

## **Supporting information**

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**Supplementary Table 1. Composition of CDMRHFD.**

	Name of nutrient	Unit	AIN-93M	AIN-93G	OYC-NASH2
<b>General ingredients</b>	Water	g/100g(diet)	9.0	9.0	9.0
	Crude protein	g/100g(diet)	12.7	18.1	17.1
	Crude fat	g/100g(diet)	4.3	7.3	27.4
	Rough grey	g/100g(diet)	3.0	3.1	2.9
	Crude fiber	g/100g(diet)	5.0	5.0	4.7
	NFE	g/100g(diet)	65.9	57.6	39.0
	Calories	kcal/100g(diet)	353.5	368.0	470.5
<b>Calorie ratio</b>	Protein calorie ratio	%/ calorie	14.4	19.6	14.5
	Fat calorie ratio	%/ calorie	11.1	17.8	52.3
	NFE calorie ratio	%/ calorie	74.5	62.6	33.2
<b>Main fatty acid composition</b>	Saturated fatty acid	%/total fatty acids	15.9	15.9	41.7
	Monounsaturated fatty acid	%/total fatty acids	23.8	23.8	46.4
	Polyunsaturated fatty acids	%/total fatty acids	60.1	60.1	10.1
<b>Others important ingredient</b>	Amount of methionine added	g	0.34	0.51	0.11
	Amount of choline added	g	0.18	0.25	-

NFE: Nitrogen-Free Extract

**Supplementary Table 2. Primer pairs used for qPCR analysis.**

<b>Gene</b>	<b>Accession #</b>	<b>Primer sequence (5'-3')</b>
<i>18S rRNA</i>	NR_003278	F 5'-CACGGACAGGATTGACAGATTG-3'
		R 5'-CAGACAAATCGCTCCACCAA-3'
<i>Casp1</i>	NM_009807	F 5'-TACCTGGCAGGAATTCTGGA-3'
		R 5'-AGTCCTGGAAATGTGCCATC-3'
<i>Ccl2</i>	NM_011333	F 5'-AGGTCCCTGTCATGCTTCTG
		R 5'-GGGATCATCTTGCTGGTGAA
<i>Ccnd1</i>	NM_007631	F 5'-CCAGAGGCGGATGAGAACAA-3'
		R 5'-ATGGAGGGTGGGTTGGAAA-3'
<i>Cdk4</i>	NM_009870	F 5'-CCTGAGGACATACCTGGACAAAG-3'
		R 5'-CCGCTTAGAAACTGACGCATT-3'
<i>Ddit3</i>	NM_007837	F 5'-CAGCGACAGAGCCAGAATAA
		R 5'-GACCAGGTTCTGCTTTCAGG
<i>Lgals3</i>	NM_010705	F 5'-GTACAGCTAGCGGAGCGG
		R 5'-CGGATATCCTTGAGGGTTTG
<i>Myc</i>	NM_010849	F 5'-AGCCCCTAGTGCTGCATGA-3'
		R 5'-GTTTGCCTCTTCTCCACAGACA-3'
<i>Nrf2</i>	NM_007527	F 5'-GGACATGGAGCAAGTTTGGC
		R 5'-GGCCTCAGCCCATCTTCTTC
<i>P47phox</i>	NM_010876	F 5'-GCCCAAAGATGGCAAGAATAAC-3'
		R 5'-TAGTCAGCAATGGCCCGATAG-3'
<i>p16</i>	NM_001040654	F 5'-ATGGAGTCCGCTGCAGACAGAC-3'
		R 5'-ACGTTGCCCATCATCATCACCTGA-3'
<i>Sqstm1</i>	NM_011018	F 5'-GTGGGACAGCCAGAGGAACAG-3'
		R 5'-TGAGGGGTCTAGAGAGCTTGG-3'
<i>Tnf</i>	NM_013693	F 5'-CCACCACGCTCTTCTGTCTAC-3'
		R 5'-AGGGTCTGGGCCATAGAACT-3'

*F*, forward sequence; *R*, reverse sequence.

*Casp1*, caspase 1

*Ccl2*, chemokine (C-C motif) ligand 2

*Ccnd1, cyclin D1*  
*Cdk4, cyclin-dependent kinase 4*  
*Ddit3, DNA damage-inducible transcript 3*  
*Lgals3, Galectin-3*  
*Myc, myelocytomatosis oncogene*  
*Nrf2, Nuclear factor erythroid 2-related factor 2*  
*p16, cyclin dependent kinase inhibitor 2A*  
*P47phox, Neutrophil cytosol factor 1*  
*Sqstm1, sequestosome 1*  
*Tnf, tumor necrosis factor alpha*

**Supplementary Table 3. Biochemical analysis of serum and liver.**

**Serum biochemical characteristics**

Time	group \ Item	T-Chol (mg/dL)	TG (mg/dL)	NEFA (mEq/L)	TBA (mg/dL)	PL (mg/dL)	Glucose (mg/dL)
3w	AIN-93 diet group (n=41)	100.9±3.9	121.9±2.4	0.84±0.07	72.1±9.07	375.7±26.9	242.4±18.2
	OYC-NASH2 diet group (n=72)	70.7±2.3	55.5±4.9	0.73±0.07	205.7±44.9	246.5±11.6	67.3±9.1
	P value	3.5301E-05	3.51887E-06	0.3893411	0.068404108	0.00038241	1.25E-06
6w	AIN-93 diet group (n=41)	90±27.2	52.6±17.5	0.54±0.1	87.8±58.5	249.1±58.2	187.9±50.8
	OYC-NASH2 diet group (n=72)	54±4.6	67.8±6.6	0.67±0.06	248.9±20.3	184.1±18.3	95.8±8.7
	P value	0.097270434	0.341045133	0.331868323	0.008208329	0.198348975	0.029601957
9w	AIN-93 diet group (n=41)	99.1±5.6	61.3±8.3	0.67±0.10	79.9±24.4	293.6±11.7	230.5±10.2
	OYC-NASH2 diet group (n=72)	51.5±2.5	62.7±9.4	0.62±0.06	225.4±40.6	184.1±14.1	82.9±5.2
	P value	3.3334E-06	0.924074415	0.565911528	0.038552191	0.000551472	4.68E-08
12w	AIN-93 diet group (n=41)	79.7±4.0	67.6±12.2	1.03±0.10	50.1±16.9	280.6±25.4	98±13.9
	OYC-NASH2 diet group (n=72)	58.6±3.0	66.5±8.9	0.64±0.04	234.0±20.7	195.7±10.3	78.5±6.3
	P value	0.001089824	0.941115762	0.000664594	6.68934E-05	0.002519746	0.160785683
24w	AIN-93 diet group (n=41)	93.0±9.8	50.3±8.5	0.73±0.10	68.9±22.5	210.8±33.8	283.4±23.1
	OYC-NASH2 diet group (n=72)	59.8±4.9	66.5±7.2	0.88±0.08	248.2±20.8	187.5±17.3	77.2±6.0
	P value	0.004748071	0.19685568	0.302497455	0.000137143	0.002519746	3.75E-08
36w	AIN-93 diet group (n=41)	92.9±12	97.6±38	0.41±0.04	97.8±13.2	309.5±50.9	212.5±20.6
	OYC-NASH2 diet group (n=72)	128.5±8.4	119.4±20.2	0.45±0.03	396.8±64.6	347.9±24.5	157.6±12.9
	P value	0.02932648	0.587159799	0.469979624	0.014651693	0.451911917	0.026624796
48w	AIN-93 diet group (n=41)	54.5±8.6	63.6±16	0.33±0.03	136.5±19.3	213.3±25.8	171.5±19.1
	OYC-NASH2 diet group (n=72)	129.5±8.6	77.5±11.2	0.44±0.04	401.4±26.7	396±25.3	180.3±16.1
	P value	0.000104321	0.484087502	0.09157195	6.96618E-05	0.000584492	0.877668848
60w	AIN-93 diet group (n=41)	88.5±1.8	87.7±11.5	0.44±0.05	166.6±14.9	362.6±33.4	229.4±9.2
	OYC-NASH2 diet group (n=72)	116.5±13.4	86.6±41.6	0.35±0.03	769.8±86.2	507.4±53.3	153.6±18.2
	P value	0.13546185	0.983268334	0.175889889	0.000213828	0.073383809	0.008717158

## Liver biochemical characteristics

Time	group \ Item		T-Chol (mg/g)	TG (mg/g)	NEFA (mEq/g)	F-Cho (mg/g)	PL (mg/g)
	group	Item					
3w	AIN-93 diet group (n=41)		0.42±0.05	21.95±1.16	0.05±0.002	1.1±0.2	11.46±0.25
	OYC-NASH2 diet group (n=72)		1.57±0.15	46.30±2.05	0.17±0.004	8.4±1.1	12.58±0.55
	P value		0.000411257	1.26091E-05	1.83E-09	1.48654E-07	0.198119294
6w	AIN-93 diet group (n=41)		0.40±0.09	25.88±4.17	0.07±0.008	3.2±0.4	8.58±0.54
	OYC-NASH2 diet group (n=72)		1.66±0.17	49.02±2.38	0.20±0.02	9.1±1.0	12.02±0.64
	P value		0.000513474	0.000396679	0.000268564	0.002806889	0.006359071
9w	AIN-93 diet group (n=41)		0.56±0.06	25.23±1.35	0.08±0.01	2.6±0.6	13.45±0.53
	OYC-NASH2 diet group (n=72)		1.55±0.06	94.74±1.53	0.22±0.013	10.2±0.7	15.78±0.74
	P value		8.70503E-07	5.6718E-11	3.0701E-05	4.45444E-05	0.066926429
12w	AIN-93 diet group (n=41)		0.50±0.12	42.29±6.12	0.11±0.01	4.6±0.6	12.55±1.36
	OYC-NASH2 diet group (n=72)		1.79±0.11	98.96±2.98	0.22±0.01	9.5±0.6	14.71±0.64
	P value		5.67067E-06	3.32359E-07	1.50737E-06	0.000179986	0.122490554
24w	AIN-93 diet group (n=41)		0.96±0.14	48.97±4.27	0.16±0.05	5.3±0.9	14.67±0.96
	OYC-NASH2 diet group (n=72)		1.67±0.09	82.24±2.47	0.20±0.013	8.5±0.6	15.86±0.57
	P value		0.000501618	6.50739E-06	0.362177621	0.010498599	0.278060887
36w	AIN-93 diet group (n=41)		1.20±0.17	61.43±4.40	0.13±0.02	2.8±0.4	17.27±2.10
	OYC-NASH2 diet group (n=72)		1.95±0.08	70.33±2.75	0.17±0.008	4.8±0.3	15.03±0.27
	P value		0.000601306	0.096455559	0.091616584	0.000763067	0.153983732
48w	AIN-93 diet group (n=41)		1.01±0.14	44.57±2.69	0.10±0.013	1.6±0.1	13.87±0.54
	OYC-NASH2 diet group (n=72)		1.72±0.13	66.20±3.47	0.16±0.006	5.1±0.4	17.21±0.68
	P value		0.004419567	0.001341769	0.00041388	2.78355E-05	0.007304479
60w	AIN-93 diet group (n=41)		1.29±0.12	66.41±4.28	0.12±0.02	2.2±0.2	18.64±1.01
	OYC-NASH2 diet group (n=72)		3.50±0.48	51.03±5.93	0.18±0.02	5.9±0.5	19.03±0.86
	P value		0.005003324	0.091401506	0.028158737	0.000194605	0.777881491

**Supplementary Figure 1. Experimental design and time course of weight change in C57BL/6J mice fed the OYC-NASH2 diet for 60 weeks.**

(A) C57BL/6J mice were divided into two groups, AIN93M diet group (n=41) and OYC-NASH2 group (n=74, two mice died at 60w), and fed corresponding diet for 60 weeks respectively. (B) Body weight and some organ weight ratios of mice fed the OYC-NASH2 / AIN93M diet during the feeding period. Data are means  $\pm$  SEM (n = 113). \*P < 0.05, \*\*P < 0.01 and \*\*\*P < 0.001 between AIN93M diet group and OYC-NASH2 diet group.



