Biome Breathe™ Probiotic

Mechanism of Action

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Asthma

Approximately 1 in 9 Australians has been diagnosed with asthma, with 441 deaths due to asthma recorded in 2017. Asthma accounts for a significant proportion of annual disease expenditure, and impacts the quality of life for many Australians. Asthma is the most common chronic disease in the developed world. Asthma is more likely to occur in those with an atopic (allergic) disposition, or a family history of atopy (allergic rhinitis, asthma, and eczema). This indicates that there is an allergic component in many cases of asthma. Recognised risk factors for asthma include: family history; c-section rather than natural birth; absence or short duration of breastfeeding; early childhood respiratory infections; early life exposure to antibiotics. Children who grow up on farms or who have pets are diagnosed with asthma at a reduced rate.

Hygiene hypothesis

The 'hygiene hypothesis' contends that reduced exposure to microbes in early life means the immune system is less effectively challenged as it matures, and may not 'learn' how to differentiate between harmless substances and those which are capable of triggering allergic asthma. Research on germ-free mice established that they exhibited significant defects in GALT (gut-associated lymphoid tissue - part of the immune system in the gut). After these mice were given various microbes it was found their GALT function was restored. This research supports the theory that exposure to microbes is important for immunomodulation. Germ-free mice were also found to show stronger airway inflammation and airway hypersensitivity than mice which had been given microbes.

Intestinal dysbiosis

Intestinal dysbiosis is associated with reduced epithelial barrier integrity and dominance of Th2 expression, where the immune system gives an inappropriate response to environmental or food antigens. This leads to the secretion of pro-inflammatory cytokines (IL-4, IL-5, IL-13, and antigen-specific IgE). Th2 cells trigger eosinophilic inflammation characteristic of allergic asthma.

The lung microbiome

Until recently, it was assumed that lung tissue was sterile. Research is now emerging that supports the hypothesis of a lung microbiome, but it is difficult to study as there is significant technical challenge accessing samples from the lungs. However, differences in lung microbiota between healthy people and asthmatics suggest bacteria may play a role in the development of asthma.

The gut-lung axis

There are many possible pathways which underlie the gut-brain axis communication. One theory is that microbiota-derived metabolites may be significant in gut-brain and gut-lung communication. The most researched of these are short-chain fatty acids (SCFAs), which are produced in the gut as bacteria act on dietary fibre. SCFAs have an immune-modulating effect on gut mucosa, and potentially have a direct effect on lung immune response. SCFAs reduce Th2-mediated inflammation

Asthma therapeutics

Currently, first-line treatment for most cases of asthma is a combination of inhaled corticosteroid and inhaled beta2 agonist (Ventolin). The steroid is given daily as a preventer, reducing inflammation in the respiratory system. The beta2 agonist is used as required, acting as a bronchodilator to increase airflow during an asthma attack. Side effects of inhaled steroid treatment include hoarse voice, sore throat, increased risk of oral thrush. Side effects of Ventolin include nervousness, tremors, palpitations, sore throat.

Probiotics - proposed method of action

Probiotics may offer a novel approach in the management of asthma. Probiotics modulate the integrity of the mucosal epithelial barrier, helping to regulate inflammatory immune response. They increase production of anti-inflammatory cytokines, and elevate Th1 expression, helping to reduce the Th2 dominance seen in many cases of asthma. Mice given Bifidobacterium breve were found to have an increase in production of regulatory T cells, which have a modulating effect on the immune system. Produced in the gut, regulatory T cells may migrate to the lung, where they provide anti-inflammatory effects. The probiotics also induced production of IL-10, a cytokine which downregulates allergic airway inflammation. B. breve has also been found to decrease production of IL-5.

In summary, probiotics reduce the inflammation associated with asthma, and help to regulate the immune system to reduce allergic response.

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Atopic dermatitis (eczema)

Atopic dermatitis (or eczema) occurs in approximately 20% of babies and children under the age of two. About 40% of these children will also develop asthma. Many of the risk factors for asthma also apply to atopic dermatitis: family history of atopy; c-section rather than natural birth; absence or short duration of breastfeeding; early exposure to antibiotics. Current treatment strategy for atopic dermatitis is to avoid potential triggers (playing in sand, swimming in chlorinated pools, dietary allergens, irritants such as soaps and laundry products); prevent the skin from drying; and apply a steroid cream to outbreaks. The steroid works by reducing inflammation.

The inflammatory profile seen in asthma also applies to atopic dermatitis: elevated levels of inflammatory cytokines along with an overexpression of Th2 cells. Probiotics will have the same mechanism of action: reducing inflammation; healing gut epithelial barriers; increasing immune-modulating SCFAs; increasing regulatory T cells.

Clinical trials investigating the effect of Lactobacillus salivarius LS01 on the symptoms of atopic dermatitis have yielded positive results: a trial published in 2011 gave 38 adults with atopic dermatitis a supplement containing either 1 billion CFU of L. salivarius LS01 or placebo twice daily for 16 weeks. Patients in the probiotic group showed statistically significant improvement in symptoms of atopic dermatitis, as well as quality of life, when compared to the placebo group. On further examination four months after completing the trial it was found that the placebo group (but not the probiotic group) exhibited a significant reduction in Th1 cytokines and Th1/Th2 ratio.

Similarly, a study examining the clinical efficacy of L. salivarius LS01 on children with atopic dermatitis found positive results: 43 patients aged 0 to 11 years were treated with the 2 billion CFU of L. salivarius for eight weeks, then 1 billion CFU for eight weeks. At the conclusion of the 16 weeks there was noted a significant reduction in symptoms. Four weeks after the end of the study, this reduction in symptoms, notably itch intensity, was still seen.

REFERENCES

Anand S, Mande S. Diet, Microbiota and Gut-Lung Connection. Frontiers in Microbiology [Internet]. 2018 [cited 2019 Oct 23]; Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edsdoj&AN=edsdoj.8f254c8a03ac4c768d51b4f130eaf385&site=eds-live

Australian Institute of Health and Welfare. Asthma. Canberra: AIWH; 2019

Drago L, Toscano M, De Vecchi E, Piconi S, Iemoli E. Changing of fecal flora and clinical Effect of L. salivarius LS01 in adults with atopic dermatitis. Journal of Clinical Gastroenterology [Internet]. [cited 2019 Oct 23];46(SUPPL. 1):S56–63. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edselc&AN=edselc.2-52.0-84866245665&site=eds-live

Frati F, Salvatori C, Incorvaia C, Bellucci A, Di Cara G, Marcucci F, et al. The Role of the Microbiome in Asthma: The Gut–Lung Axis. International Journal of Molecular Sciences [Internet]. 2018 [cited 2019 Oct 22];(1):123. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edsdoj&AN=edsdoj.7a25d4cb9c64704a00f71cf488fcc16&site=eds-live

Hajavi J, Esmaeili S-A, Varasteh A-R, Vazini H, Atabati H, Mardani F, et al. The immunomodulatory role of probiotics in allergy therapy. Journal of Cellular Physiology [Internet]. 2019 [cited 2019 Oct 22];(3):2386. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edsgao&AN=edsgcl.563825655&site=eds-live

Niccoli A, Artesi A, Candio F, Ceccarelli S, Cozzali R, Ferraro L, et al. Preliminary results on clinical effects of probiotic Lactobacillus salivarius LS01 in children affected by atopic dermatitis. Journal Of Clinical Gastroenterology [Internet]. 2014 Nov [cited 2019 Oct 24];48 Suppl 1:S34–6. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=cmedm&AN=25291124&site=eds-live

Ozturk AB, Turturice BA, Perkins DL, Finn PW. The Potential for Emerging Microbiome-Mediated Therapeutics in Asthma. Current Allergy and Asthma Reports [Internet]. 2017 [cited 2019 Oct 21];17(9):1. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edssjs&AN=edssjs.B38D0B72&site=eds-live

Probiotics in Adults: do They Improve Atopic Dermatitis? [cited 2019 Oct 23]; Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edsclt&AN=edsclt.NCT01500941&site=eds-live

Sokolowska M, Frei R, Lunjani N, Akdis C, O'Mahony L. Microbiome and asthma. Asthma Research and Practice [Internet]. 2018 [cited 2019 Oct 21];(1):1. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=edsdoj&AN=edsdoj.1901eec473214334bc68da8003560bf9&site=eds-live

Toh Z, Anzela A, Tang M, Licciardi P. Probiotic therapy as a novel approach for allergic disease. Front. Pharmacol [Internet]. 2012 Sep [cited 2019 Oct 22]. Available from: https://doi.org/10.3389/fphar.2012.00171

Wilson NG, Hernandez-Leyva A, Kau AL. The ABCs of wheeze: Asthma and bacterial communities. PLoS Pathogens [Internet]. 2019 Apr 25 [cited 2019 Oct 21];15(4):1–7. Available from: http://search.ebscohost.com.ezproxy.utas.edu.au/login.aspx?direct=true&db=asn&AN=136082275&site=eds-live