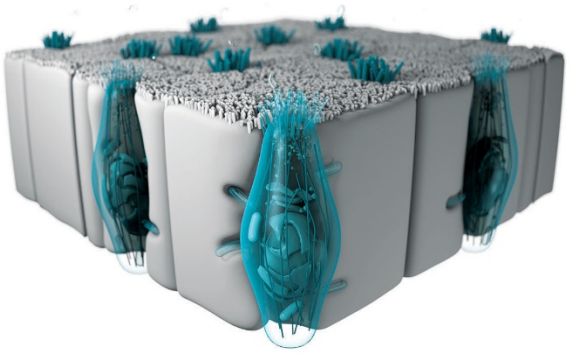
STANDARD DEVIATIONS: Does this Taste Bad to You?

Greetings,

Cell function. Sometimes it surprises us with a diversity and significance we don't anticipate. Our concepts, expectations and understanding are being challenged by discoveries that change and enhance our views of what happens at a cellular level.

Tuft cells are an unusual *chemosensory* cell finding new notoriety in the different ways they function and the places they show up.

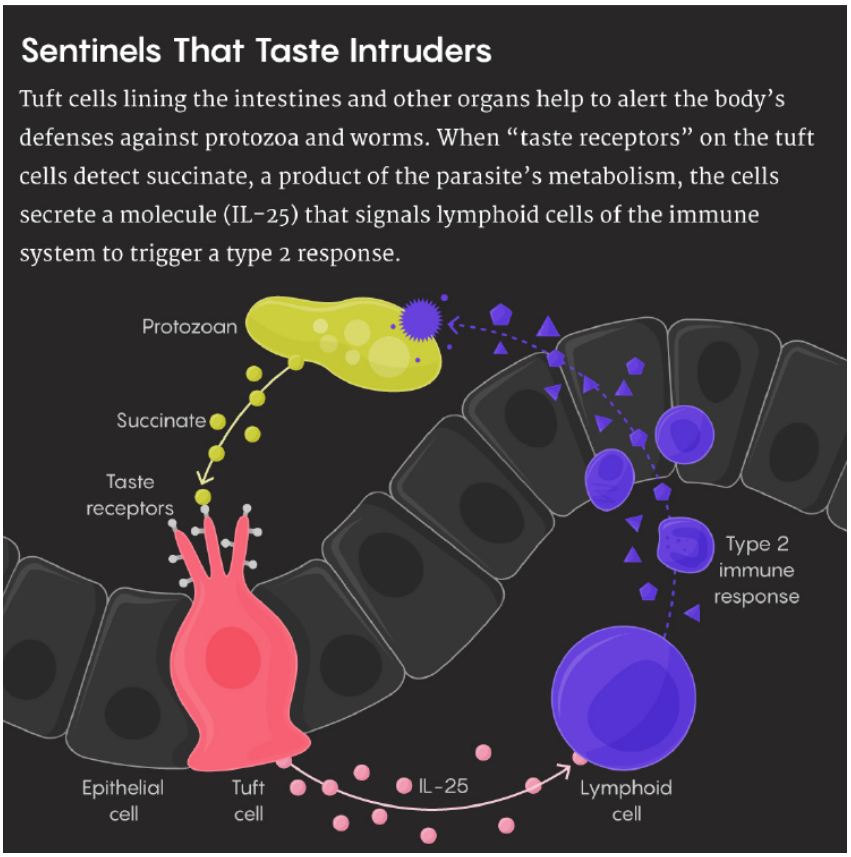


{Tuft cells. Sentries of pathogen detection?}

Oddball shaped and sparsely distributed in epithelial tissues, tuft cell functions are diverse and the focus of some interesting research. Receptors found in the "brush-like" villi that extends into the lumen trigger responses that influence an inflammatory cascade. They recognize parasitic invaders like protozoa, they also detect allergens and other molecules. It's a mechanism similar to the way cells detect molecules that we associate with taste, like bitter and umami. The chemosensory trigger promotes changes in the surrounding cells and environment. Tuft cells produce bunches of signal proteins and cytokines (acetylcholine and interleukins) that tell other cells to step up. Their role in type 2 immune response is probably under-stated.

Just about every tube in the body has a tuft cell population. They're found in the gut, lung, trachea, nasal passage, gall bladder, and pancreas; just about anywhere outsiders are knocking around our insides. When activated, they participate in the mediation of the classical type 2 immune response. This results in the inflammatory and cellular changes observed in the tissue.

The classical and notable way we understand this immune activation is the response to **helminthic worm infections**. Tuft cells recognize, or taste, *succinate* produced by the parasite and signal differentiation of T helper cells, immunoglobulins (IgE, IgA), eosinophils, basophils, and mucus production and muscle contraction. This "weep and sweep" reaction is our defense, ultimately resulting in worm expulsion.



{Tuft cells "taste" invasive worms, parasitic protozoa and allergens, all of which trigger type 2 immune response.}

Helminths are parasitic worms (nematodes, filarial worms, flatworms, flukes, trematodes, and tapeworms). They are the most common infectious agents of humans in developing countries and produce a global burden of disease that exceeds more infamous conditions, including malaria and tuberculosis. Eggs of intestinal helminths can be found in the mummified feces of humans dating back thousands of years.

So helminth infections are bad, right?

Well, yes, they are. As far as neglected tropical disease goes, these are pretty serious. BUT, here's a weirdly wacky relationship …. people who live in endemic areas of helminth infection see LESS problems with other conditions that may be related to the things going on with our immunities! When our inflammatory processes get out of control we experience reactions that result in some serious conditions, such as asthma, rhinitis, dermatitis, and anaphylaxis.

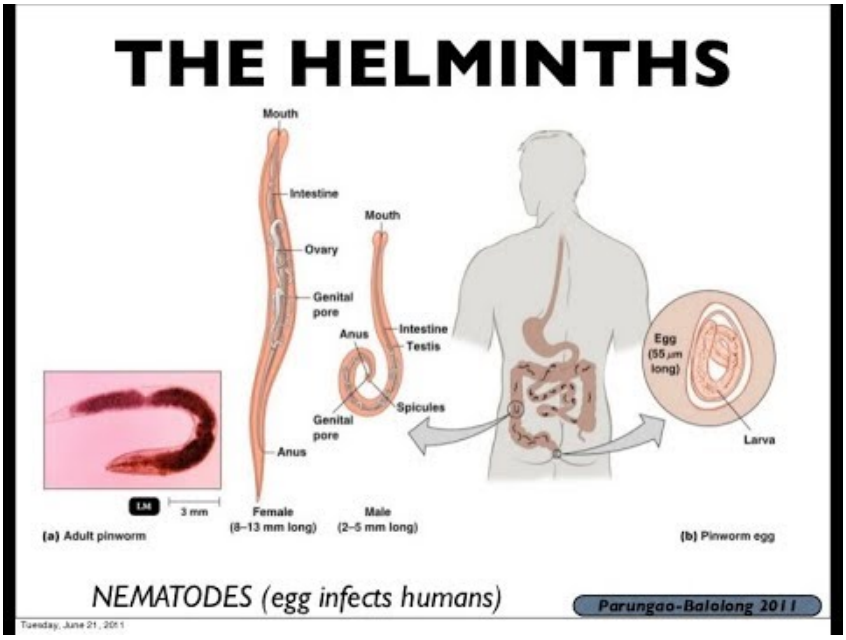
Epidemiological studies have pointed to the **lower frequency of allergies** (such as asthma, eczema, and allergic rhinitis) in developing countries **where the parasites are common** than in economically developed countries. Helminth species have been shown to suppress IgE and anaphylaxis in dietary peanut allergy. And **autoimmune disorders,** such as MS, **are also lower in helminth affected areas.** Crazy.

Only in the last couple years have we started exploring the tuft cell role in the gut and other organs as real players. Inflammatory response studies show tuft cell proliferation in tissues where they are not common and expression of tumorigenic factors. Tuft cells are being implicated in cancers of the stomach, pancreas, and intestine. They are suspected to be targeted by norovirus and may contribute to chronic norovirus infections.

A curious finding was seen in mice studies with flu. Infected mice show tuft cells suddenly appearing in the lung in greater numbers. Unsure exactly why this proliferation of tuft cells happens after the flu, speculations are that it might be the body's attempt to repair damage from the virus as part of the broader type 2 immune response. Stimulation of lymphocytes, mucus, and cytokine swarms is a blessing, or a curse?

The ability to continually "taste" the environment for different compounds provides a key opportunity for the body to respond to even minute parasitic threats. Then, with help from tuft cells and their cascading effects on the immune system, the body can fight off the invaders before they've gotten a foothold. But the sudden emergence of tuft cells in tissues, like the lungs, where they are not always present, might also cause its own pathologies?

Helminth and protozoan parasites are the most common infectious agents of humans living in developing countries and represent an important disease burden. Tuft cells found in the gut epithelium recognize the insult and react with a response that informs the immune system. Type 2 immune responses promote efficient expulsion of intestinal parasites such as helminths by driving a "weep and sweep" response that involves mucous production, fluid secretion, and increased intestinal motility. The generation of type 2 immunity in response to helminth parasites requires the secretion of cytokines by intestinal tuft cells.



These same chemosensory responses in susceptible individuals (without parasite) can cause the symptoms of allergy after exposure to pollens and certain food antigens, may have tumorigenic characteristics, and may be targeted by viral agonists. If the type 2 immune response is activated without parasitic provocation then we may see adverse clinical outcomes. The tuft cell may be a contributor to this paradox.

In an evolutionary sense, the tuft cell demonstrates a conserved mechanism that offers protection from parasitic insult. This defense strategy is likely related to the origin of our sense of taste, our diarrheal reactions, and mucus production in the gut, oral, and respiratory tracts. It might also be activating the pathways for allergy and autoimmune pathologies.

Have a great week and be safe,

Bryan