like molecules		
Glycineamideribotide	Nucleosides, nucleotides and analogues		
Heptyl ketone	Organic oxygen compounds		
Indoleacetyl glutamine	Organic acids and derivatives	0.0469	0.6225
Mesoporphyrin IX	Organoheterocyclic compounds		
N- Acetylaspartylglutamic acid	Organic acids and derivatives	0.0251	0.5533

N-Acetylhistamine	Organic acids and derivatives				
Palmitoyl glucuronide	Lipids and lipid-like molecules			<b>0.0239</b>	0.5533
<b>Pentadecanoylglycine</b>	Organic acids and derivatives			<b>0.0197</b>	0.5463
Pentaporphyrin I	Organoheterocyclic compounds	<b>0.0379</b>	0.9617		
Perillic acid	Lipids and lipid-like molecules				
Phosphocreatinine	Organic acids and derivatives				
Ribose-1-arsenate	Organic oxygen compounds				
<b>SAICAR</b>	Nucleosides, nucleotides and analogues	<b>0.0126</b>	0.9617		
Stearic acid	Lipids and lipid-like molecules				
Stigmastanol	Lipids and lipid-like molecules				
Tetracosanoic acid	Lipids and lipid-like molecules	<b>0.0119</b>	0.9617	<b>0.0318</b>	0.5549
Vanilloylglycine	Benzenoids	<b>0.0386</b>	0.9617		

<sup>1</sup>Metabolites in bold are significant in 2 comparisons. P value is given for metabolites that correlate significantly with myocardial external efficiency (MEE) or myocardial oxygen consumption (MVO<sub>2</sub>), together with the adjusted p value for multiple testing.

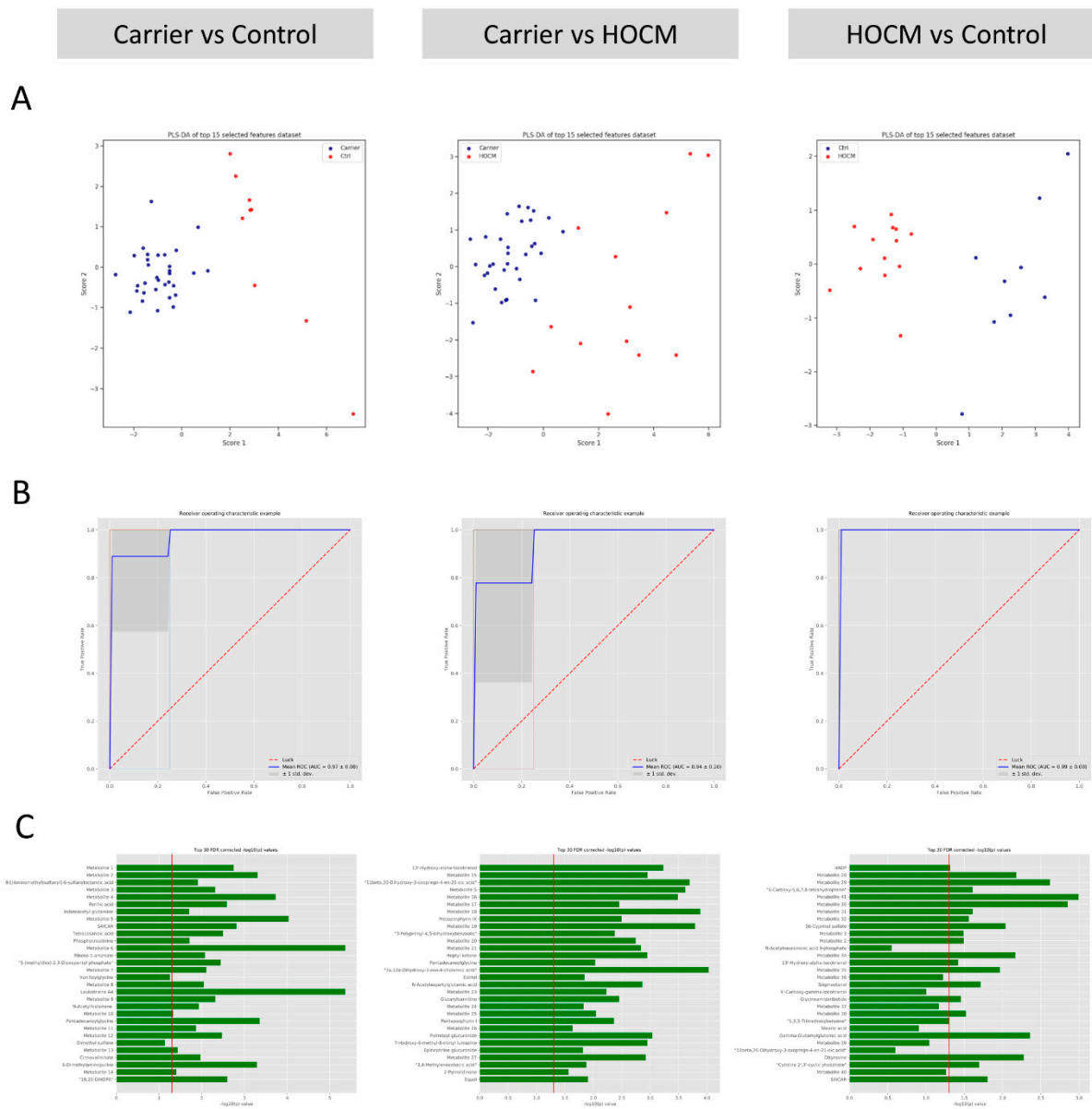
**Table S3:** Metabolite-Protein links identified with MetaBridge.

Carrier vs Ctrl	Carrier vs HOCM	HOCM vs Ctrl
LTA4H	DDAH1	ALDH9A1
LYPLA1		ALDH3A2
		ALDH7A1
		GART



**Figure S1:** Overview of gene variants in this study. (A) shows the protein domains in which the gene variants are located. Image with permission granted by Vasco Sequeira. (B) indicates the location of the gene variants in the structural context. Image adapted from Sequeira et al. Circ Res 2013 with permission Circ Res.

Figure S2

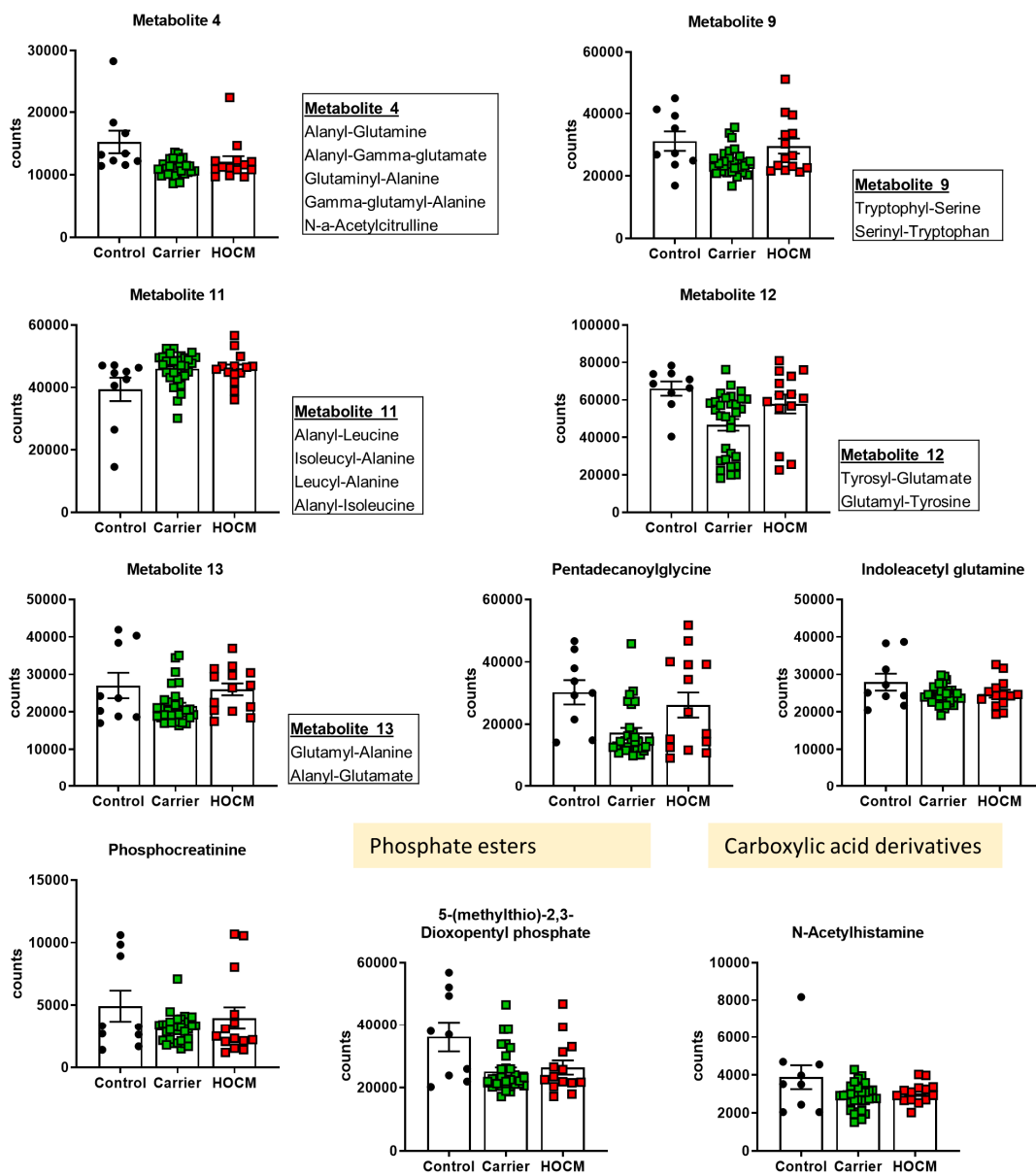


**Figure S2:** Multivariate modelling. (A) Partial least square-discriminant analysis plots (PLS-DA) for the three group-wise comparisons Carrier vs Ctrl, Carrier vs HOCM and HOCM vs Ctrl. (B) ROC curves of the three group-wise comparisons presenting the performance of the metabolomics data in distinguishing the groups. (C) Top 30 most predictive metabolites with corresponding  $-\log_{10}(p)$ -values.

## Carrier vs Ctrl

### Organic acids and derivatives

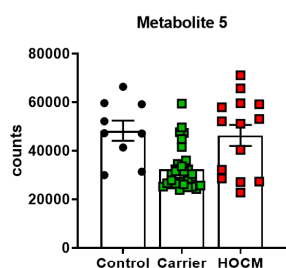
#### Amino acids, peptides and analogues



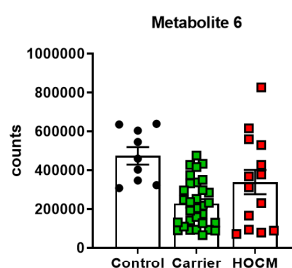
## Carrier vs Ctrl

### Lipids and lipid-like molecules

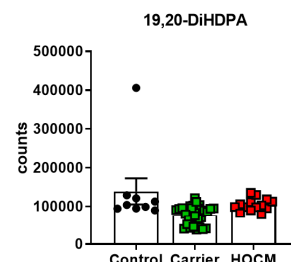
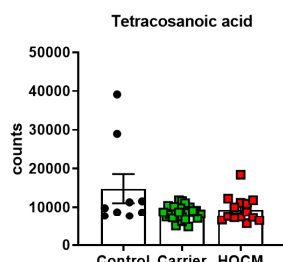
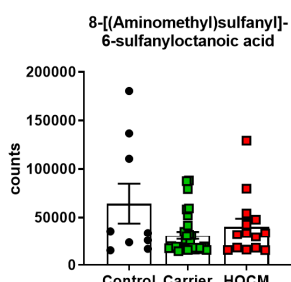
#### Fatty acids and conjugates



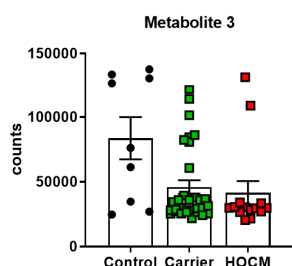
**Metabolite 5**  
11-peroxy-5Z,8Z,12E,14Z-eicosatetraenoate  
9-peroxy-5Z,7E,11Z,14Z-eicosatetraenoate



**Metabolite 6**  
5-HEPE  
Leukotriene A4  
12-HEPE  
14,15-EpETE  
15-HEPE  
15-KETE  
17,18-EpETE  
5-KETE  
11R-HEPE  
18R-HEPE  
9-HEPE

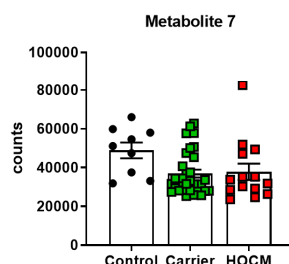


#### Ceramides



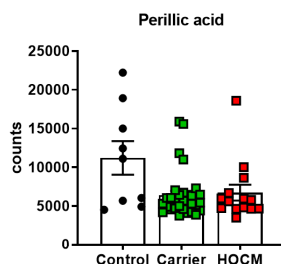
**Metabolite 3**  
Ceramide (d18:1/18:0)  
Cer(d18:0/18:1(11Z))  
Cer(d18:0/18:1(9Z))  
N-Stearyl sphingosine

#### Eicosanoids

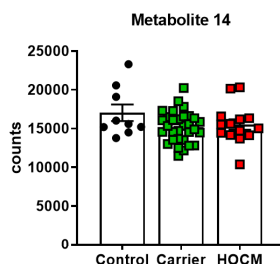


**Metabolite 7**  
Prostaglandin E3  
Prostaglandin D3  
15-Keto-prostaglandin E2  
Resolvin E1  
12-Oxo-20-hydroxy-leukotriene B4  
15-Epi-lipoxin B5  
15-Oxo-lipoxin A4  
20-oxo-leukotriene B4  
PGH3  
5,12,18R-TriHEPE  
8-iso-15-keto-PGE2

#### Monoterpenoids

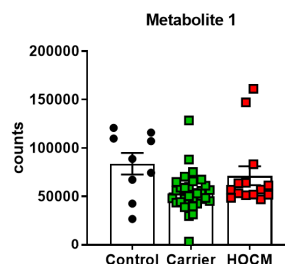


#### Glycerophosphoethanolamines

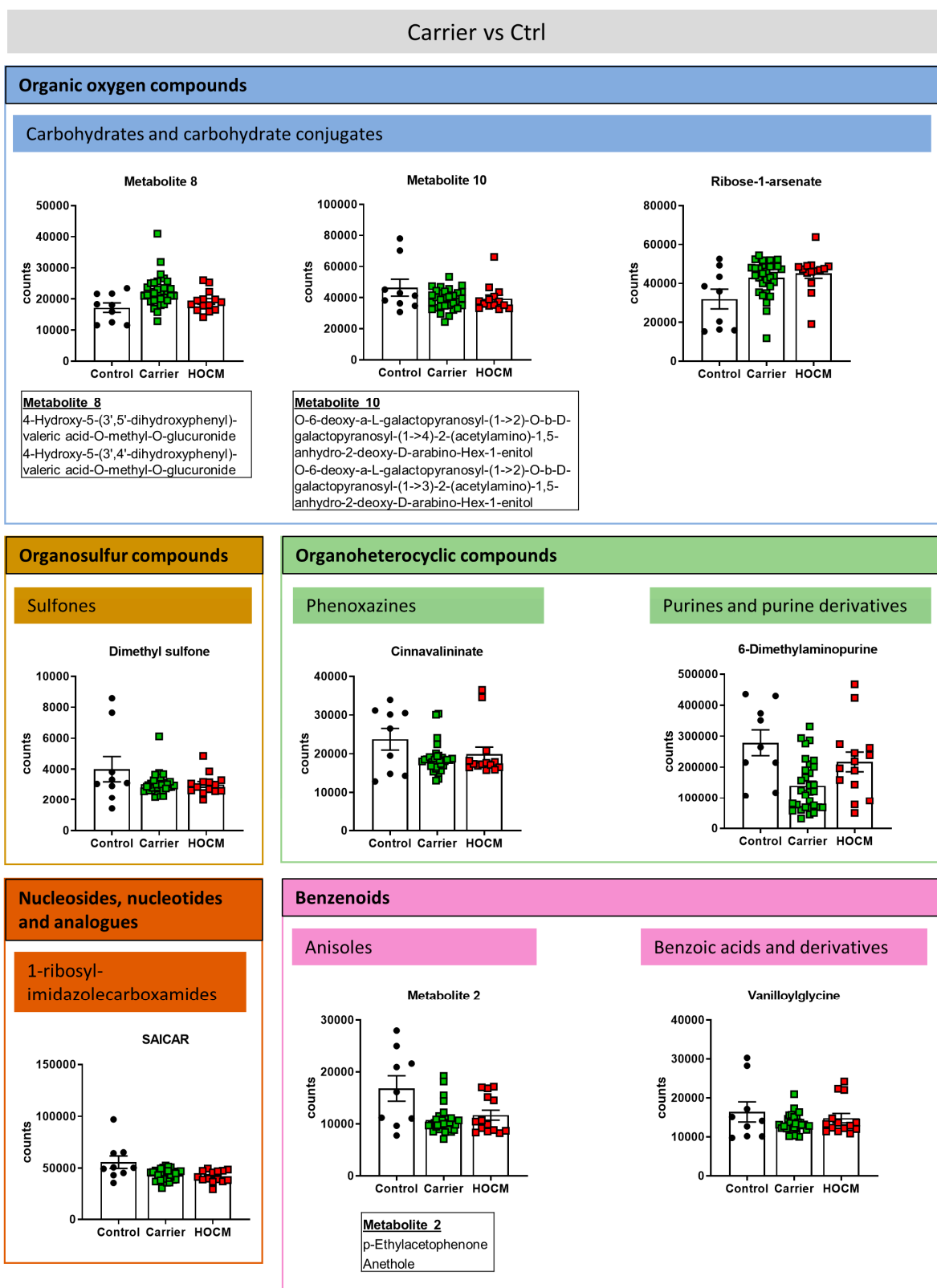


**Metabolite 14**  
sn-glycero-3-Phosphoethanolamine  
Glycerolphosphorylethanolamine

#### Androstane steroids



**Metabolite 1**  
19-Hydroxyandrost-4-ene-3,17-dione  
19-Oxotestosterone  
7a-Hydroxyandrost-4-ene-3,17-dione  
11b-Hydroxyandrost-4-ene-3,17-dione  
16a-Hydroxyandrost-4-ene-3,17-dione  
4-Methoxy-17beta-estradiol  
2-Hydroxyestradiol-3-methyl ether

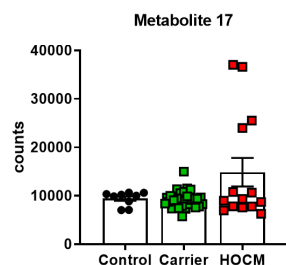


**Figure S3:** Bar graphs with individual data points of the top 30 most important metabolites in distinguishing the Carrier vs Ctrl group. Data from the third group is included in all graphs.

## Carrier vs HOCM

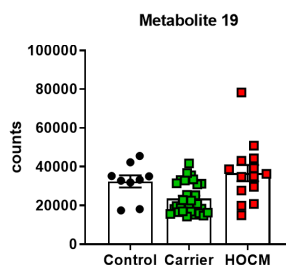
### Organic acids and derivatives

#### Amino acids, peptides and analogues



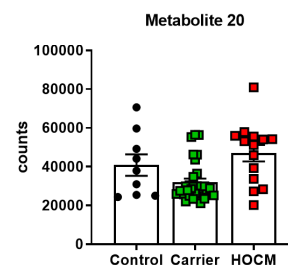
**Metabolite 17**

Aspartyl-Glutamate  
Glutamyl-Aspartate



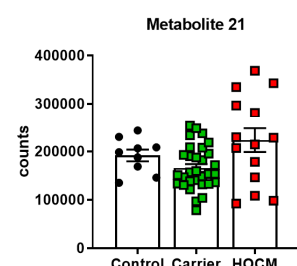
**Metabolite 19**

Hydroxyprolyl-Valine  
Valyl-Hydroxyproline



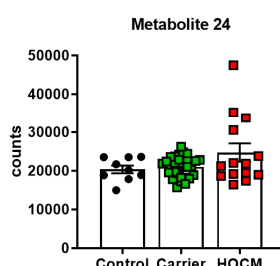
**Metabolite 20**

Asparaginy-Tryptophan  
Histidinyl-Tyrosine  
Tryptophyl-Asparagine  
Tyrosyl-Histidine



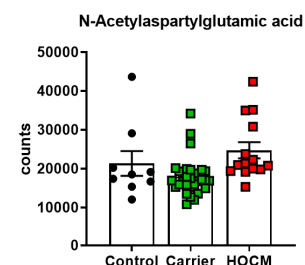
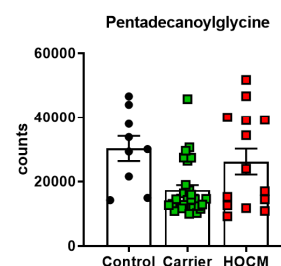
**Metabolite 21**

Asymmetric dimethylarginine  
Symmetric dimethylarginine



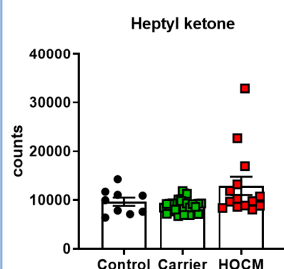
**Metabolite 24**

Asparaginy-Lysine  
Lysyl-Asparagine

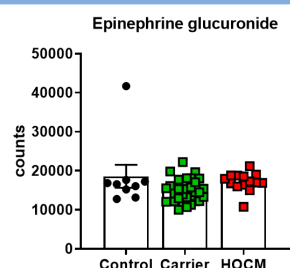


### Organic oxygen compounds

#### Carbonyl compounds

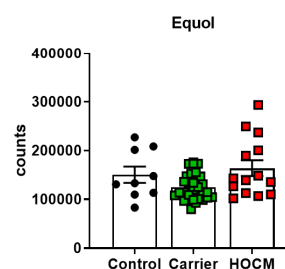


#### Carbohydrates and carbohydrate conjugates



### Phenylpropanoids and polyketides

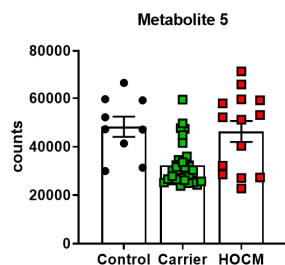
#### Isoflavans



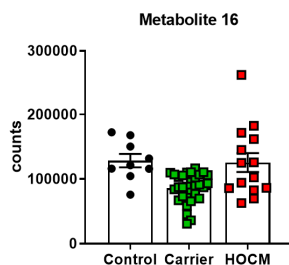
## Carrier vs HOCM

### Lipids and lipid-like molecules

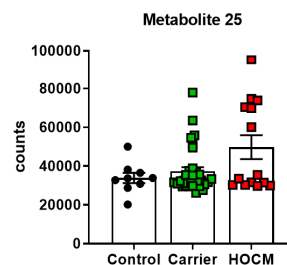
#### Fatty acids and conjugates



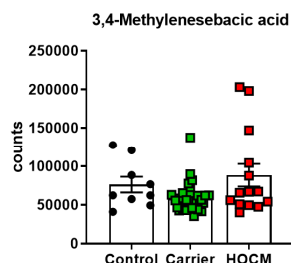
**Metabolite 5**  
11-peroxy-5Z,8Z,12E,14Z-eicosatetraenoate  
9-peroxy-5Z,7E,11Z,14Z-eicosatetraenoate



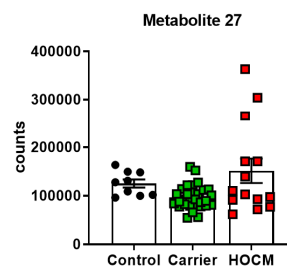
**Metabolite 16**  
Medroxyprogesterone  
17-HDoHE  
19(20)-EpDPE  
16(17)-EpDPE  
10-HDoHE  
11-HDoHE  
16-HDoHE  
20-HDoHE  
4-HDoHE  
7-HDoHE  
8-HDoHE  
4-Hydroxy-all-trans-retinyl acetate



**Metabolite 25**  
Tetracosahexaenoic acid  
Tetracosahexaenoic acid, n-3

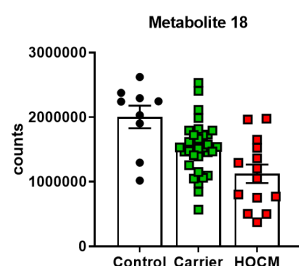


#### Eicosanoids

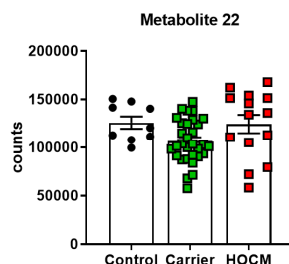


**Metabolite 27**  
15-Keto-13,14-dihydroprostaglandin A2  
Prostaglandin J2  
Prostaglandin A2  
12-Keto-leukotriene B4  
Prostaglandin B2  
Delta-12-Prostaglandin J2  
Leukotriene B5  
5-Oxo-6-trans-leukotriene B4  
7'-Carboxy-gamma-chromanol  
15d PGD2  
bicyclo-PGE2  
Prostaglandin-c2

#### Linoleic acids and derivatives

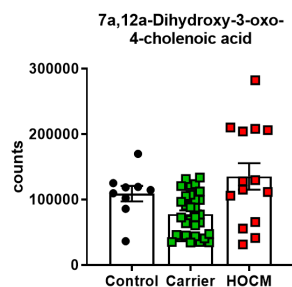


**Metabolite 18**  
MG(0:0/18:3(6Z,9Z,12Z)/0:0)  
MG(0:0/18:3(9Z,12Z,15Z)/0:0)  
MG(18:3(6Z,9Z,12Z)/0:0/0:0)  
MG(18:3(9Z,12Z,15Z)/0:0/0:0)

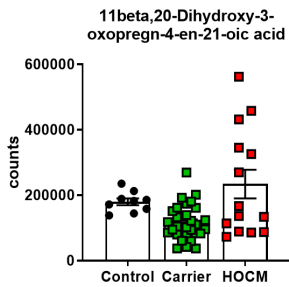


**Metabolite 22**  
Estriol  
2-Hydroxyestradiol  
16b-Hydroxyestradiol  
17-Epiestril  
16,17-Epiestril  
4-Hydroxyestradiol  
2-Polyprenyl-3-methyl-6-methoxy-1,4-benzoquinone  
4-hydroxystradiol

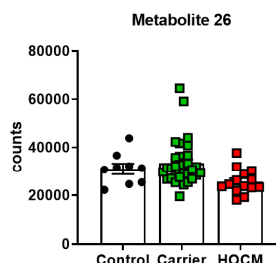
#### Cholestane steroids



#### Oxosteroids



#### Tetraterpenoids

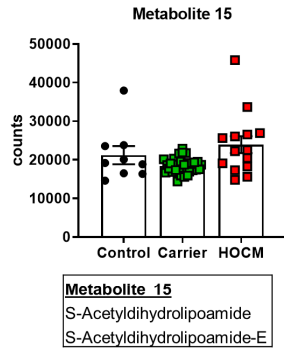


**Metabolite 26**  
3'-Hydroxy-e,e-caroten-3-one  
3-Hydroxy-b,e-caroten-3'-one

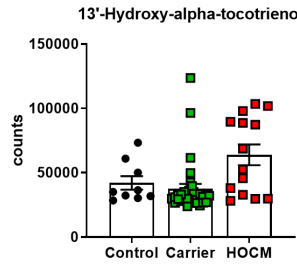
## Carrier vs HOCM

### Lipids and lipid-like molecules

#### Fatty amides

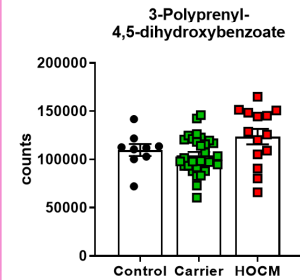


#### Quinone and hydroquinone lipids

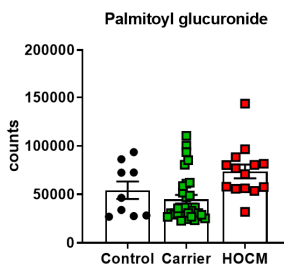


### Benzenoids

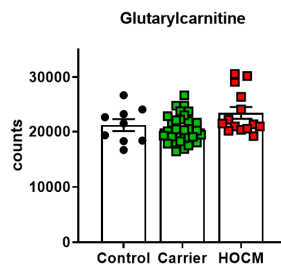
#### Benzoic acids and derivatives



#### Fatty acyl glycosides

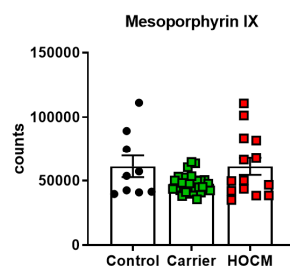
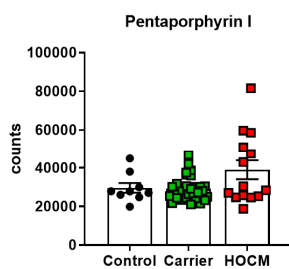


#### Fatty acid esters

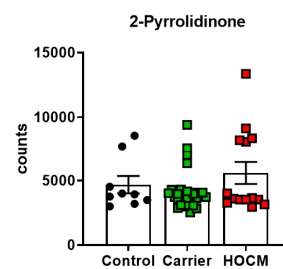


### Organoheterocyclic compounds

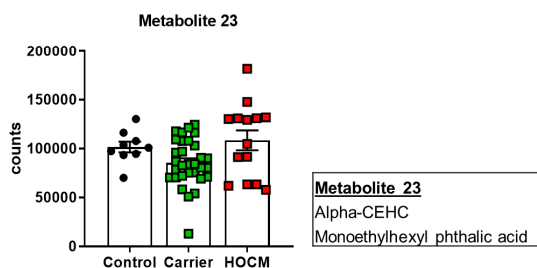
#### Porphyrins



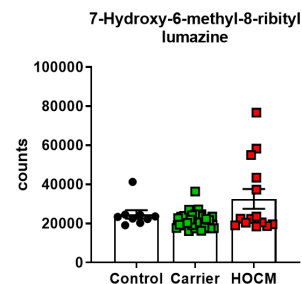
#### Pyrrolidones



#### 1-benzopyrans



#### Pteridines and derivatives

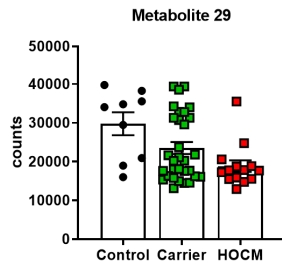


**Figure S4:** Bar graphs with individual data points of the top 30 most important metabolites in distinguishing the Carrier vs HOCM group. Data from the third group is included in all graphs.

## HOcm vs Ctrl

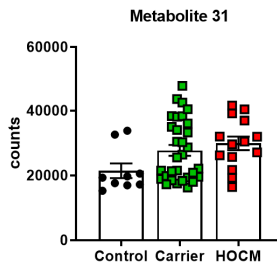
### Organic acids and derivatives

#### Amino acids, peptides and analogues



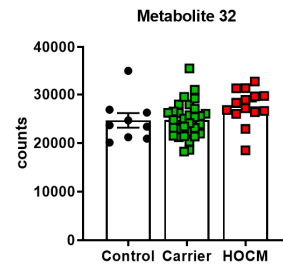
##### Metabolite 29

Lysyl-Glutamine  
Lysyl-Gamma-glutamate  
Gamma-glutamyl-Lysine  
Glutamyl-Lysine



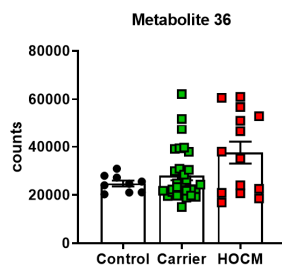
##### Metabolite 31

Cysteinyl-Leucine  
Isoleucyl-Cysteine  
Leucyl-Cysteine  
Cysteinyl-Isoleucine



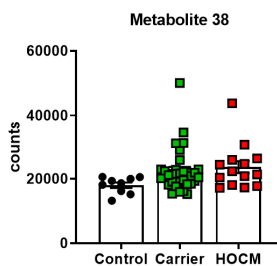
##### Metabolite 32

Tyrosyl-Glutamine  
Tyrosyl-Gamma-glutamate  
gln-tyr  
Glutamyl-Tyrosine



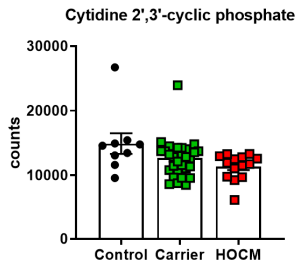
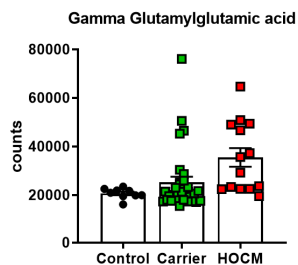
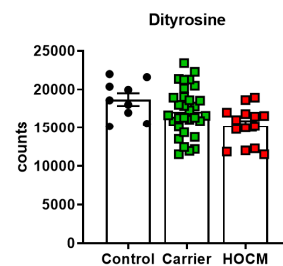
##### Metabolite 36

Tyrosyl-Cysteine  
Cysteinyl-Tyrosine



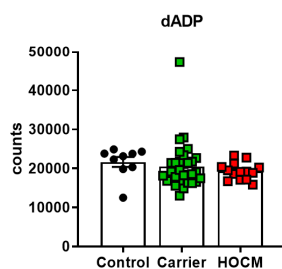
##### Metabolite 38

Histidinyl-Threonine  
Threoninyl-Histidine  
2-(3-Carboxy-3-aminopropyl)-L-histidine

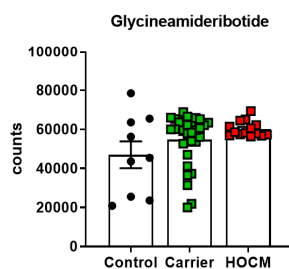


### Nucleosides, nucleotides and analogues

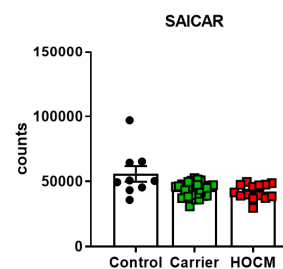
#### Purine deoxyribonucleotides



#### Glycinamide ribonucleotides



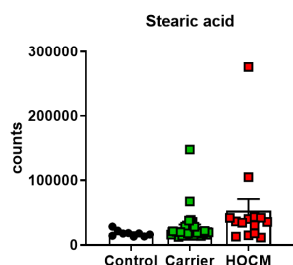
#### 1-ribosyl-imidazolecarboxamides



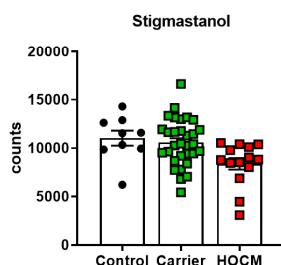
## HOCM vs Ctrl

### Lipids and lipid-like molecules

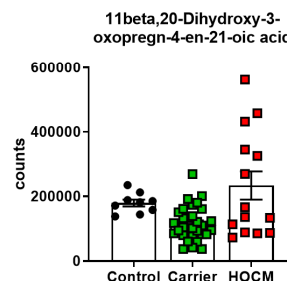
#### Fatty acids and conjugates



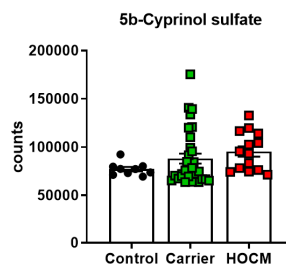
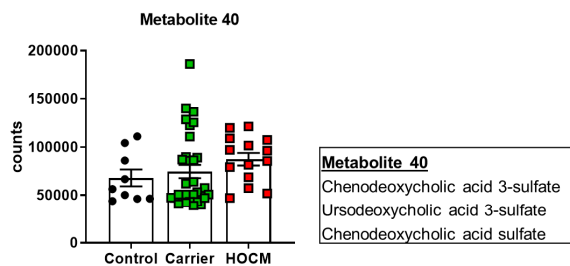
#### Stigmastanes and derivatives



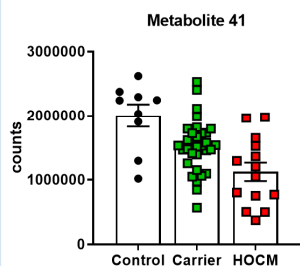
#### Oxosteroids



### Bile acids, alcohols and derivatives

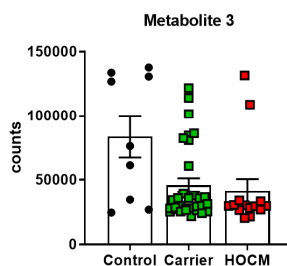


### Lineolic acids and derivatives



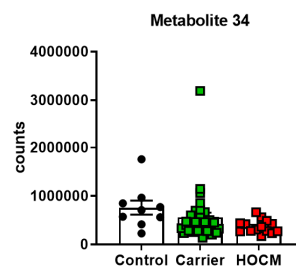
**Metabolite 41**  
MG(0:0/18:3(6Z,9Z,12Z)/0:0)  
MG(0:0/18:3(9Z,12Z,15Z)/0:0)  
MG(18:3(6Z,9Z,12Z)/0:0/0:0)  
MG(18:3(9Z,12Z,15Z)/0:0/0:0)

### Ceramides



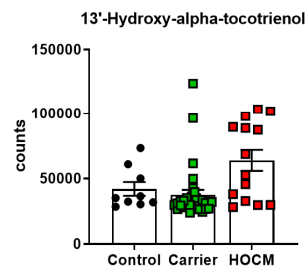
**Metabolite 3**  
Ceramide (d18:1/18:0)  
Cer(d18:0/18:1(11Z))  
Cer(d18:0/18:1(9Z))  
N-Stearoylsphingosine

### Monoradylglycerols

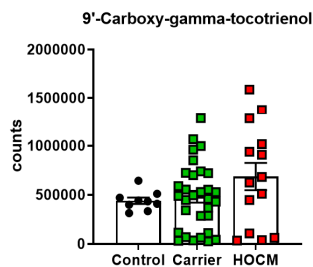


**Metabolite 34**  
MG(20:5(5Z,8Z,11Z,14Z,17Z)/0:0/0:0)  
9'-Carboxy-gamma-chromanol  
MG(0:0/20:5(5Z,8Z,11Z,14Z,17Z)/0:0)

### Quinone and hydroquinone lipids



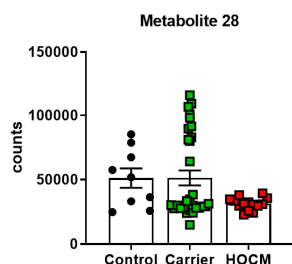
### Monoterpenoids



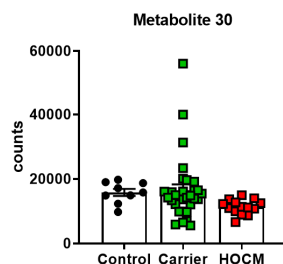
## HOCM vs Ctrl

### Lipids and lipid-like molecules

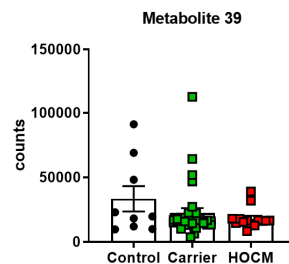
#### Diradylglycerols



**Metabolite 28**  
 DG(16:0/15:0/0:0)  
 DG(15:0/0:0/16:0)  
 DG(15:0/16:0/0:0)



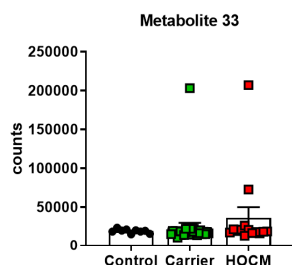
**Metabolite 30**  
 DG(15:0/14:0/0:0)  
 DG(14:0/0:0/15:0)  
 DG(14:0/15:0/0:0)



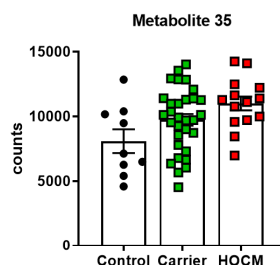
**Metabolite 39**  
 DG(14:1(9Z)/20:0/0:0)  
 DG(16:0/18:1(11Z)/0:0)  
 DG(16:0/18:1(9Z)/0:0)  
 DG(16:1(9Z)/18:0/0:0)  
 DG(18:0/16:1(9Z)/0:0)  
 DG(18:1(11Z)/16:0/0:0)  
 DG(18:1(9Z)/16:0/0:0)  
 DG(20:0/14:1(9Z)/0:0)  
 DG(20:1(11Z)/14:0/0:0)  
 DG(14:0/0:0/20:1n9)  
 DG(16:0/0:0/18:1n7)  
 DG(16:0/0:0/18:1n9)  
 DG(18:0/0:0/16:1n7)  
 DG(20:0/0:0/14:1n5)  
 DG(14:0/20:1(11Z)/0:0)

### Organic oxygen compounds

#### Carbohydrates and carbohydrate conjugates



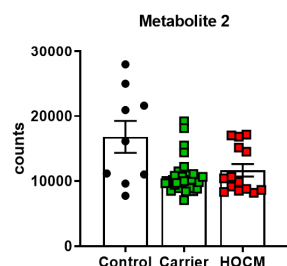
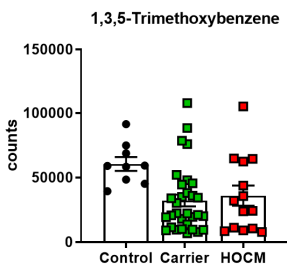
**Metabolite 33**  
 N-Acetyl-a-neuraminic acid  
 N-Acetylneuraminic acid



**Metabolite 35**  
 5-(3',4',5'-trihydroxyphenyl)-gamma-valerolactone-O-methyl-5'-O-glucuronide  
 5-(3',4',5'-trihydroxyphenyl)-gamma-valerolactone-O-methyl-4'-O-glucuronide

### Benzenoids

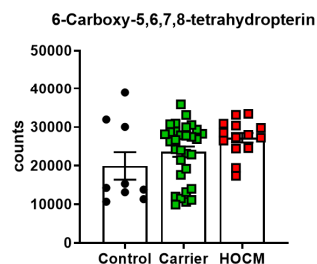
#### Anisoles



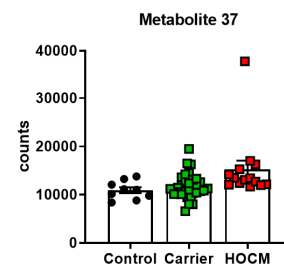
**Metabolite 2**  
 p-Ethylacetophenone  
 Anethole

### Organoheterocyclic compounds

#### Pterins and derivatives



#### Hydroxyindoles



**Metabolite 37**  
 5-Hydroxyindoleacetaldehyde  
 Indoleacetic acid

**Figure S5:** Bar graphs with individual data points of the top 30 most important metabolites in distinguishing the HOCM vs Ctrl group. Data from the third group is included in all graphs.