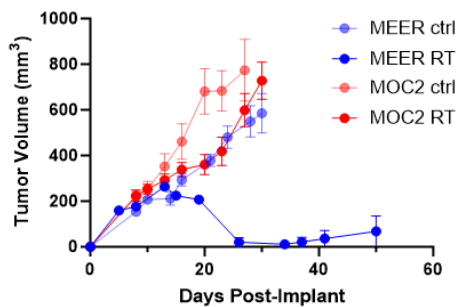


A

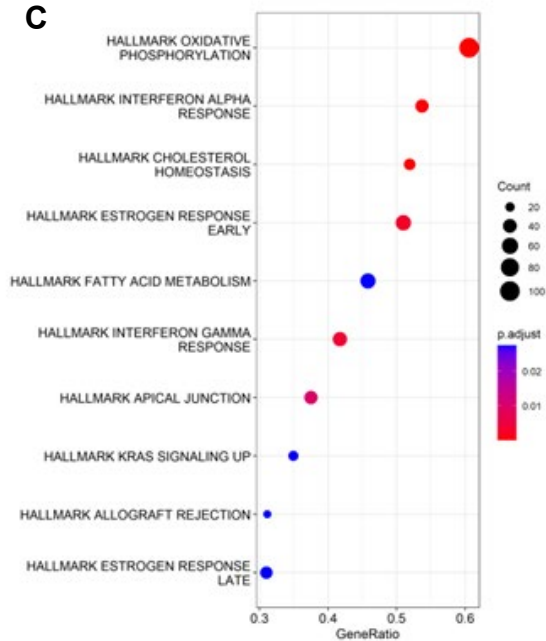
MEER vs MOC2



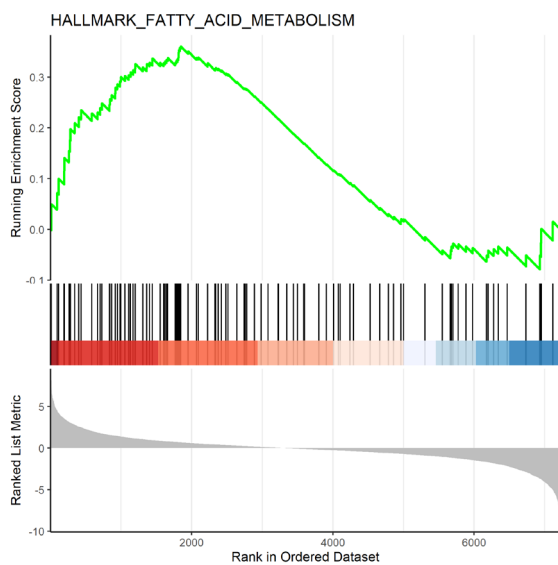
B



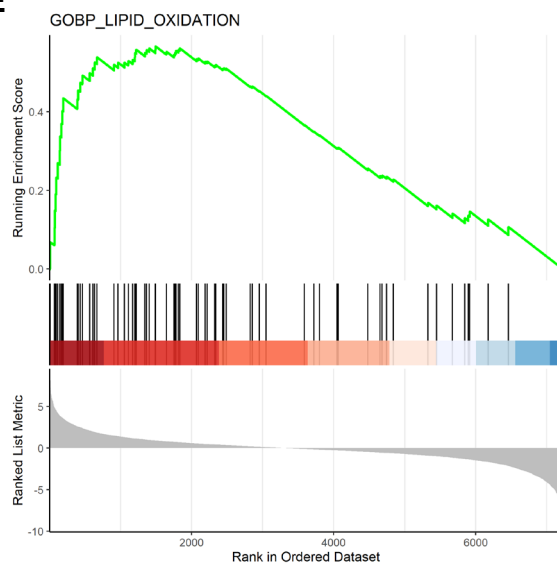
C



D



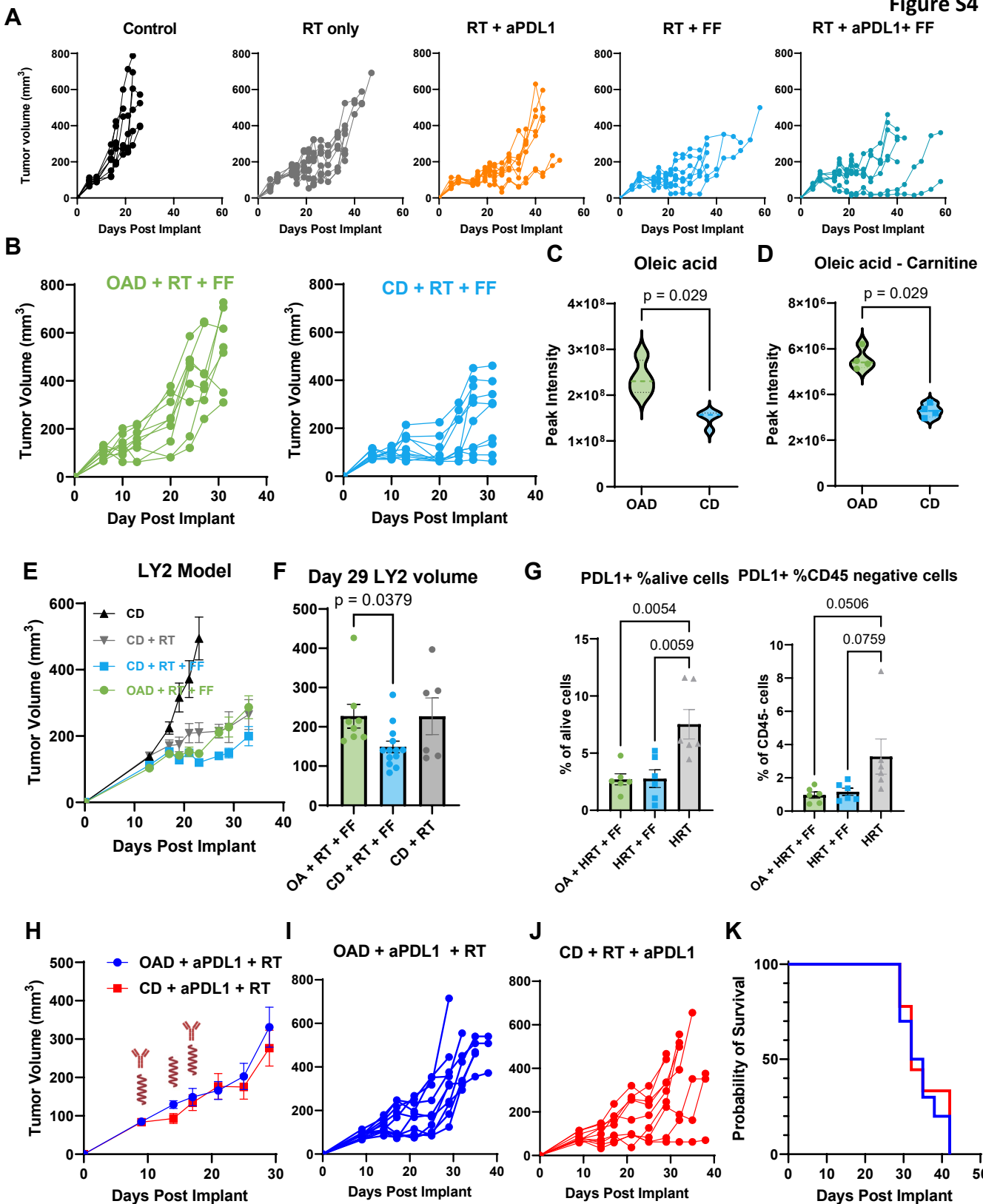
E

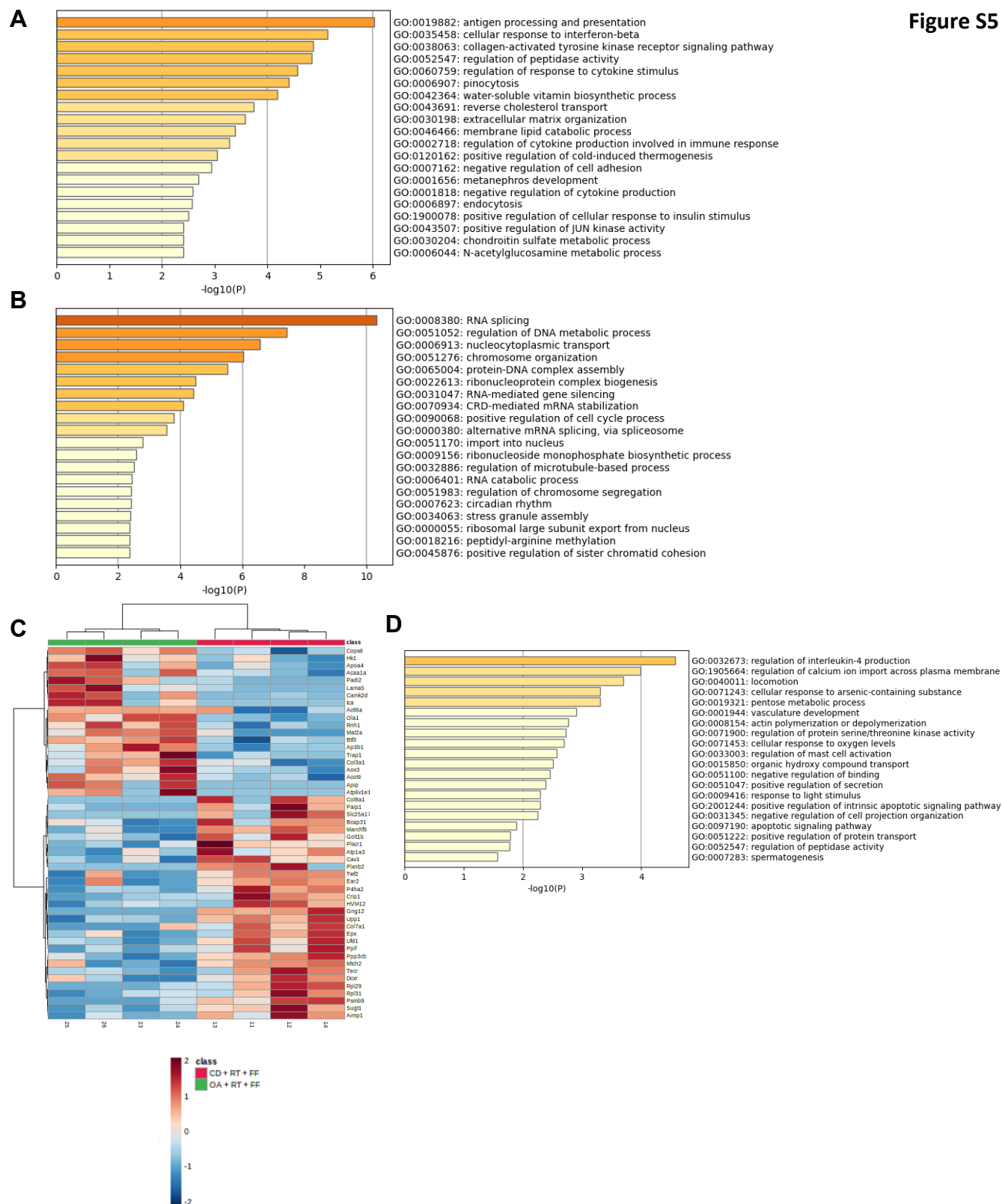


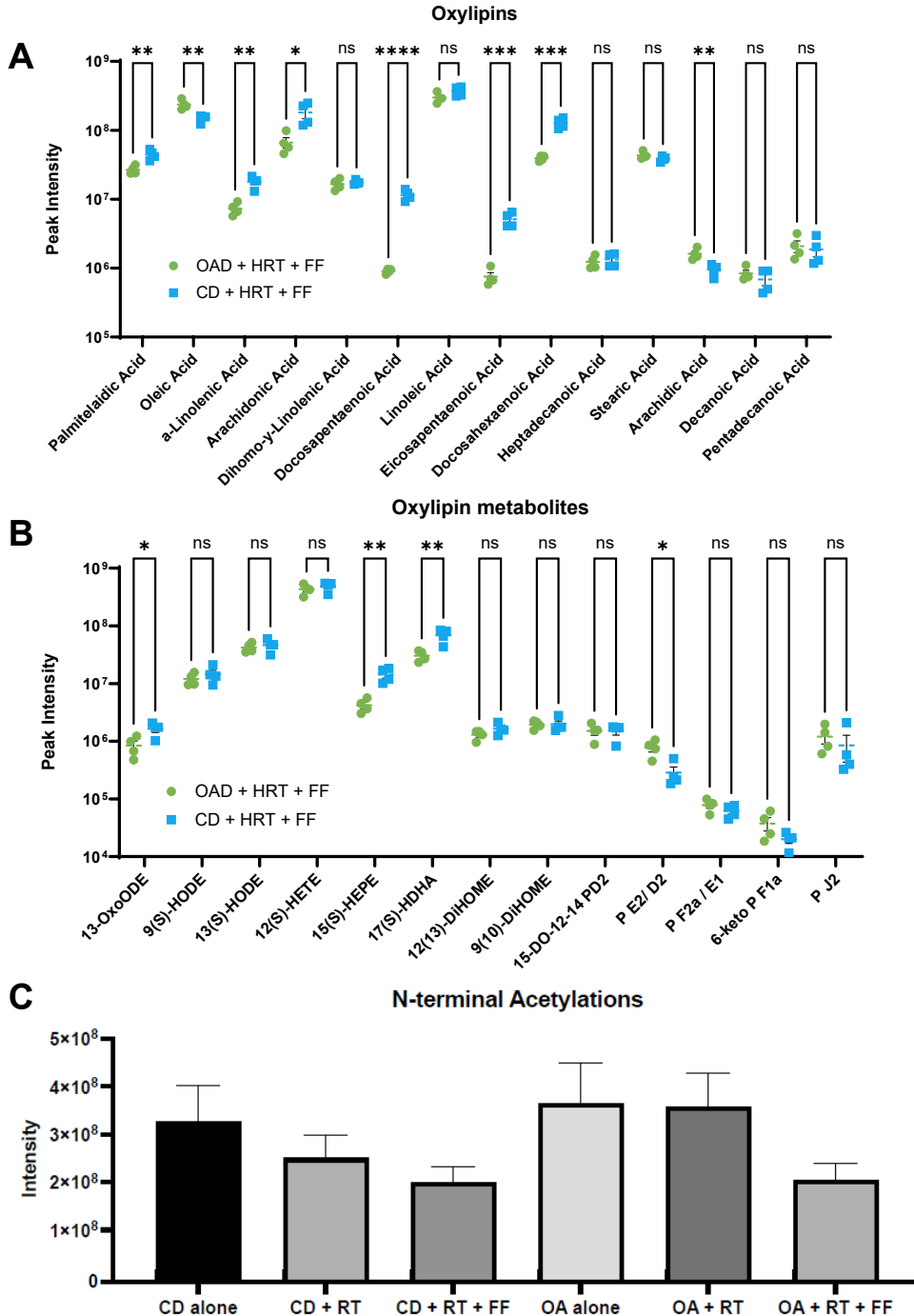
	Control diet ¹	Oleic acid diet ²
Protein (%kcal)	24%	20%
Carbohydrate (%kcal)	60%	35%
Source	Wheat, corn	Wheat
Fat (%kcal)	16%	45%
% Saturated	16.7%	6.7%
% Monounsaturated	22.9%	85.4%
% Polyunsaturated	60.4%	7.9%
Source	Soybean oil	High oleic acid sunflower oil
Oleic acid (% weight)	1.1%	19.7%
Oleic acid (% kcal)	3.67% of total kcal	37.6% of total kcal
Linoleic acid (% weight)	2.6%	1.8%
Linolenic acid (% weight)	0.3%	0.02%
Palmitic acid (% weight)	0.6%	0.8%
Stearic acid (% weight)	0.1%	0.8%
Kcal/gram chow	3.1 kcal/g	4.73 kcal/g

¹ Teklad Diets Global Soy Protein-Free Extruded Rodent Diet 2020X

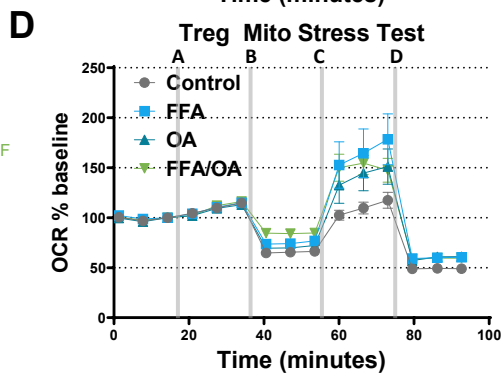
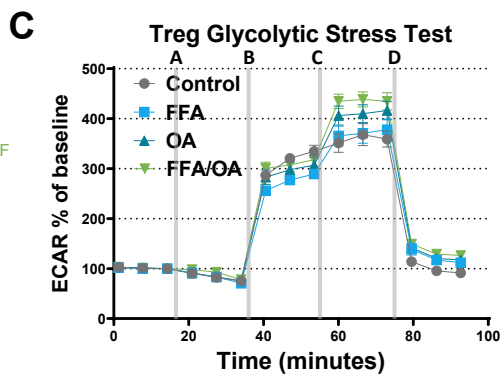
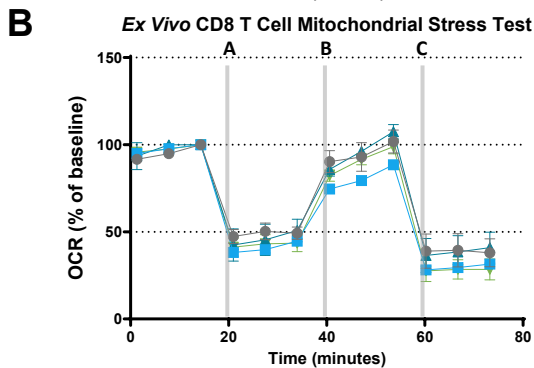
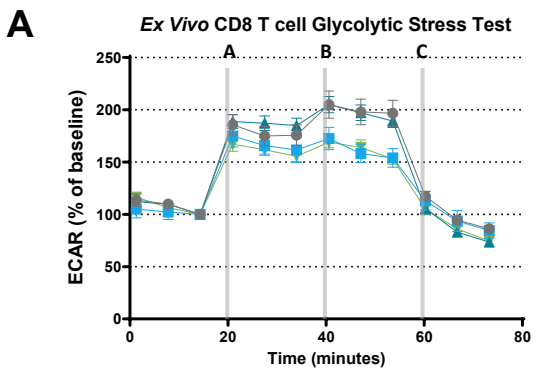
² Research Diets D22083002 Rodent Diet with 45% kcal Fat from High Oleic Sunflower Oil and Wheat Starch with Green Dye







Comparison	P-value	Comparison	P-value
CD alone vs. CD + HRT	0.6246	CD + HRT vs. OA + HRT + FF	0.9282
CD alone vs. CD + HRT + FF	0.2047	CD + HRT + FF vs. OA alone	0.055
CD alone vs. OA alone	0.9796	CD + HRT + FF vs. OA + HRT	0.074
CD alone vs. OA + HRT	0.993	CD + HRT + FF vs. OA + HRT + FF	>0.9999
CD alone vs. OA + HRT + FF	0.2386	OA alone vs. OA + HRT	>0.9999
CD + HRT vs. CD + HRT + FF	0.8945	OA alone vs. OA + HRT + FF	0.0662
CD + HRT vs. OA alone	0.2241	OA + HRT vs. OA + HRT + FF	0.0887
CD + HRT vs. OA + HRT	0.2904		



Supplemental Figure 1

A-F: Log₂ CPM figures of data from figure 1A with Mann-Whitney test p-values generated. Responders (R) shown in red, non-responders (NR) shown in grey.

G-I: TCGA H&N data for overall survival based on high or low genetic expression of PPARGC1A (G), CPT1C (H), or PDK1 (I).

J: Trypan blue viability assay comparing surviving fraction of MOC2 HPV-unrelated HNC model cancer cells at 24 hours after culturing with either 0.1% DMSO control, 100µM FF or 100µM OA.

K: Baseline serum oleic acid of responders or non-responders from Darragh, et al.

L: ROC graph for baseline oleic acid as a predictor of response from Darragh, et al. (AUC of 0.885).

M&N: Extracellular flux analyses measuring normalized ECAR (mean and SEM, n=5 replicates) of MOC2 cancer cells (M) or LY2 cancer cells (N) after injection of specified drug at the third time point: DMSO control (grey), 100µM FF (light blue), 100µM OA (light green), or combination 100µM FF and OA (dark green).

O: ATP production rate assay performed on an Agilent Seahorse for surviving MOC2 cells 24h after irradiation with 0 Gy or 8 Gy. Drug injections for this assay with final concentrations were 1.5µM oligomycin (A), and 0.5 µM rotenone and antimycin A (B).

Supplemental Figure 2

A: Tumor volume curves comparing mice implanted with MEER (blue) or MOC2 (red) cell lines and treated with RT (opaque) or without RT (translucent).

B-E: GSEA graphics derived from tumor proteomics from MEER vs MOC2 implanted mice that underwent RT.

Supplemental figure 3: comparison of diets

Supplemental Figure 4

A: Spaghetti plots of tumor volume for each group from Figure 2A.

B: Spaghetti plots of the mice fed either the OAD or CD and then treated with HRT and FF (Figure 2H)

C-D: Serum metabolomic data shown as violin plots of mice on the OAD (green) vs. CD (blue) regarding levels of OA (C) and OA attached to carnitine (D). Mann-Whitney test of means used to generate p-values.

E-F: Repeated experiment from figure 3 in the LY2 murine HNC model. FF was started on day 5 after the 1st HRT fraction. HRT delivered as 24 Gy in 3 fractions on day 13, 17 and 21.

G: Flow cytometry gating for PD-L1 positivity on all alive cells as well as CD45 negative alive cells

H-K: Tumor volume curves for oleic acid diet (OAD) vs. control diet (CD) with aPDL1 and HRT. Spaghetti plots for this experiment (F,G) and survival curve (H).

Supplemental Figure 5

A: GO pathways up in HRT alone compared to control

B: GO pathways down in HRT alone compared to control

C: Unsupervised clustering heatmap of top X proteins of CD + HRT + FF vs OAD + HRT + FF

D: GO pathways upregulated in OAD + HRT + FF in comparison to CD + HRT + FF

Supplemental Figure 6

A: Oxylipin profiles comparing OAD + HRT + FF to CD + HRT + FF

B: Oxylipin metabolite profiles comparing OAD + HRT + FF to CD + HRT + FF

C: N-terminal acetylation profiles shown for CD, CD + HRT, CD + HRT + FF, OAD, OAD + HRT, and OAD+HRT+FF. P-values shown from Tukey's multiple comparison test between groups.

Supplemental Figure 7

A: Glycolytic stress test of ex vivo CD8 T cells harvested from mice on the OAD treated with HRT (teal) or with HRT and FF (green), or on the CD and treated with HRT and FF (blue) or HRT alone (grey). The final drug concentration injections were as follows: 10mM glucose (A), 1.5 μ M oligomycin (B), 50mM 2-DG (C). Values shown are percent of baseline ECAR with SEM.

B: Mitochondrial stress test of ex vivo CD8 T cells harvested from mice on the OAD treated with HRT (teal) or with HRT and FF (green) or on the CD and treated with HRT and FF (blue) or HRT alone (grey). Drug injections include 1.5 μ m oligomycin (A), 1.5 μ m FCCP (B), and 0.5 μ m rotenone/antimycin A (C). Data shown is percent of baseline OCR with standard error.

C: Glycolytic stress test of cultured Tregs with final dilution of injections of experimental drug (A, DMSO, FFA, OA, or FFA/OA), 10 mM glucose (B), 1.5 μ m oligomycin (C), and 50 mM 2-DG (D). Data shown is percent of baseline ECAR with standard error.

D: Mitochondrial stress stress test of cultured Tregs with final dilution of injections of experimental drug (A, DMSO, FFA, OA, or FFA/OA), 1.5 μ m oligomycin (B), 1.5 μ m FCCP (C), and 0.5 μ m rotenone/antimycin A (D). Data shown is percent of baseline OCR with standard error.