

Supplementary Table 1. Ingredient profiles of diets.

Diet	Low Fat	High Fat	Western	Inulin	Pectin	Psyllium	American	Aspartame	Vegan	Ketogenic	Mediterranean	Japanese
Product #	D1245 0J	D12492	D12079B	D21021102	D21021103	D21021104	D12052705C	D21021101	D18041701	D12052706	D12052702DM	D12052703CM
Ingredient	gm	gm	gm	gm	gm	gm	gm	gm	gm	gm	gm	gm
Casein	200	200	195	200	200	200	38.5	38.5	0	160	44	0
Soy Protein, Supro 661	0	0	0	0	0	0	0	0	16	0	0	16
Fish Protein Isolate	0	0	0	0	0	0	8.5	8.5	0	0	27	27
Egg White	0	0	0	0	0	0	55	55	0	0	9	6
Beef, Cooked, Powdered, 5013	0	0	0	0	0	0	76.9	76.9	0	0	61.9	7
Pea Protein 85% - PureBulk	0	0	0	0	0	0	0	0	50	0	0	0
L-Cystine	3	3	3	3	3	3	3	3	0	3	3	3
L-Methionine	0	0	0	0	0	0	0	0	4.4	0	0	0
L-Phenylalanine	0	0	0	0	0	0	0	0	4.7	0	0	0
L-Leucine	0	0	0	0	0	0	0	0	2.4	0	0	0
L-Threonine	0	0	0	0	0	0	0	0	2	0	0	0
L-Tryptophan	0	0	0	0	0	0	0	0	0.5	0	0	0
L-Valine	0	0	0	0	0	0	0	0	2.2	0	0	0
L-Histidine	0	0	0	0	0	0	0	0	0.5	0	0	0
L-Isoleucine	0	0	0	0	0	0	0	0	1.3	0	0	0
Corn Starch	506.2	0	50	506.2	506.2	506.2	30	30	0	0	0	0
Maltodextrin	125	125	100	125	125	125	0	0	0	0	0	0
Wheat Starch	0	0	0	0	0	0	195	195	143	0	365	0
Rice Starch	0	0	0	0	0	0	0	0	143	0	0	763.5
Potato Starch	0	0	0	0	0	0	30	30	0	0	0	0
Sucrose	68.8	68.8	341	68.8	68.8	68.8	205	205	70	0	61	70
Fructose	0	0	0	0	0	0	22	22	6	0	19	6
Organic Spinach Powder (Nubeleaf)	0	0	0	0	0	0	0	0	53	0	0	0
Organic Broccoli Powder (Nubeleaf)	0	0	0	0	0	0	0	0	53	0	0	0
Organic Apple Powder (Nubeleaf)	0	0	0	0	0	0	0	0	53	0	0	0

[illegible]

Vitamin Mix V10001	10	10	10	10	10	10	10	10	10	10	10	10
Biotin 1%	0	0	0	0	0	0	0.1	0.1	0	0	0.014	0.014
Choline Bitartrate	2	2	2	2	2	2	2	2	2	2	2	2
Cholesterol	0	0	1.5	0	0	0	1.5	1.5	0	1.5	0	0.19
Ethoxyquin	0	0	0.04	0	0	0	0	0	0	0	0	0
Resveratrol (50% Trans Resveratrol)	0	0	0	0	0	0	0	0	0	0	0.045	0
Green Tea Extract	0	0	0	0	0	0	0	0	0	0	0	0.215
Aspartame	0	0	0	0	0	0	0	0.924	0	0	0	0
FD&C Red Dye #5	0	0	0	0.05	0	0	0.01	0.01	0	0.025	0	0.1
FD&C Yellow Dye #40	0.04	0	0	0	0.05	0.025	0.04	0.04	0	0	0.1	0
FFD&C Blue Dye #1	0.01	0.05	0	0	0	0.025	0	0	0	0.025	0	0
Total	1055.05	773.85	1001.54	1055.05	1055.05	1055.05	864.7547	865.6787	1015.4049	609.5533	855.5613	1034.7229

Supplementary Table 2. Macronutrient content of diets.

Diet	Low Fat	High Fat	Western	Inulin	Pectin	Psyllium	American	Aspartame	Vegan	Ketogenic	Mediterranean	Japanese
Product #	D12450J	D12492	D12079B	D21021102	D21021103	D21021104	D12052705C	D21021101	D18041701	D12052706	D12052702DM	D12052703CM
g												
Protein	178	177	173	178	178	178	136.9	136.9	139.3	142.2	112.6	120.5
Carbohydrate	639.7	196.8	501	658.5	639.7	639.7	465.9	465.9	561	14.7	418.4	703.9
Fat	47.4	272.4	210	47.4	47.4	47.4	143.2	143.2	102.9	339.9	175.2	44.9
Cholesterol	0.05	0.21	2.1	0.05	0.05	0.05	1.65	1.65	0	2.09	0.07	0.22
Fiber	50	50	50	48.1	40	45.9	24	24	90.7	49.5	53.7	58
Insoluble Fiber	50	50	50	0.1	0	32.9	18.2	18.2	69	37.5	40.7	19.6
Soluble Fiber	0	0	0	48.1	40	12.8	5.8	5.8	21.7	12	13	38.4
g%												
Protein	16.9	22.9	17	16.9	16.9	16.9	15.8	15.8	13.7	23.3	13.2	11.6
Carbohydrate	60.6	25.4	50	62.4	60.6	60.6	53.9	53.9	55.2	2.4	48.9	68
Fat	4.5	35.2	21	4.5	4.5	4.5	16.6	16.6	10.1	55.8	20.5	4.3
Fiber	4.7	6.5	5	4.6	3.8	4.3	2.8	2.8	8.9	8.1	6.3	5.6
Insoluble Fiber	4.7	6.5	5	0	0	3.1	2.1	2.1	6.8	6.2	4.8	1.9
Soluble Fiber	0	0	0	4.6	3.8	1.2	0.7	0.7	2.1	2	1.5	3.7
kcal												
Protein	712	708	704	712	712	712	548	548	557	569	450	482
Carbohydrate	2559	787	2004	2634	2559	2559	1863	1863	2244	59	1674	2816
Fat	427	2452	1890	427	427	427	1289	1289	926	3059	1577	404
Total	3698	3947	4598	3773	3698	3698	3700	3700	3727	3687	3701	3701
Kcal/gm	3.5	5.1	4.6	3.58	3.5	3.5	4.28	4.27	3.67	6.05	4.33	3.58
Kcal %												
Protein	19	18	15	19	19	19	15	15	15	15	12	13
Carbohydrate (Digestible, Non-Fiber)	69	20	44	70	69	69	50	50	60	2	45	76
Fat	12	62	41	11	12	12	35	35	25	83	43	11
Cholesterol (mg/kg)	51.4	276.5	2096.8	51.4	51.4	51.4	1907.7	1905.7	0	3422.9	86.4	210.9
Aspartame (mg/kg)	0	0	0	0	0	0	0	1067.4	0	0	0	0

Supplementary Table 3. Clinical information for non-responder lung cancer patient donor.
Stool samples were collected prior to the patient's first ICI treatment.

Age	70 years
Sex	Male
BMI	20.8
Histology	Adenocarcinoma
PD-L1 status	≥50%
Stage	IV
First line ICI?	Yes
Treatment	Pembrolizumab

Supplementary Table 8. Clinical information for plasma metabolomics from lung cancer patients. All plasma samples were collected prior to the first immunotherapy treatment, except for n=5 (2 NR, and 3 R) which were collected at later timepoints.

	NR n=21		R n=32	
Median age	67 years		66 years	
Sex				
Male	n=12	57.1%	n=18	56.3%
Female	n=9	42.9%	n=14	43.8%
Average BMI	24.6		25.4	
Histology				
Adenocarcinoma	n=15	71.4%	n=25	78.1%
Squamous	n=6	28.6%	n=6	18.8%
Adenosquamous	n=0	0.0%	n=1	3.1%
PD-L1 status				
<1%	n=7	33.3%	n=6	18.7%
1-49%	n=6	28.6%	n=7	21.9%
>50%	n=7	33.3%	n=18	56.3%
Unknown	n=1	4.8%	n=1	3.1%
Stage				
IIA	n=0	0.0%	n=1	3.1%
IIB	n=0	0.0%	n=2	6.3%
IIIA	n=3	14.3%	n=2	6.3%
IIIB	n=2	9.5%	n=1	3.1%
IV	n=16	76.2%	n=26	81.3%
First line ICI?				
Yes	n=17	81.0%	n=27	84.4%
No	n=4	19.0%	n=5	15.6%
Treatment				
Nivolumab	n=3	14.3%	n=3	9.4%
Pembrolizumab	n=5	23.8%	n=15	46.9%
Atezolizumab	n=1	4.8%	n=0	0.0%
Nivolumab + chemotherapy	n=2	9.5%	n=3	9.4%
Pembrolizumab + chemotherapy	n=9	42.9%	n=9	28.1%
Unknown	n=1	4.8%	n=2	6.3%
Oncogene Status				
<i>EGFR</i>				
Exon 18	n=1	4.8%	n=0	0.0%
Exon 21 L858R	n=1	4.8%	n=0	0.0%
Unknown	n=5	23.8%	n=7	21.9%

Negative	n=14	66.7%	n=25	78.1%
<i>ALK</i>				
Unknown	n=3	14.3%	n=8	25.0%
Negative	n=18	85.7%	n=24	75.0%
<i>MET</i>				
Unknown	n=17	81.0%	n=8	25.0%
Negative	n=4	19.0%	n=24	75.0%
<i>ROS</i>				
Unknown	n=7	33.3%	n=11	34.4%
Negative	n=14	66.7%	n=21	65.6%
<i>KRAS</i>				
G12F	n=0	0.0%	n=1	3.1%
G12V	n=0	0.0%	n=5	15.6%
G12C	n=4	19.0%	n=4	12.5%
Q61L	n=0	0.0%	n=1	3.1%
G12A	n=1	4.8%	n=1	3.1%
Unknown	n=9	42.9%	n=12	37.5%
Negative	n=7	33.3%	n=8	25.0%
<i>BRAF</i>				
Positive	n=1	4.8%	n=0	0.0%
Unknown	n=9	42.9%	n=10	31.3%
Negative	n=11	52.4%	n=22	68.8%
<i>TP53</i>				
Unknown	n=19	90.5%	n=26	81.3%
Negative	n=2	9.5%	n=6	18.8%

Supplementary Table 9. Clinical information for FMT donor lung cancer patients. All fecal samples were collected prior to the first ICI treatment.

	BMI < 25 n=3		BMI ≥ 25 n=6	
Median age	51 years		63 years	
Sex				
Male	n=0	0%	n=1	16.7%
Female	n=3	100%	n=5	83.3%
Average BMI	21.4		29	
Histology				
Adenocarcinoma	n=3	100%	n=6	100%
PD-L1 status				
<1%	n=0	0%	n=3	50%
1-49%	n=1	33.3%	n=0	0%
>50%	n=2	66.7%	n=3	50%
Stage				
IIIA	n=1	33.3%	n=0	0%
IV	n=2	66.7%	n=6	100%
First line ICI?				
Yes	n=1	33.3%	n=3	50%
No	n=2	66.7%	n=3	50%
Treatment				
Nivolumab	n=1	33.3%	n=2	33.3%
Pembrolizumab	n=1	33.3%	n=4	66.7%
Pembrolizumab + Chemotherapy	n=1	33.3%	n=0	0%
Oncogene Status				
<i>EGFR</i>				
Unknown	n=0	0%	n=2	33.3%
Negative	n=3	100%	n=4	66.7%
<i>ALK</i>				
Negative	n=3	100%	n=6	100%
<i>MET</i>				
Unknown	n=3	100%	n=5	83.3%
Negative	n=0	0%	n=1	16.7%
<i>ROS</i>				
Unknown	n=2	66.7%	n=3	50%
Negative	n=1	33.3%	n=3	50%
<i>KRAS</i>				
G12C	n=1	33.3%	n=0	0%
Unknown	n=1	33.3%	n=1	16.70%

Negative	n=1	33.3%	n=5	83.3%
<i>BRAF</i>				
Unknown	n=1	33.3%	n=4	66.7%
Negative	n=2	66.7%	n=2	33.3%
<i>TP53</i>				
Unknown	n=3	100%	n=6	100%

Supplementary Table 10. Weight-adjusted anti-PD-1 dosing at 10 mg/kg of body weight*.

Diet	Model	Mean body weight (g)	Mean anti-PD-1 dose (µg)
Japanese	15 week	22.8	228
Pectin	15 week	27.6	276
Inulin	15 week	29.4	294
Low Fat	15 week	27.0	270
Psyllium	15 week	29.9	299
Vegan	15 week	35.7	357
American	15 week	35.5	334
Ketogenic	15 week	33.4	355
Aspartame	15 week	39.3	393
Mediterranean	15 week	40.1	401
Western	15 week	39.5	395
High Fat	15 week	45.5	455
Psyllium	3 week	30.6	306
High Fat	3 week	37.2	372

**Mean values are used here as an illustrative example; actual dosing was calculated for each individual cohort, based on corresponding body weights.*

Supplementary Table 11. Flow cytometry antibodies.

Antibody	Fluorophore	Clone	Dilution	Vendor	Catalogue
CD45	APC/Fire 810	30-F11	200	BioLegend	103174
CD3	FITC	17A2	200	BioLegend	100203
CD3	Spark YG 570	17A2	400	BioLegend	100266
CD3	Brilliant Ultra Violet 805	17A2	100	eBioscience	368-0032-82
CD4	PE/Fire 700	GK1.5	200	BioLegend	100484
CD8	PE/Fire 640	53-6.7	200	BioLegend	100790
PD-1	APC/Cy7	29F.1A12	200	BioLegend	135224
CD19	PE/Cy5	6D5	100	BioLegend	115510
CD11a	Percp-Cy5.5	M17/4	100	BioLegend	101123
CD11b	Brilliant Violet 570	M1/70	100	BioLegend	101233
CD11c	Brilliant Violet 750	N418	200	BioLegend	117357
CD44	APC	IM7	100	BioLegend	103011
MHC II	APC	M5/114.15.2	100	BioLegend	107614
Ly6G	Alexa Fluor 700	IA8	200	BioLegend	127622
Ly6C	Brilliant Violet 421	HK1.4	200	BioLegend	128031
Foxp3	Pacific Blue	MF-14	400	BioLegend	126410
IFN γ	Brilliant Violet 711	XMG1.2	50	BioLegend	505835
TNF α	Alexa Fluor 700	MP6-XT22	100	BioLegend	506338
Ki67	PE-Dazzle 594	16A8	100	BioLegend	652428
Isotype	PE-Dazzle 594	RTK2758	100	BioLegend	400558