

## Context-dependent roles for SIRT2 and SIRT3 in tumor development upon calorie restriction or high fat diet

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### Supplementary Tables and Figures:

Diet Group		Ctrl			CR			HFD		
<i>Genotype</i>		<i>Sirt2</i> <sup>+/+</sup>	<i>Sirt2</i> <sup>-/-</sup>	<i>Sirt2</i> <sup>+/-</sup>	<i>Sirt2</i> <sup>+/+</sup>	<i>Sirt2</i> <sup>-/-</sup>	<i>Sirt2</i> <sup>+/-</sup>	<i>Sirt2</i> <sup>+/+</sup>	<i>Sirt2</i> <sup>-/-</sup>	<i>Sirt2</i> <sup>+/-</sup>
		<i>Sirt3</i> <sup>+/+</sup>	<i>Sirt3</i> <sup>+/-</sup>	<i>Sirt3</i> <sup>-/-</sup>	<i>Sirt3</i> <sup>+/+</sup>	<i>Sirt3</i> <sup>+/-</sup>	<i>Sirt3</i> <sup>-/-</sup>	<i>Sirt3</i> <sup>+/+</sup>	<i>Sirt3</i> <sup>+/-</sup>	<i>Sirt3</i> <sup>-/-</sup>
<i>p53</i> (+/-)	Sex (M:F)	6:5	6:5	5:6	5:6	6:5	5:6	5:6	5:5	5:7
	Median age (days)	446	471	413	550	309	415	293	353	406
	Hazard Ratio (HR)	-	-	-	0.46	1.67	0.65	4.01	1.58	1.13
<i>p53</i> (-/-)	Sex (M:F)	6:6	6:5	5:4	5:7	5:6	5:5	6:5	5:6	7:4
	Median age (days)	179	181.5	169	189	148	158	139.5	111	112
	Hazard Ratio (HR)	-	-	-	0.55	1.16	0.45	1.58	3.55	1.24

**Supplementary Table (1): Diet-induced changes in median survival and hazard ratios of tumor incidence.** The hazard ratios, indicating changes in tumor incidence rate compared to control diet group, were calculated from the slopes of tumor-free survival curves (Fig. 2-5) and estimated based on log-rank test.

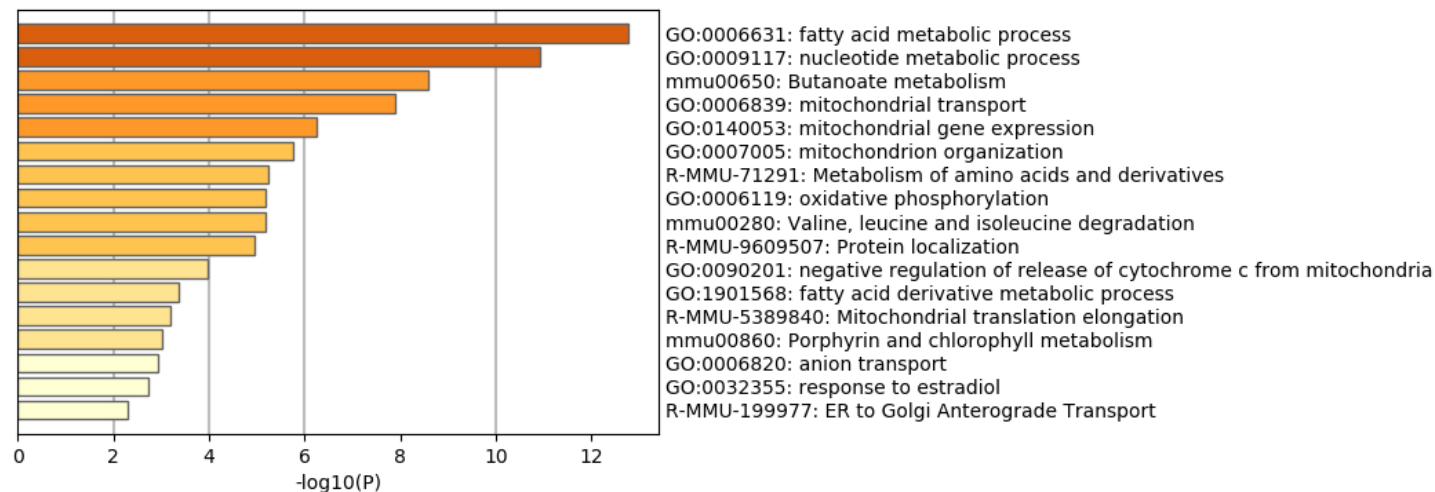
Diet	Genotype		Gender	Age (days)	Tumors observed							
	<i>p53</i>	<i>Sirt2/3</i>			Sarcoma	Lymphomas	Liver	Colon/Intestinal	Mammary	Head and Neck	Renal	Splenomegaly
CTRL	<i>p53</i> (-/-)	wt	Male	229		x						
CTRL	<i>p53</i> (-/-)	wt	Male	162*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (-/-)	wt	Male	215								
CTRL	<i>p53</i> (-/-)	wt	Male	196	x	x						
CTRL	<i>p53</i> (-/-)	wt	Male	108		x						
CTRL	<i>p53</i> (-/-)	wt	Female	285	x							
CTRL	<i>p53</i> (-/-)	wt	Female	248		x						
CTRL	<i>p53</i> (-/-)	wt	Female	49								
CTRL	<i>p53</i> (-/-)	wt	Female	97								
CTRL	<i>p53</i> (-/-)	wt	Female	222	x							
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	181								
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	198				x				
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	107								
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	220								
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	102								
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Male	182		x						
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Female	141				x				
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Female	186								
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Female	172	x							
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Female	244				x		x		
CTRL	<i>p53</i> (-/-)	<i>Sirt2</i> (-/-)	Female	221								
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Male	116								
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Male	187		x	x					
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Male	168	x							
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Male	190								
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Male	148	x							
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Female	170								
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Female	192								
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Female	196*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (-/-)	<i>Sirt3</i> (-/-)	Female	149					x			
CTRL	<i>p53</i> (+/-)	wt	Male	211								
CTRL	<i>p53</i> (+/-)	wt	Male	474								x
CTRL	<i>p53</i> (+/-)	wt	Male	190								
CTRL	<i>p53</i> (+/-)	wt	Male	518								x
CTRL	<i>p53</i> (+/-)	wt	Male	410*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	wt	Female	196								
CTRL	<i>p53</i> (+/-)	wt	Female	534								
CTRL	<i>p53</i> (+/-)	wt	Female	441*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	wt	Female	446								
CTRL	<i>p53</i> (+/-)	wt	Female	473								
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	186								
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	265								
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	570	x			x				
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	521		x						
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	563						x		
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Male	529								
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Female	505				x				x
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Female	557*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Female	421								
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Female	301					x			
CTRL	<i>p53</i> (+/-)	<i>Sirt2</i> (-/-)	Female	315								x
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Male	343*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Male	471			x					
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Male	391	x							
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Male	428*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Male	448			x					x
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	404*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	413*				found dead / macroscopic analysis for tumors was not possible				
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	405	x		x					
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	297								x
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	469					x			x
CTRL	<i>p53</i> (+/-)	<i>Sirt3</i> (-/-)	Female	351							x	





**Supplementary Table (2): Tumors developed in the *Sirt2<sup>wt</sup>/Sirt3<sup>wt</sup>*, *Sirt2<sup>-/-</sup>* and *Sirt3<sup>-/-</sup>* mice.** Table shows diet, genotype, gender, age and types of tumors for all mice included in the study.

**A**



**B**

Acadl|Aldh3a2|Cpt2|Ggt1|Anxa1|Echdc2|Mlycd|Them4|Acox3|Hadha|Cyp2c50|Acsm1|Acad9|Hadhb|Acsm2|Acsf3|Acsm5|Cyp2c68

**Supplementary Figure 1. Proteomics based approach to analyze the acetylome in *Sirt3<sup>+/+</sup>* and *Sirt3<sup>-/-</sup>* mice.** Proteins with increased acetylation in *Sirt3<sup>-/-</sup>* liver tissue as compared to *Sirt3<sup>+/+</sup>* tissue were detected by mass spectrometry following immunoprecipitation with an anti-acetyllysine antibody (ICP0388; ImmunoChem Pharmaceuticals, Inc.). (A) Pathway analysis was performed using Metascape. Bar graph of enriched terms across input protein list, colored by p-values is shown. (B) List of proteins with increased acetylation in *Sirt3<sup>-/-</sup>* liver tissue as compared to *Sirt3<sup>+/+</sup>* tissue included in the Fatty acid metabolic process cluster is shown.

