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Diet and Immunology

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Diet and Immunology

It is well accepted that diet has far-reaching effects on the physiology of lab animals. Targeted phenotypes can be purposely induced by using specific diets, allowing the researcher to test their hypotheses. Like other areas of study, immunology is a field in which attention must be paid to the diet being fed, since changing the diet composition could result in a different immunological phenotype. This requires that researchers understand the differences between grain-based (GB) chows and purified ingredient diets, and unfortunately, many investigators (immunologists or not) are unaware of these differences.

Briefly, GB chows are made with unrefined grains and animal ingredients each of which contain multiple nutrients and non-nutrients. These ingredients include ground corn, ground wheat, ground oats, soybean meal, alfalfa meal, and animal by-products such as fish meal and porcine animal meal. Because these are relatively unrefined, the composition of these ingredients will naturally vary due to soil conditions, climate, and timing of harvest. As a result, the GB chow from which they are made will have batch to batch variation. Furthermore, GB chows can also contain varying levels of phytoestrogens and heavy metals, both of which can unintentionally affect research outcomes (3, 4).

In contrast, purified ingredient diets are made with refined ingredients that contain one main nutrient and are commonly phytoestrogen-free, depending on the protein source. This means that they have consistent nutrient composition, can be reported from one batch to the next, can be easily modified to the researchers' advantage while containing little to no confounding non-nutrients. In other words, they provide a more stable and 'cleaner' diet base compared to GB chows.

So how might the type of diet impact immunology research?

Non-nutrients

The aryl hydrocarbon receptor (AhR) is expressed on intraepithelial lymphocytes and helps to maintain these cells in places like the intestine. Li et al. (1) found that a GB chow contained an unidentified ligand for the AhR, because when this GB chow was fed to mice, it affected mRNA levels of the AhR and Cyp1a1 in the small intestine. However, the authors could not attribute this effect to any one specific diet-derived chemical entity since "The chemical complexity of the diet makes it difficult to determine the exact nature of all potential AhR ligands." They then chose to add specific amount of purified indole-3-carbinole (I3C; a phytochemical found in cruciferous plants that can be converted in *vivo* to an AhR ligand) to a purified ingredient diet. The purified ingredient diet was used to provide a clean diet background, devoid of any confounding plant phytochemicals that are often found in GB chow diets. The authors reported that I3C supplementation in this way increased the number of small intestinal intraepithelial lymphocytes and importantly, the reason for this increase had a direct and identifiable cause.

Purified Diet Control vs. Grain Based Chow

	Purified High Fat Diet	Purified Low Fat Control Diet	Grain Based Chow	
	Ingredient*	Matched	NOT Matched	Reason
Fat	Lard, soybean oil	✓	X	Variable Sources
Protein	Casein	✓	X	Variable Sources
Carbohydrate	Corn starch, sucrose, maltodextrin	✓	X	Variable Sources
Fiber	Cellulose, insoluble	✓	X	Variable Sources/ 4X Higher
Micronutrients	Vitamins, minerals	✓	X	Variable Level
Phytoestrogens	NONE	✓	X	Variable Level
Heavy Metals	NONE	✓	X	Variable Level

*Ingredients typical of a purified diet, though other purified sources can be used.

Gut microbiome

The mammalian gut hosts a very dense population of gut microbes, with estimations of ~10^{12} bacteria per ml for humans, making it the most densely populated bacterial ecosystem known (5). The types and levels of gut bacteria are affected by the composition of the diet, with fiber probably being the dietary constituent thought to have the greatest effect on the gut microbiome. These gut microbes are thought to play a role in maintaining a healthy gut barrier and in gut innate immune responses (6). Changes in gut microbe populations may therefore affect barrier function and inflammation. Because GB chows typically have increased levels and more diverse (and undefined) types of fibers (both fermentable and non-fermentable fibers) compared to traditional purified ingredient diets, which typically have one source (i.e. cellulose, a non-fermentable fiber), it would be expected that effects on gut microbiota would be different between these diet types and indeed they are (7). Therefore researchers studying immunology, especially as it pertains to the gut, should be aware of these diet differences. Sources of soluble fiber (those fermentable by gut bacteria, e.g. inulin, fructooligosaccharides) have been added to purified ingredient diets and been shown to affect gut microbiota populations (8) and so provide the opportunity to study the effects of dietary fibers on gut microbiome-induced changes in gut immunity in a stable, controllable diet background.

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