Supplementary Table 1 – Detailed composition of the experimental diets used in the study

Diet formulation provided as gram of ingredients per 100g for each of the 10 diets used in the study. The diets are isocaloric at 14.5 MJ/kg with the following net metabolizable energy (NME) assigned: casein (13.3 kJ/g; 3.2 kCal/g), L-methionine (18 kJ/g; 4.3 kCal/g), Canola oil (36.6 kJ/g; 8.7 kCal/g), Wheat starch (14.13 kJ/g; 3.4 kCal/g), Dextrinized Starch (14.6 kJ/g; 3.49 kCal/g), Sucrose 14.92 kCal/g and cellulose was given a NME of 0 kCal/g.

		Diet 1	**Diet 2**	**Diet 3**	**Diet 4**	**Diet 5**	**Diet 6**	**Diet 7**	**Diet 8**	**Diet 9**	**Diet 10**
	%P	60	5	5	33	33	5	14	14	42	24
	%C	20	75	20	47	20	47	29	57	29	38
	%F	20	20	75	20	47	48	57	29	29	38
INGREDIENTS											
Protein	**Casein**	64.87	5.04	5.04	35.50	35.50	5.04	14.83	14.83	45.29	25.71
	L-Methionine	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
Fat	**Canola Oil**	7.91	7.91	29.65	7.91	18.58	18.98	22.53	11.46	11.46	15.03
Carbohydrate	**Wheat Starch**	12.59	47.87	12.60	29.91	12.60	29.91	18.37	36.34	18.37	24.13
	Dextrinized Starch	4.10	15.57	4.10	9.73	4.10	9.73	5.98	11.82	5.98	7.85
	Sucrose	3.11	11.81	3.11	7.38	3.11	7.38	4.54	8.97	4.54	5.96
Minerals	**$CaCO_3$**	1.31	1.31	1.31	1.31	1.31	1.31	1.31	1.31	1.31	1.31
	NaCl	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26
	AIN93 Trace Minerals	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14
	KH_2PO_4	0.69	0.69	0.69	0.69	0.69	0.69	0.69	0.69	0.69	0.69
	K_2SO_4	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16
	KCl	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
	$C_5H_{14}ClNO$	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Vitamins	**AIN93 vitamins**	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cellulose	**Cellulose**	3.06	7.44	41.15	5.21	21.75	24.60	29.39	12.23	10.00	16.97

Supplementary Table 2 – Statistical output for mixture models relating to sIgA

Model (Scheffé Polynomials)	Akaike Information Criterion	Degrees of freedom
1	1168.363	4
2	1168.552	7
3	1156.861	11
4	1170.262	8
Null	1181.324	2

Model 1 Coefficients			
Components	**Estimate (Std. Error)**	**t value**	**P(>|t|)**
Protein	2094.2 (264.7)	7.913	2.05e−11
Fat	517.6 (214.5)	2.413	0.018334
Carbohydrate	868.8 (220.6)	3.939	0.000185
Adjusted R-squared	0.8076		
p-value	< 2.2e−16		

Supplementary Table 3 – Statistical output for mixture models relating to plasma IgA

Model (Scheffé Polynomials)	Akaike Information Criterion	Degrees of freedom
1	1160.604	4
2	1142.835	7
3	1149.336	11
4	1144.762	8
Null	1171.433	2

Model 2 Coefficients			
Components	**Estimate (Std. Error)**	**t value**	**P(>|t|)**
Protein	1244.4 (600.3)	2.073	0.041706
Fat	2042.4 (371.3)	5.501	5.31e−07
Carbohydrate	2110.2 (375.5)	5.619	3.30e−07
Protein:Fat	−3432.3 (1666.8)	−2.059	0.043043
Protein:Carbohydrate	−4738.6 (1667.2)	−2.842	0.005804
Fat:Carbohydrate	−6169.1 (1657.3)	−3.722	0.000385
Adjusted R-squared	0.7243		
p-value	< 2.2e−16		

Supplementary Table 4 – Statistical output for mixture models relating to plasma IgM

Model (Scheffé Polynomials)	Akaike Information Criterion	Degrees of freedom
1	696.561	4
2	700.119	7
3	701.771	11
4	700.027	8
Null	693.555	2

Supplementary Table 5 – 16S rRNA sequencing quality control

	Total reads	Reads post filtering	Reads post merging and chimera filtering	Reads retained
HP 1	135805	119366	97727	71.96%
HP 2	49009	43630	43301	88.35%
HP 3	120743	107426	91056	75.41%
HP 4	59370	51662	50927	85.78%
HP 5	71171	62355	61855	86.91%
HP 6	55324	49431	49288	89.09%
HP 7	24290	21876	21826	89.86%
HP 8	111569	96616	95494	85.59%
HC 1	89660	79158	78435	87.48%
HC 2	133887	119303	102883	76.84%
HC 3	52702	47334	46964	89.11%
HC 4	29954	26904	26437	88.26%
HC 5	121070	100002	94779	78.28%
HC 6	86078	71337	71144	82.65%
HC 7	69380	59366	59010	85.05%
HC 8	136477	117920	101334	74.25%
HF 1	44447	41330	40566	91.27%
HF 2	135418	126495	117867	87.04%
HF 3	13618	12835	12692	93.20%
HF 4	19284	18178	17971	93.19%
HF 5	23368	22069	21948	93.92%
HF 6	19495	18154	18134	93.02%
HF 7	120323	113333	103573	86.08%
HF 8	102020	95906	84963	83.28%

Supplementary Table 6 – Antibodies used for flow cytometry

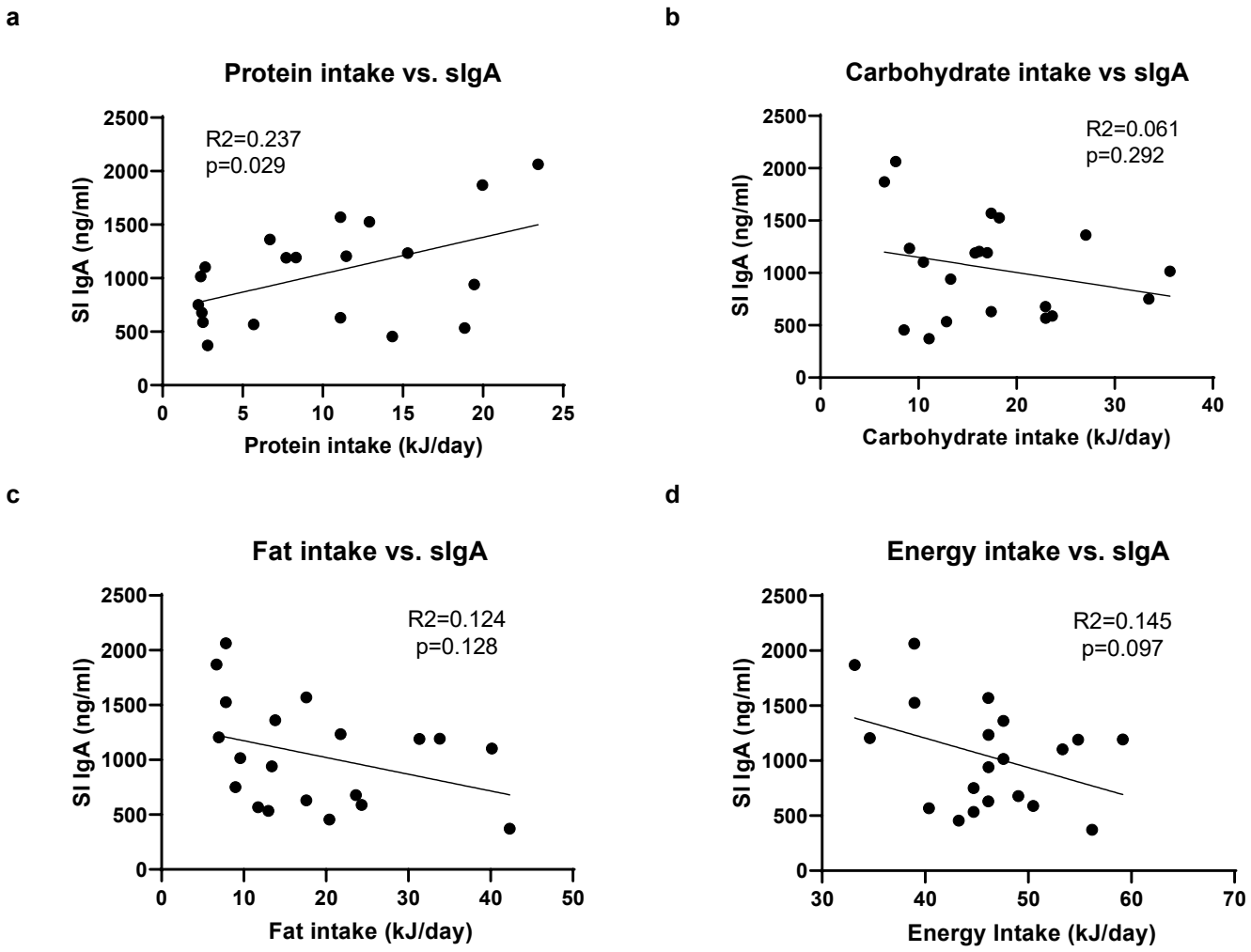
Target	Conjugate	Clone	Manufacturer
CD45	BV785	30-F11	BioLegend
CD95	APC	SA367H8	BioLegend
GL-7	FITC	GL7	BioLegend
B220	VioGreen	REA755	Miltenyi Biotec
IgA	PE	11-44-2	eBioscience

Supplementary Table 7 – Primers used in this study and their sequence

Pre-designed and validated primers used in this study. All primers were purchased from Sigma-Aldrich (KiCqStart SYBR® Green primers).

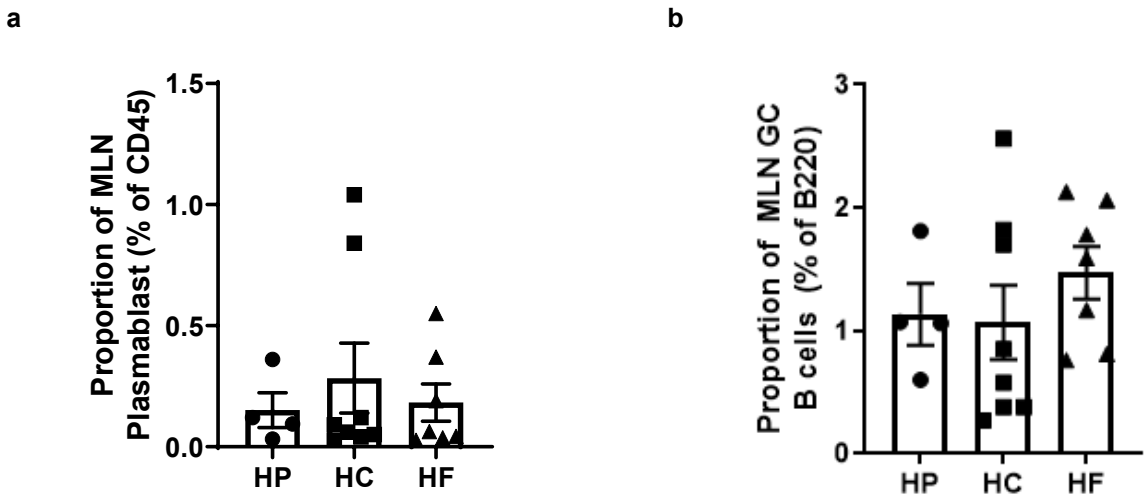
Gene target	Specie	Forward (5'-3')	Reverse (5'-3')
Pigr	Mouse	AAGAACTCCAGAGATTTGGG	GTGGTAGTCACGATTTCATC
Ccl28	Mouse	GAGGTGTCTCATCATGTTTC	ATACGTTTTCTCTGCCATTC
Tnfsf13	Mouse	TCTATAGTCAGGTCCTGTTTC	GGCATACTTCTGATACATCG
Baff	Mouse	ATCTACAGCCAGGTTCTATAC	AGCTGAATCTCATCTCCTTC
Tgfb	Mouse	GGATACCAACTATTGCTTCAG	TGTCCAGGCTCCAAATATAG
Tslp	Mouse	CCTGAAACTGAGAGAAATGAC	ACACCCTTAGTATTCTGTCC
Il10	Mouse	AAGGGTTACTTGGGTTGCCA	AAATCGATGACAGCGCCTCAG
Il4	Mouse	CTGGATTCATCGATAAGCTG	TTTGCATGATGCTCTTTAGG
Rpl13a	Mouse	ATCCCTCCACCCTATGACAA	GCCCCAGGTAAGCAAACTT
GAPDH	Human	GAAGGTGAAGGTCGGAGTCA	CAGAGTTAAAAGCAGCCCTGG
CCL28	Human	GAGGTGTCTCATCATGTTTC	ATACGTTTTCTCTGCCATTC
APRIL	Human	CAGGTGTCTTCCATTTACAC	TGGAGAGAGGTTAAGTTTCG
PIGR	Human	GACCGAGTTTCAATCAGAAG	TTGTCATTGGCTCCAAATTC

Supplementary Figure 1



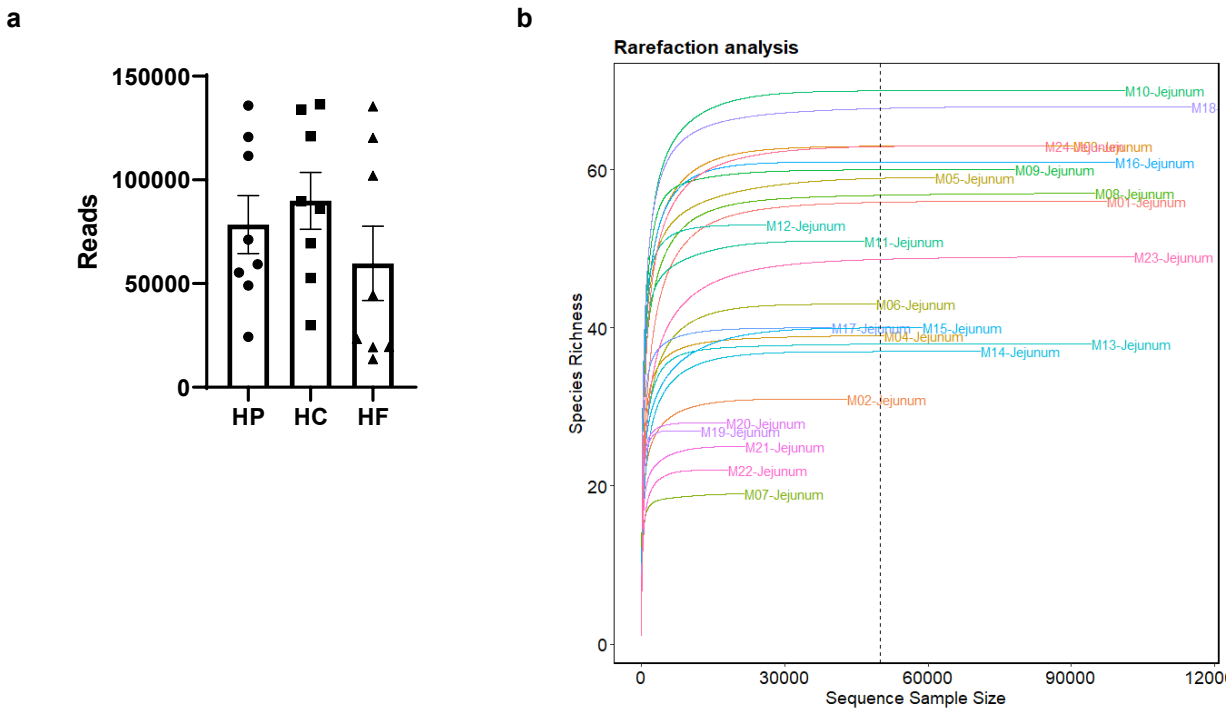
Supplementary Figure 1: Mice were fed on one of 10 diets encompassing a macronutrient range of 5-60% protein, 20-75% carbohydrate, and 20-75% fat and average food intake as well as sIgA quantified. Linear regression of (a) protein eaten, (b) carbohydrate eaten, (c) fat eaten or (d) total energy intake vs. sIgA levels were performed. Each dot represents the average intake versus the average quantified sIgA of a single cage (n=4 animals per cage). Macronutrient eaten and total energy intake is represented as kJ/day.

Supplementary Figure 2



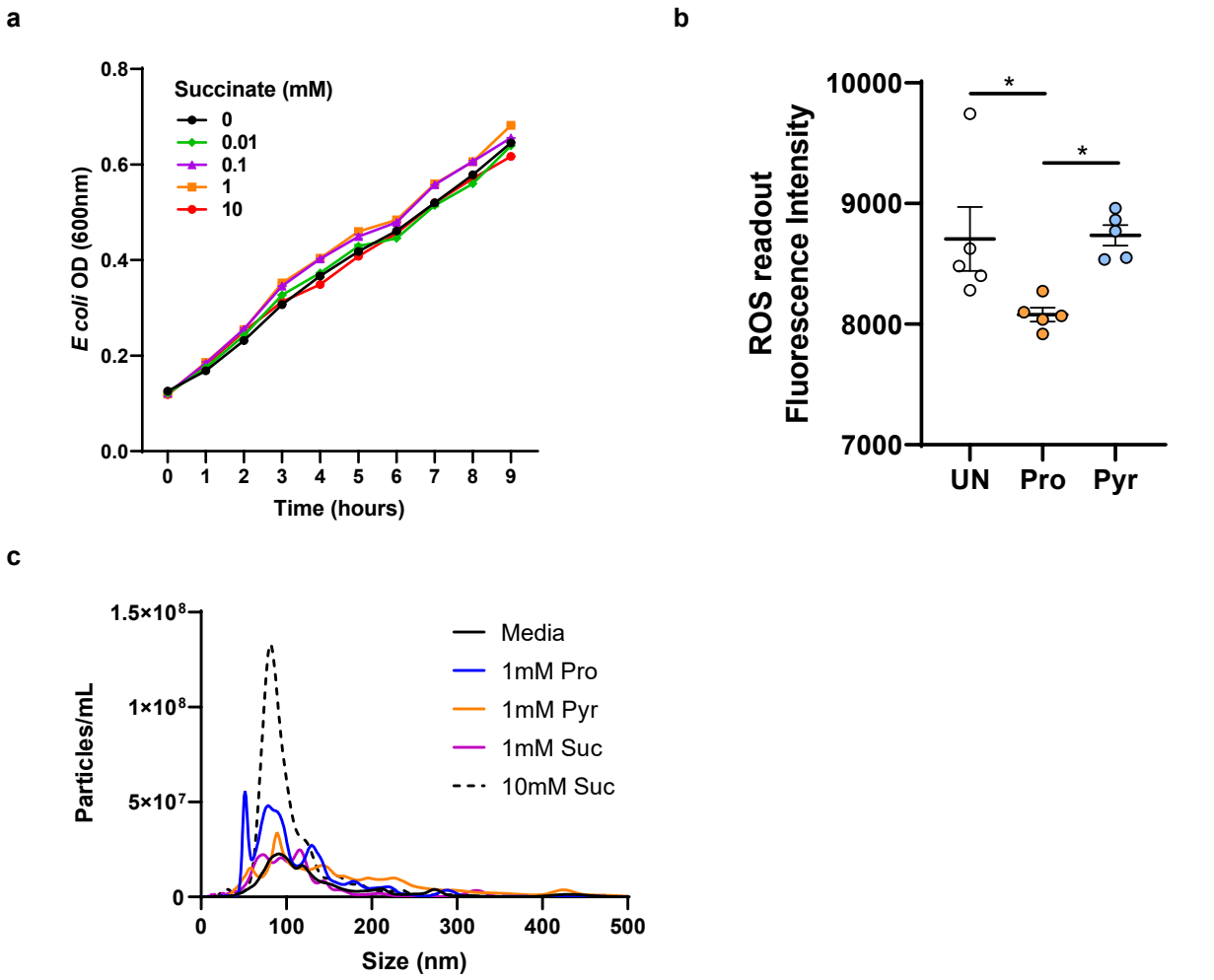
Supplementary Figure 2: (a) Proportion of $B220^{+}IgA^{+}$ plasmablast and (b) $CD95^{+}GL7^{+}$ germinal centre B cells in the mesenteric lymph nodes (n=4-8 per diet) were determined by flow cytometry from mice fed on either a HP, HC, or HF diet for 5 weeks. Data are represented as mean ± SEM.

Supplementary Figure 3



Supplementary Figure 3: DNA from luminal content was extracted for 16S rRNA DNA sequencing from mice fed on a high-protein, high-carbohydrate or high-fat diet for 5 weeks. (a) The total number of reads per samples were identified and no statistical significance between groups were found (Kruskal-Wallis test). (b) Rarefaction analysis was performed. Data are represented as mean ± SEM.

Supplementary Figure 4



Supplementary Figure 4: (a) *E coli* was grown in LB broth in the presence of varying concentration of succinate and growth quantified by spectrophotometry (OD 600nm). (b) *E coli* was grown in LB broth in the presence of varying concentration of propionate (Pro) or pyruvate (Pyr) for 2 hours and ROS production quantified by the conversion of 2',7'-dichlorofluorescein diacetate to 2',7'-dichlorofluorescein (n=5 per condition). (c) *E coli* was grown in the presence of propionate (Pro), pyruvate (Pyr) or succinate (Suc) for 16 hours and extracellular vesicle was isolated and then quantified by nanoparticle tracking analysis (n=5-6 per condition) Data are represented as mean ± SEM. *p <0.05