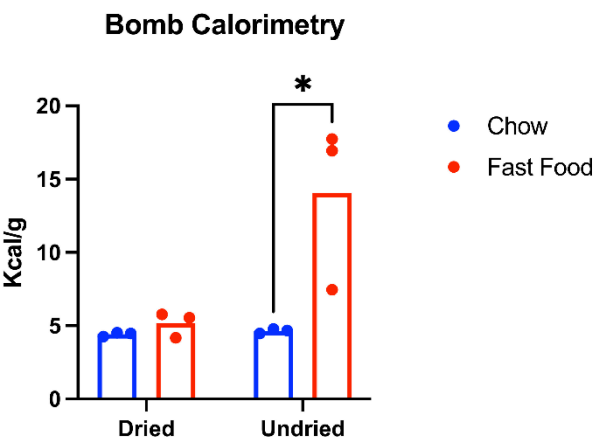
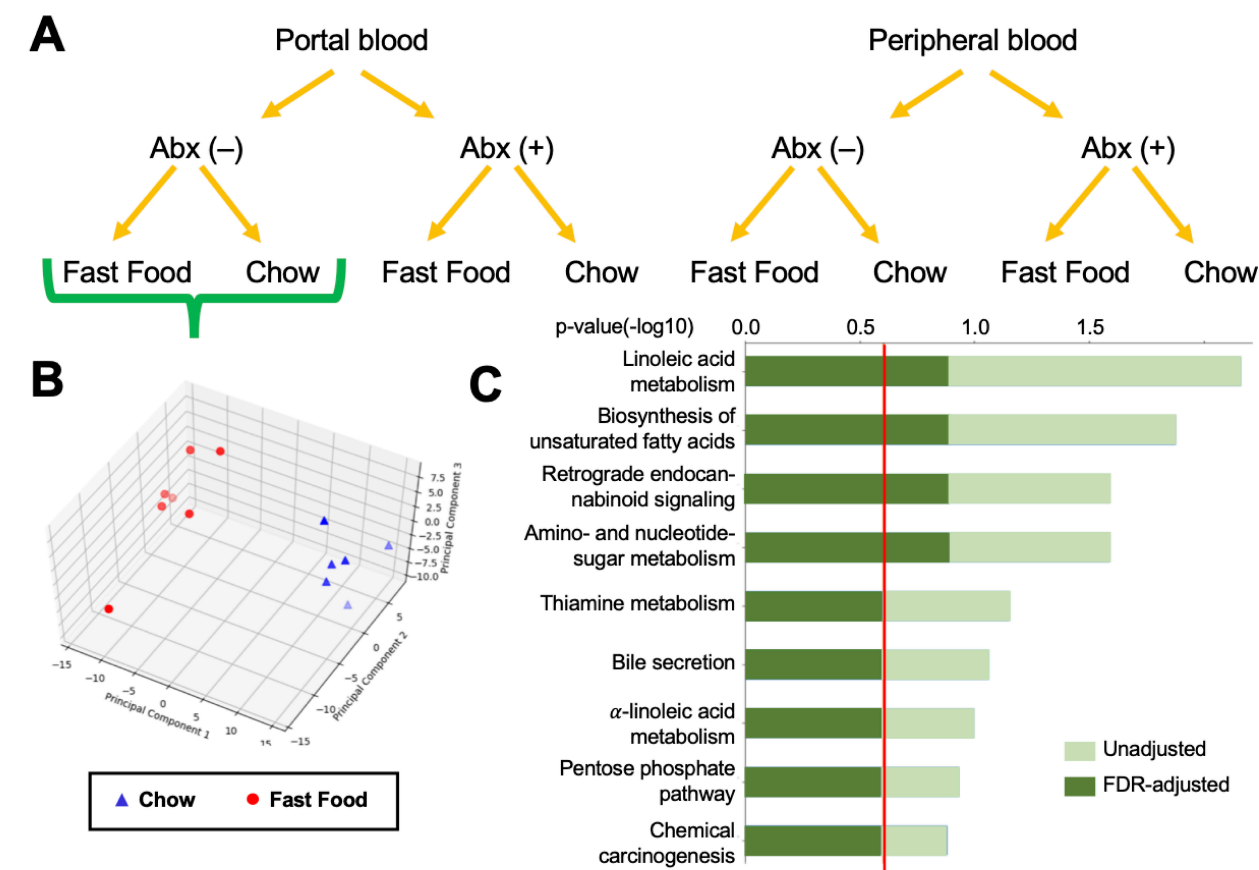
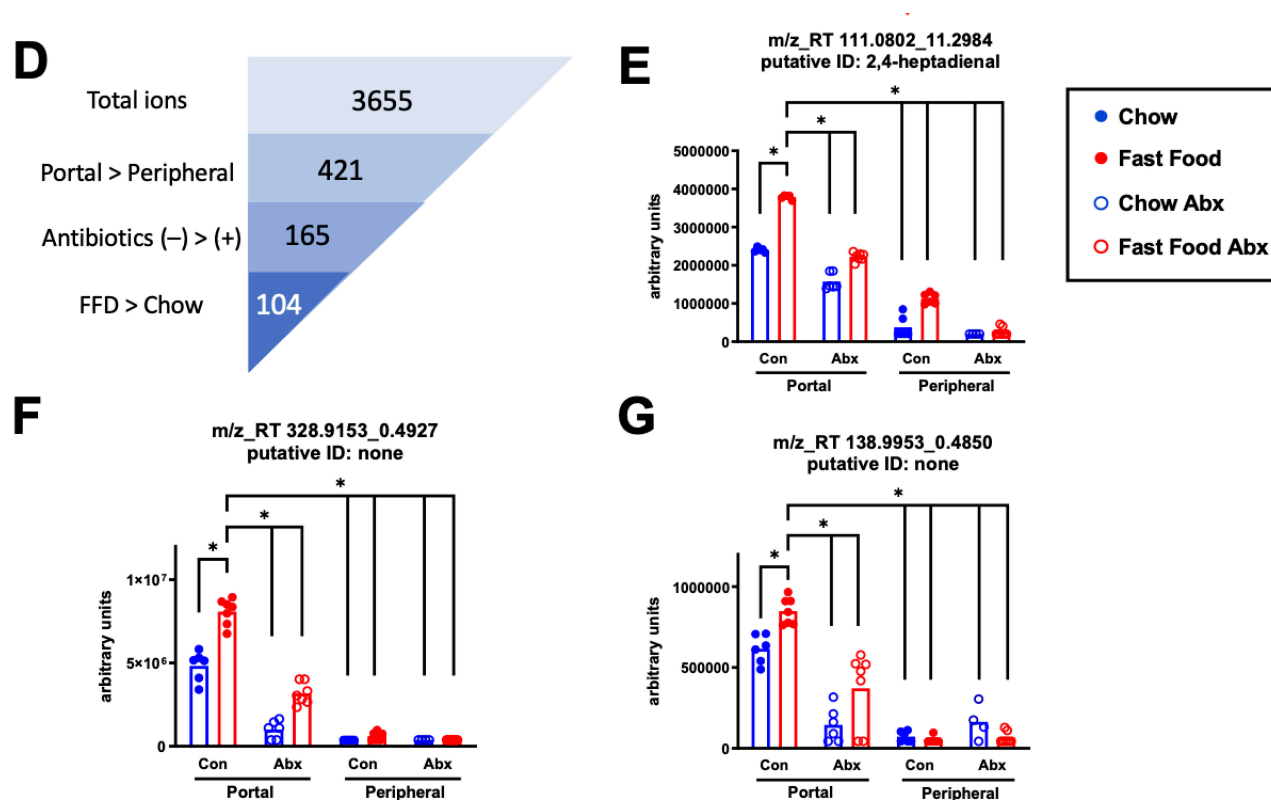


Supplementary Figures and Tables

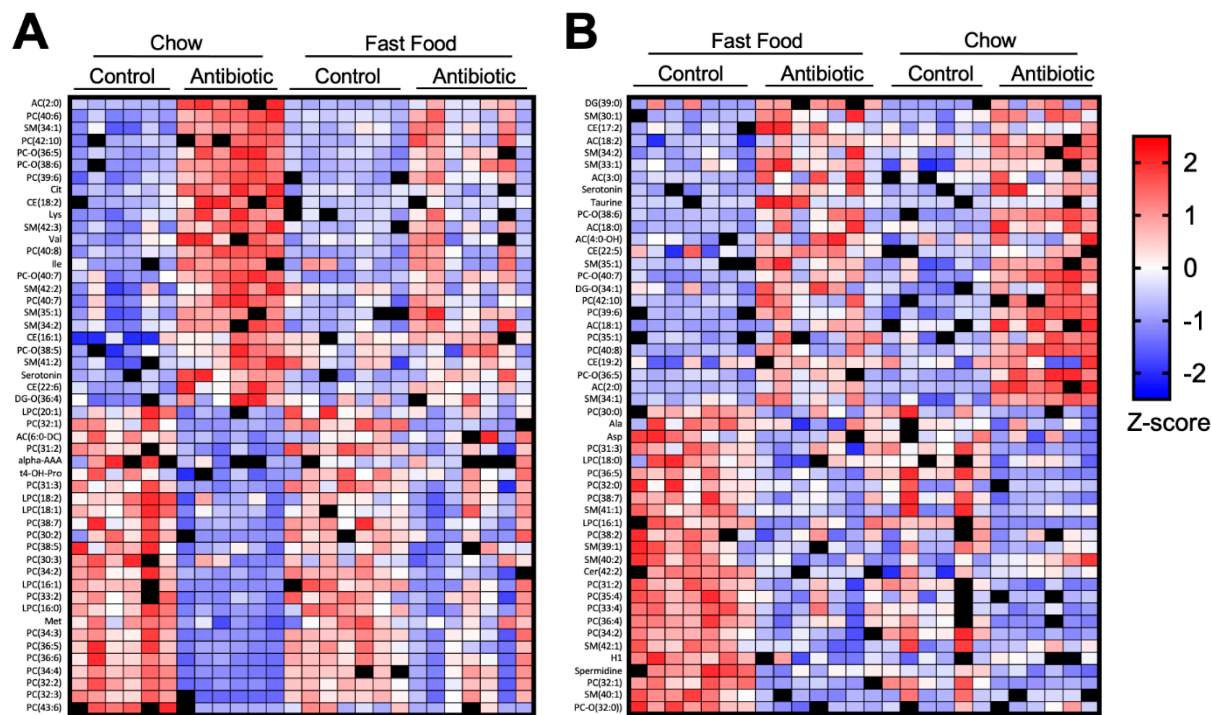


**Supplementary Figure S1. Bomb Calorimetry Reveals Caloric Density of Chow and Fast Food Slurries.** Samples of the chow and fast food slurries were dried down before oxygen bomb calorimetry. The heat of combustion is recorded as calories/gram of dry weight. The undried calorie density is then back-calculated based on the original undried weight of each sample. 3 samplings of each diet were analyzed in duplicate with averaged values plotted. Statistical analysis was performed using two-way ANOVA with Tukey’s multiple comparisons test and significance is displayed for differences within type of sample preparation. \*  $P<0.05$ .

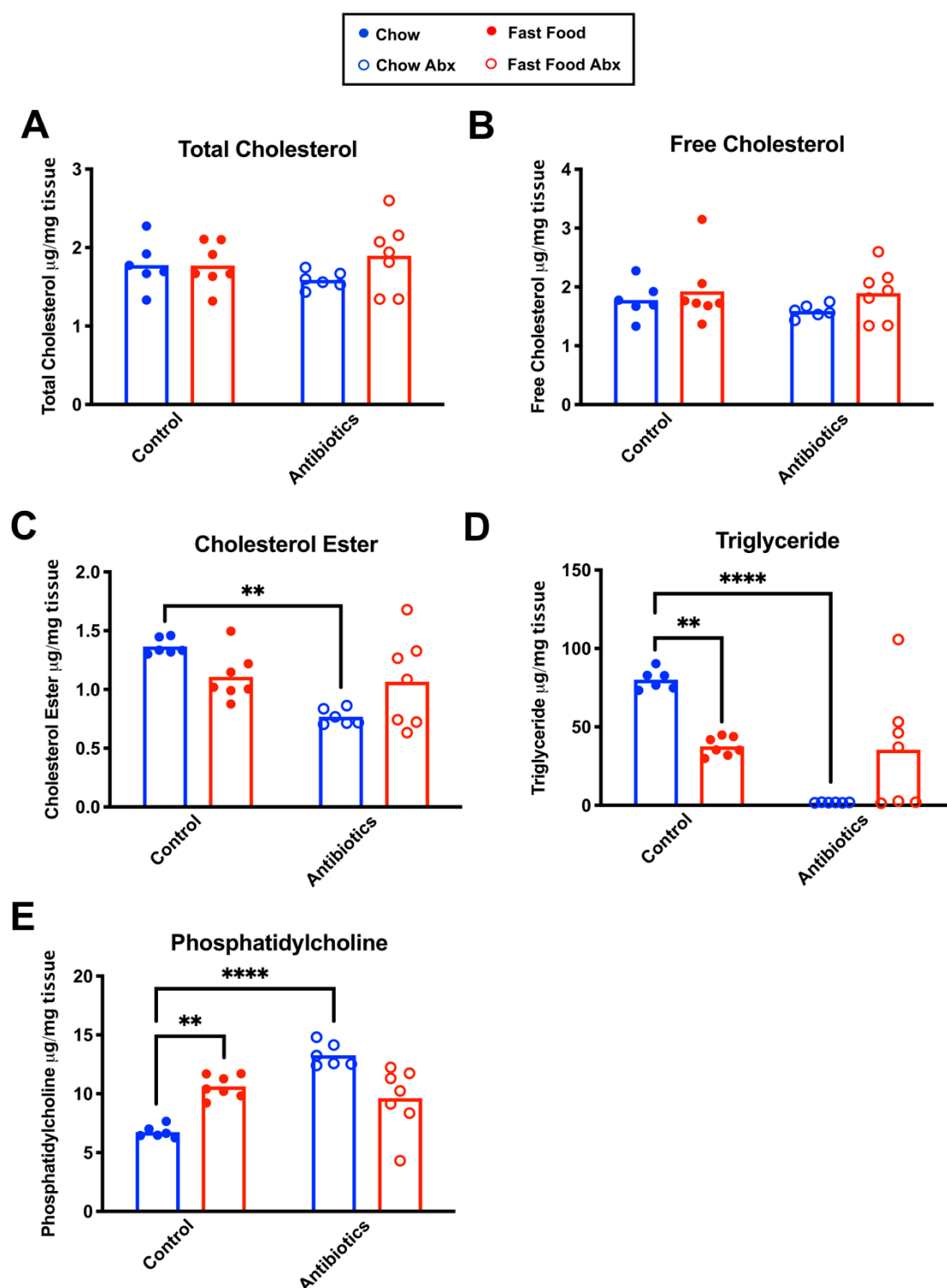




**Supplementary Figure S2. Plasma Metabolomic Signatures – Positive Ionization Mode.** (A) 6-week old male C57BL6/J mice were randomly assigned to control drinking water or drinking water supplemented with broad spectrum antibiotics for two weeks. Following an overnight fast, mice were given a single oral gavage of either chow slurry or fast food slurry and sacrificed exactly 4 hours later. Portal and peripheral blood were taken for plasma and LCMS-based untargeted metabolomics was performed in the positive ESI mode. (B) PCA and (C) KEGG pathway analysis of portal blood from chow versus fast food gavage of control water mice generated using MetaboLyzer. (D) Multiple two-group comparisons were made to identify ions enriched within the portal blood that were greater in the control water, fast food gavage group. 104 ions satisfy all criteria. (E) The comparison tests performed are shown with overlying horizontal comparison bars. Ion mass charge\_retention time (m/z\_RT) 111.0802\_11.2984 satisfies all criteria and is putatively identified as 2,4-heptadienal. (F) Ions m/z\_RT 328.9153\_0.4927 and (G) 138.9953\_0.4850 satisfy all criteria but do not have a putative identification. \* $q < 0.10$  (Mann-Whitney U test). Con = control; Abx = antibiotics.  $n = 4-7$  per group.



**Supplementary Figure S3. A Single Fast Food Meal Alters the Hepatic Phospholipid Metabolism in a Gut Microbe-Dependent Manner.** 6-week old male C57BL6/J mice were randomly assigned to control drinking water or drinking water supplemented with broad spectrum antibiotics for two weeks. Following an overnight fast, mice were given a single oral gavage of either chow slurry or fast food slurry and the liver was harvested exactly 4 hours later for targeted metabolomics. Shown is a heatmap of the top 50 differentially expressed molecules across drinking type within (A) the chow diet groups, or within (B) the fast food diet groups. Groups listed above with samples contained within columns; row metabolite identification listed on left; z-score normalized values scaled by row (red = increase, blue = decrease, black = missing value or excluded outlier); order of metabolites (vertically) determined solely by z-score differences across the first two columns. Abx = antibiotics, AC, acylcarnitine, PC = phosphatidylcholine, SM, sphingomyelin, CE = cholesteryl ester, DG = diglyceride, LPC = lysophosphatidylcholine, Cer = ceramide, alpha-AAA = alpha-aminoadipic acid. *n* = 6-7 per group.



**Supplementary Figure S4. A Single Fast Food Meal Alters the Major Hepatic Lipid Classes in a Gut Microbe-Dependent Manner.** 6-week old male C57BL6/J mice were randomly assigned to control drinking water or drinking water supplemented with broad spectrum antibiotics for two weeks. Following an overnight fast, mice were given a single oral gavage of either chow slurry or fast food slurry and the liver was harvested exactly 4 hours later for enzymatic determination of (A) total cholesterol, (B) free cholesterol, (C) cholesterol esters, (D) total hepatic triglycerides, and (E) phosphatidylcholine. Statistical analysis was performed using two-way ANOVA with Tukey's multiple comparisons test and significance is displayed for

differences within each meal-type between gut microbiota groups (control vs antibiotic ablated) and within gut microbiota groups, between meal type. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$ .  $n = 6-7$  per group.

**Supplementary Table S1. Nutritional information for oral gavage slurry components.** Nutritional information was obtained from the official website of each fast food chain, as well as Teklad for the chow diet.

	Food	Calories	Total Fat (g)	Saturated Fat (g)	Trans Fat (g)	Cholesterol (mg)	Sodium (mg)	Carbohydrates (g)	Dietary Fiber (g)	Sugars (g)	Protein (g)	Calories (kcal/g)	Protein (% kcal)	Carbohydrate (% kcal)	Fat (% kcal)
McDonald's	Double Quarter Pounder with Cheese	740	42	19	2.5	155	1380	40	3	9	48				
	Chicken Tenders	326	14.3	1.6	<i>no data available</i>	<i>no data available</i>	1400	28	0.4	0.14	21				
	French Fries (Large)	500	25	3.5	0	0	350	63	6	0	6				
	Chocolate Milkshake	580	14	8	1	50	250	102	1	84	13				
Burger King	Whopper with Cheese	740	46	16	2	115	1340	50	2	11	32				
	Original Chicken Sandwich	660	40	7	0	75	1170	48	2	5	28				
	Cheesy Tots (8 piece)	316.2	15.6	4.7	0.2	15.7	794.5	34.6	3	0.8	9.3				
	French fries (Large)	430	18	2.5	0	0	410	66	7	2	5				
Taco Bell	Beef Crunchy Taco	170	9	3.5	0	25	310	13	3	<1	8				

	Chicken Quesadilla	510	26	12	0.5	75	1250	38	4	2	27				
	5 Layer Burrito	490	18	7	0	30	1250	63	9	5	18				
Coca Cola	Coca Cola (20 Oz.)	240	0	0	0	0	75	65	0	65	0				
	Rodent Diet											3.1	23.5	59.4	17.1

**Supplementary Table S2. Ingredients list for oral gavage slurry components.** The ingredients of each dietary component are listed as described on the official website of each fast food chain.

	Food	Ingredients
McDonald's	Double Quarter Pounder with Cheese	<b>Quarter Pound 100% Beef Patty:</b> 100% Pure USDA 4 oz. Inspected Beef; No Fillers, No Extenders. Prepared With Grill Seasoning (Salt, Black Pepper). <b>Quarter Pound Bun:</b> Enriched Flour (Wheat Flour, Malted Barley Flour, Niacin, Reduced Iron, Thiamine Mononitrate, Riboflavin, Folic Acid), Water, Sugar, Yeast, Soybean Oil, Contains 2% or Less: Sesame Seeds, Salt, Wheat Gluten, Dextrose, Guar Gum, Vinegar, Vegetable Proteins (Pea, Potato, Rice), Sunflower and/or Canola Oil, Maltodextrin, Natural Flavors, May Contain One or More Dough Conditioners (DATEM, Ascorbic Acid, Mono and Diglycerides, Enzymes), Modified Food Starch. Contains: Wheat. <b>Pasteurized Process American Cheese:</b> Milk, Cream, Water, Sodium Citrate, Salt, Cheese Cultures, Citric Acid, Enzymes, Soy Lecithin, Color Added. Contains: Milk, Soy. <b>Ketchup:</b> Tomato Concentrate from Red Ripe Tomatoes, Distilled Vinegar, High Fructose Corn Syrup, Corn Syrup, Water, Salt, Natural Flavors. <b>Pickle Slices:</b> Cucumbers, Water, Distilled Vinegar, Salt, Calcium Chloride, Alum, Potassium Sorbate (Preservative), Natural Flavors, Polysorbate 80, Extractives of Turmeric (Color). Onions. <b>Mustard:</b> Distilled Vinegar, Water, Mustard Seed, Salt, Turmeric, Paprika, Spice Extractive.

	Chicken Tenders	Chicken meat, water, toasted wheat crumb, sodium phosphates, corn maltodextrin, flavour (rosemary extract), salt, seasoning [salt, sugar, spice, yeast extract, onion powder, disodium inosinate and disodium guanylate, flavour (rosemary extract), corn maltodextrin, modified corn starch], polysorbate 80, chicken fat (soybean oil), silicon dioxide, breaded with: wheat flour, toasted wheat crumbs, water, corn starch, salt, wheat starch, onion powder, garlic powder, spices, baking powder, dehydrated parsley, sodium aluminum phosphate, cooked in 100% vegetable oil (canola oil, corn oil, soybean oil, hydrogenated soybean oil, citric acid, dimethylpolysiloxane). Contains: Wheat. May contain milk.
	French Fries	Potatoes, Vegetable Oil (canola Oil, Corn Oil, Soybean Oil, Hydrogenated Soybean Oil, Natural Beef Flavor [wheat And Milk Derivatives]*), Dextrose, Sodium Acid Pyrophosphate (maintain Color), Salt. *natural Beef Flavor Contains Hydrolyzed Wheat And Hydrolyzed Milk As Starting Ingredients. Contains Wheat, Milk.
	Chocolate Milkshake	<b>Vanilla Ice Milk:</b> Milk ingredients, sugar, modified milk ingredients, glucose, mono and diglycerides, guar gum, dextrose, carrageenan, cellulose gum, natural flavour, sodium hydroxide, sodium carbonate. Triple <b>Thick Milkshake Chocolate Syrup:</b> Sugar, glucose, water, glycerol, cocoa, fruit and vegetable juice (colour), natural flavours (plant source), salt, potassium sorbate.



Burger King	Whopper with Cheese	<p><b>Sesame Seed Buns:</b> Enriched Wheat Flour (Wheat Flour, Malted Barley Flour, Niacin, Iron, Thiamin Mononitrate, Riboflavin, Folic Acid), Water, High Fructose Corn Syrup, Yeast, Sesame Seeds, Contains 2% or less of the following: Soybean Oil, Salt, Yeast Nutrients (Monocalcium Phosphate, Calcium Sulfate), Dough Conditioners (Monoglycerides, DATEM), Calcium Propionate (Preservative), Wheat Starch. <b>WHOPPER® Patties:</b> 100% USDA inspected Ground Beef (Fire-Grilled). <b>American cheese (pasteurized process):</b> Cultured Milk, Water, Cream, Sodium Citrate, Salt, Sorbic Acid (Preservative), Sodium Phosphate, Artificial Color, Enzymes, Acetic Acid, Soy Lecithin. <b>Ketchup:</b> Tomato concentrate made from Red Ripe Tomatoes, Distilled Vinegar, High Fructose Corn Syrup, Corn Syrup, Salt, Spice, Onion Powder, Natural Flavoring, Natural flavoring is plant in origin. <b>Mayonnaise:</b> Soybean Oil, Eggs, Water, Distilled Vinegar, Contains 2% or Less of the Following: Egg Yolks, Salt, Sugar, Lemon Juice Concentrate, Natural Flavor, Calcium Disodium EDTA Added to Protect Flavor, Dehydrated Garlic, Dehydrated Onion, Paprika or Paprika Oleoresin. <b>Pickles:</b> Cucumbers, water, vinegar, salt, calcium chloride, 1/10 of 1% sodium benzoate (preservative), natural spice extractives, extractives of turmeric, polysorbate 80, propylene glycol and fd&amp;c yellow #5.</p>
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	Original Chicken Sandwich	<p><b>Sesame Seed Buns:</b> Enriched Wheat Flour (Wheat Flour, Malted Barley Flour, Niacin, Iron, Thiamin Mononitrate, Riboflavin, Folic Acid), Water, High Fructose Corn Syrup, Yeast, Sesame Seeds, Contains 2% or less of the following: Soybean Oil, Salt, Yeast Nutrients (Monocalcium Phosphate, Calcium Sulfate), Dough Conditioners (Monoglycerides, DATEM), Calcium Propionate (Preservative), Wheat Starch. <b>Breaded Original Chicken Patty (Fried):</b> Chicken Breast with Rib Meat, Water, Salt and Monosodium Glutamate. Breaded with: Bleached Wheat Flour, Salt, Spices, Partially Hydrogenated Vegetable Oil (Soybean and/or Cottonseed), Dried Whey, Monosodium Glutamate, Yeast, Dehydrated Sweet Pepper, Onion Powder, Garlic Powder, Dextrose, Leavening (Monocalcium Phosphate, Sodium Bicarbonate). BATTERED WITH : Water, Bleached Wheat Flour, Leavening (Sodium Acid Pyrophosphate, Sodium Bicarbonate), Salt, Corn Starch, Oat Flour and Natural Flavoring.</p> <p><b>Mayonnaise:</b> Soybean Oil, Eggs, Water, Distilled Vinegar, Contains 2% or Less of the Following: Egg Yolks, Salt, Sugar, Lemon Juice Concentrate, Natural Flavor, Calcium Disodium EDTA Added to Protect Flavor, Dehydrated Garlic, Dehydrated Onion, Paprika or Paprika Oleoresin.</p>
	Cheesy Tots	<p><b>Cheesy Tots</b> Potatoes, Wheat Flour, Pasteurized Processed Cheese (Cheddar Cheese [Milk, Cheese Culture, Salt, Enzymes], Water, Milkfat, Sodium Phosphate, Sodium Hexametaphosphate, Salt, Sorbic Acid [preservative], Color [Annatto, Paprika]), Vegetable Oil (Contains One or More of the Following: Canola, Palm, Soybean, Sunflower), Mozzarella Cheese (Pasteurized Milk, Non-Fat Milk, Cultures, Salt, Enzymes), Enriched Wheat Flour (Flour, Niacin, Iron, Thiamin Mononitrate, Riboflavin, Folic Acid), Salt, Modified Potato Starch, Sugar, Natural Cheese Flavor, Dextrin, Dehydrated Potato, Yeast, Disodium Dihydrogen Pyrophosphate (to promote color retention).</p>
	French fries	<p><b>French Fries (Fried):</b> Potatoes, Soybean Oil or Canola and Palm Oil, Modified Potato Starch, Rice Flour, Potato Dextrin, Salt, Leavening (Disodium Dihydrogen Pyrophosphate, Sodium Bicarbonate), Dextrose, Xanthan Gum, Sodium Acid Pyrophosphate added to preserve natural color.</p>

Taco Bell	Beef Crunchy Taco	<p><b>Seasoned Beef:</b> Beef, water, seasoning [cellulose, chili pepper, maltodextrin, salt, oats, soy lecithin, spices, tomato powder, sugar, onion powder, citric acid, natural flavors (including smoke flavor), torula yeast, cocoa, disodium inosinate &amp; guanylate, dextrose, lactic acid, modified corn starch], salt, sodium phosphates. <b>Contains:</b> Soy, Iceberg Lettuce: Fresh iceberg lettuce [certified vegan], <b>Taco Shell:</b> Ground corn, vegetable oil (soybean, corn and/or cottonseed oil), oat fiber. [certified vegan], <b>Cheddar Cheese:</b> Cheddar cheese (cultured pasteurized milk, salt, enzymes, annatto (VC)), anti-caking agent. <b>Contains:</b> Milk [certified vegetarian]</p>
	Chicken Quesadilla	<p><b>Flour Tortilla:</b> Enriched wheat flour, water, vegetable shortening (soybean, hydrogenated soybean and/or cottonseed oil), sugar, salt, leavening (baking soda, sodium acid pyrophosphate), molasses, dough conditioner (fumaric acid, distilled monoglycerides, enzymes, vital wheat gluten, cellulose gum, wheat starch, calcium carbonate), calcium propionate, sorbic acid, and/or potassium sorbate (P). <b>Contains:</b> Wheat. [certified vegan], <b>Three Cheese Blend:</b> Low-Moisture Part-Skim Mozzarella Cheese, Cheddar Cheese, Pasteurized Process Monterey Jack and American Cheese with Peppers (Cultured Milk, Cultured Part-Skim Milk, Water, Cream, Salt, Sodium Citrate, Jalapeno Peppers, Sodium Phosphate, Lactic Acid, Sorbic Acid [P], Color Added, Annatto and Paprika Extract Blend [VC], Enzymes), Anticaking Agents (Potato Starch, Cornstarch, Powdered Cellulose). <b>Contains:</b> Milk [certified vegetarian], <b>Grilled Chicken:</b> White meat chicken with rib meat, water, seasoning (modified potato starch, salt, yeast extract, spices, sugar, citric acid, disodium inosinate and guanylate, torula yeast, maltodextrin, dextrose, natural flavors, and 2% or less of soybean oil added as a processing aid), sodium phosphates, <b>Creamy Jalapeno Sauce:</b> Soybean oil, water, vinegar, jalapeno peppers, buttermilk, spices, cage-free egg yolk, 2% or less of: dextrose, chili powder, salt, natural flavors, sugar, onion powder, paprika (VC), minced onion, garlic powder, cocoa powder processed with alkali, dried onion, glucono-delta-lactone, modified food starch, xanthan gum, potassium sorbate (P), sodium benzoate (P), sorbic acid (P), disodium inosinate and disodium guanylate, lactic acid, propylene glycol alginate, citric acid, acetic acid (PF), calcium disodium edta (P). <b>Contains:</b> Milk, Egg [certified vegetarian]</p>

	5 Layer Burrito	<p><b>Flour Tortilla:</b> Enriched wheat flour, water, vegetable shortening (soybean, hydrogenated soybean and/or cottonseed oil), sugar, salt, leavening (baking soda, sodium acid pyrophosphate), molasses, dough conditioner (fumaric acid, distilled monoglycerides, enzymes, vital wheat gluten, cellulose gum, wheat starch, calcium carbonate), calcium propionate, sorbic acid, and/or potassium sorbate (P).</p> <p><b>Contains:</b> Wheat. [certified vegan], <b>Refried Beans:</b> Pinto beans, soybean oil, seasoning (salt, sugar, spice, beet powder (VC), natural flavors, sunflower oil, maltodextrin, corn flour, trehalose, modified cornstarch). [certified vegan], <b>Seasoned Beef:</b> Beef, water, seasoning [cellulose, chili pepper, maltodextrin, salt, oats, soy lecithin, spices, tomato powder, sugar, onion powder, citric acid, natural flavors (including smoke flavor), torula yeast, cocoa, disodium inosinate &amp; guanylate, dextrose, lactic acid, modified corn starch], salt, sodium phosphates. <b>Contains:</b> Soy, <b>Nacho Cheese Sauce:</b> Nonfat milk, cheese whey, water, vegetable oil (canola oil, soybean oil), modified food starch, maltodextrin, natural flavors, salt, dipotassium phosphate, jalapeno puree, vinegar, lactic acid, cellulose gum, potassium citrate, sodium stearoyl lactylate, citric acid, annatto and oleoresin paprika (VC). <b>Contains:</b> Milk [certified vegetarian], <b>Reduced-Fat Sour Cream:</b> Milk, cream, modified corn starch, lactic acid, maltodextrin, citric acid, sodium phosphate, natural flavor, cellulose gel, potassium sorbate (P), cellulose gum, guar gum, locust bean gum, carrageenan, vitamin A. <b>Contains:</b> Milk [certified vegetarian], <b>Cheddar Cheese:</b> Cheddar cheese (cultured pasteurized milk, salt, enzymes, annatto (VC)), anti-caking agent. <b>Contains:</b> Milk [certified vegetarian]</p>
Coca Cola	Coca Cola	Carbonated water, high fructose corn syrup, caramel color, phosphoric acid, natural flavors, caffeine.
	Rodent Diet	Ground wheat, ground corn, wheat middlings, soybean meal, corn gluten meal, soybean oil, calcium carbonate, dried brewer's yeast, dicalcium phosphate, sodium chloride, L-lysine HCl, DL-methionine, ferrous sulfate, magnesium oxide, manganous oxide, zinc oxide, copper sulfate, cobalt carbonate, vitamin A acetate, vitamin D3, vitamin E, niacin, thiamin mononitrate, folic acid, menadione bisulfite complex, vitamin B12, riboflavin, pyridoxine, hydrochloride, calcium pantothenate, biotin, red food color.