

Alpha Times

Newsletter of Alpha-1 Organisation Australia inc

Issue 20 Autumn '25

From the President's Pen

I recently shared the exciting press release from BEAM Therapeutics (via our Alpha-1 Organisation Australia Inc Public Facebook page) about their initial positive data from the "BEAM-302" Phase 1/2 clinical trial. The initial results show an increase in total and functional (normal) Alpha-1 antitrypsin levels and a decrease in mutated Z-type antitrypsin. The safety findings are pleasing showing that the intervention is welltolerated. While further study phases are required to support eventual product commercialization, it is looking hopeful that a product could be available (hopefully within 10 years) to improve life-expectancy and limit organ damage due to normal antitrypsin circulating throughout the body. Patient participation in clinical trials allows testing of new therapeutics and the Alpha-1 community is extremely thankful to everyone who participates in clinical trials. Closer to home, I hope that everyone affected by extreme weather events has been able to access medication and fresh food and maintain usual health practices. Going out on windy days brings challenges e.g. avoiding tree branches and breathing in extra dust. People with lung damage such as emphysema should avoid going out on windy days as fine and very fine dust particles can get deep into your lungs, causing irritation and inflammation. Inflammation plays a pivotal role in many lung diseases, so avoiding inflammation where possible is advised. Precautions include staying indoors and avoiding outdoor activity. If you need to venture outdoors on windy days covering your nose and mouth will limit fine dust particles entering the lungs.

Cyclone Alfred affected fresh-food supplies to some locations and panic buying resulted in limited or no access to fresh fruit and vegetable for some. With the knowledge that eating fresh fruit and vegetables is associated with better health, we are aways interested in sharing evidence in our newsletter showing the link between dietary components and health, including lung inflammation.

If you have evidence-based tips associated with staying healthy and leading your best life we would love to hear from you. Share your ideas and experiences contactus.aloa@gmail.com.

Best wishes Gaynor President, A1OA

Mental Health First Aid

Alpha-1 Organisation Australia has an accredited Mental Health First Aider who is ready to help if you are not coping after a diagnosis of A1AD for yourself or a family member. A new diagnosis can cause mental distress, anxiety, or depression. Please reach out to mentalhealth.aloa@gmail.com



Zoom Events/Meetings:

Our friendly monthly support group meetings are open to everyone diagnosed with Alpha-1.

Meetings are held on the third Wednesday of each month in 2025, at 3pm AEST / AEDT.

If you are interested in joining us for a chat at one of these friendly, supportive meetings please email us for the Zoom link –

Email pres.a1oa@gmail.com.



Food Matters

In this edition we are exploring some links between food and health with a focus on lungs and livers as these organs are more commonly affected by Alpha-1 antitrypsin deficiency.

A Diet Rich in Fruit and Vegetables is Linked to Better Lung Health

Fruit and vegetable intake has been reported to have many health benefits, including an association with better respiratory and lung health. There are many health-related components in fresh fruit and vegetables including antioxidants, vitamins, minerals, fibre and phytochemicals.

In regard to lung health, some studies have found an association between increased fruit intake over two years and an increase in FEV1 (forced expiratory volume – the amount of air than someone can force out of their lungs in one second). There is also a growing body of evidence that links diets rich in fresh fruit and vegetables to reduced lung inflammation. Diets higher in fibre reduces inflammation while excessive consumption of saturated fat is linked to high circulating fatty acids which creates an inflammatory response. Fast food diets and ones heavy in processed food are linked to more neutrophils in sputum and more toll-like receptors (TLR) which are pro-inflammatory. So called "Western diets" are also associated with higher asthma risk and more wheeze in a dose-dependent manner i.e. the more processed food eaten the more wheezing occurs. (REF: Wood, L. G.).

Chronic Obstructive Pulmonary Disease (COPD) is linked to an increased risk of lung cancer. While not smoking is the most important strategy to reduce lung cancer risk, eating fruits and vegetables containing carotenoids and other antioxidants has been found to reduce lung cancer risk. A systematic review and meta-analysis of the literature has identified that lung cancer risk can be decreased by 8-18% by eating fruits and vegetables. The flavonoids and carotenoids are some of the protective compounds in fruit and vegetables. It is interesting to note that 400g of fruits and vegetables daily is enough to reduce risk with a higher consumption not linked to further risk reduction. (REF: Vieira AR, Abar, L, Vingeliene S, et al.)

The benefits of antioxidants from diet associated with lung health was also reported in 2024 by Wharton et al. They noted associations of a nutritionally rich plant-based diet and significantly better lung function, with a slower decline in lung function through time. They also name dietary fibre as a key component that reduces inflammatory responses, possibly through alterations in the gut microbiome and increased production of anti-inflammatory metabolites such as short-chain fatty acids. (REF: Wharton RC, Wang JG, Choi Y, et al.)

Conclusion

Alpha-1 antitrypsin plays an important anti-inflammatory role. Until such times that Alphas can access clinical trials and new treatments that result in normal antitrypsin levels it seems important to try to reduce inflammation. A healthy diet can play a role in reducing inflammation. This seems important especially when considering that the science tells us that inflammation if linked to worse health outcomes.





Fresh fruit and vegetables for better health

Probiotics for liver health

In the last edition of Alpha Times, we gave an overview of probiotics and their benefits for liver health, specifically in relation to cirrhosis. Non-alcoholic fatty liver disease (NAFLD) may progress to fibrosis, compensated cirrhosis, advanced cirrhosis, or hepatocellular carcinoma, so a way to slow or prevent progression would be of benefit to patients.

In this issue, we examine which probiotics have been shown to be helpful in relieving or reversing NAFLD.

A variety of Lactobacillus strains have been shown to affect the progression of NAFLD by reducing cholesterol. Bifidobacterium lactis has also been shown to help with liver health by reducing inflammation, improving gut permeability, and restoring the balance of gut microbiota.

These are some specific strains of probiotics that have been shown to reduce liver inflammation:

- 1. **Lactobacillus acidophilus**: This strain can reduce liver inflammation and improve liver function in individuals with liver disease.
- 2. **Lactobacillus plantarum**: This strain can reduce liver inflammation in individuals with non-alcoholic fatty liver disease.
- 3. **Other lactobacillus strains.** Ingestion of Lactobacillus, such as L. paracasei and L. fermentum, ameliorates the progression of non-alcoholic steatosis by lowering cholesterol.
- 4. Bifidobacterium lactis: This strain can reduce inflammation in the liver and improve gut health.
- 5. Bifidobacterium animalis ssp. lactis MG741: Can reduce body weight and improve gut permeability
- 6. Bifidobacterium lactis TY-S01: Can protect against alcohol-induced liver injury
- 7. Bifidobacterium animalis ssp. lactis 420: Can alleviate experimental autoimmune hepatitis
- 8. **Bifidobacterium animalis subsp. lactis V9**: Can attenuate hepatic steatosis and inflammatory responses
- 9. Bifidobacterium lactis Probio-M8

Good probiotic food choices

The most common fermented foods that naturally contain probiotics, or have probiotics added to them, include yogurt, kefir, kombucha, sauerkraut, pickles, miso, tempeh, kimchi, sourdough bread, and some cheeses.



Air Matters

The air we breathe is an important factor in our lung health. Wearing a mask when there is smoke around, staying indoors on days with a high pollution index, and using an air purifier can all help.

How do air purifiers work?

When indoor air is sucked into the air purifier it passes through a filter inside. The filters capture airborne pollutants like dust and then pushes clean air back out into the room. Some purifiers are designed to remove specific types of contaminants and others remove gases.

Are there any downsides to air purifiers?

Many ionizers, especially older models, can generate ozone when they are operating, which is known to exacerbate asthma. When selecting an air purifier be sure to buy one that doesn't produce ozone.

What things should you consider before buying an air purifier?

Look for True HEPA filters. These are the most effective at removing ultra-fine particles, such as dust mites, pet dander, pollen and mould.

Find a unit that meets the size guidelines for the area of the room you will have it in.

How efficient is your HEPA air purifier? To qualify as a HEPA filter, the filter must be able to remove at least 99.97% of airborne particles as small as $0.3\mu m$ in size, as defined in the Australian Standard AS4260:1997. This Australian Standard classifies HEPA filters into several grades based on their efficiency.

Other ways to improve air quality.

To improve the air quality in your home, don't leave it to the air purifier alone.

These can help you and your family breathe easier:

- Put allergy-proof covers on your pillows and mattress.
- Wash bedding weekly in hot water.
- Keep pets out of the bedroom, especially cats.
- Sleep with the windows closed to prevent irritants from entering the home.
- Change the air filter in your home's HVAC system regularly.
- Avoid smoking in the home and avoid second-hand smoke on your clothing.
- Avoid standing water and damp areas in your home. Water condensation leads to mould growth which can be a trigger for sensitive individuals. Live plants and live Christmas trees are often a "hidden trigger" that people forget about.
- Vacuum your home regularly, especially in your bedroom.



Portable air filters

Using an air filter to eliminate pollen, pollutants and other irritants can reduce the chances of health issues like headaches, fatigue, asthma, and allergies due to breathing in polluted air.

For people, such as lung affected Alpha-1 sufferers, concerned with quality of air when they travel, be it in a hotel room or an aeroplane, using a portable air filter can be of benefit.

Modern aeroplanes are equipped with HEPA filters that ensure the air circulating in the cabin is purified. This might reduce the necessity of using a personal air purifier.

Portable air filters can significantly improve the air quality in your accommodation when travelling, making your stay more comfortable and healthier, and give peace of mind.

Travelling with a portable air filter

These devices are compact and lightweight, so are easy to carry in your stowed or carry-on luggage.

- 1. **Airline Regulations**: Most airlines allow portable air filters in both carry-on and checked luggage. However, always check the specific regulations of the airline you are flying with.
- 2. **Health Benefits**: helps ensure that you breathe cleaner air in your accommodation. This is therefore beneficial for individuals with A1AD with its attendant respiratory conditions.
- 3. **Convenience**: Portable air filters are easy to use and maintain, and many models come with features like USB charging, making them convenient for travel.

Using portable air filters in hotels

Generally, there are no restrictions on using portable air filters in hotels but check with the hotel.

- 1. **Room Size**: Portable air filters are designed for small to medium-sized rooms. Check the size of the hotel room you will be staying in.
- 2. **Power Supply**: Check for compatibility with the power supply in the country you are traveling to or bring a power adapter or converter if the voltage is different.
- 3. **Noise Level**: Some portable air filters can be noisy. Make sure you choose a guiet model.

Using Portable air filter on an aeroplane

- 1. Airline Regulations: as above.
- 2. **Usage During Flight**: Some airlines may have policies against using electronic devices that emit noise or require a power source during the flight.
- 3. **Power Supply**: Ensure that your portable air filter can operate on battery power or has a USB charging option, as using in-seat power outlets may not always be feasible.
- 4. **Noise Level**: Choose a model that operates quietly to avoid disturbing other passengers.

Using a portable air filter effectively:

- 1. Placement: Place the air filter in a central location in the room for optimal air circulation.
- 2. **Keep Doors and Windows Closed** to maximize the effectiveness of the air filter.
- 3. **Run Continuously**: For the best results, run the air filter continuously.
- 4. **Adjust Settings**: Adjust the airflow rate and fan speed according to the size of the room and the level of air pollution.
- 5. **Regular Maintenance**: Clean or replace the filter according to the manufacturer's instructions to ensure the air filter continues to work effectively9.
- 6. **Avoid Heat Sources**: Do not place the air filter near heat sources or humidifiers, as this can affect its performance.



Wearable Portable Air Purifier

There is a number of wearable air purifiers available. These have been somewhat controversial, with some companies making unwarranted claims about their efficacy. However, there is evidence that some do work.

Zhang et al (2023) have developed breathable shape memory fibre-based material with antibacterial and waterproof properties. This is important for multitiered wearable protection to address the increasing concerns of air pollution.

The individual wearable air purifier Respiray Wear A+ was evaluated by Bergman et al (2024) and found to protect significantly against airborne pollen, HDM, and cat allergens and so may be a very useful device for avoiding indoor allergens.

An interesting development is The Dyson Zone[™], an unusual combination of noise-cancelling headphones with a removable face visor that helps purify air, particularly around polluted areas. The Dyson Zone[™] purifies the air you breathe on the move by delivering a plume of fresh air without touching your face, using high-performance filters and two miniaturized air pumps.

What are the side effects of wearable air purifiers?

- Reduced humidity: Continuous air purification can lower humidity levels, leading to dry skin, eyes, and throat irritation.
- Respiratory issues: Prolonged exposure to dry air can cause nosebleeds, congestion, and other respiratory discomforts.

Clinical Trials

To keep up to date with clinical trials in Australia, visit
https://www.australianclinicaltrials.gov.au/
Also keep abreast with international happenings via the US site
Home | ClinicalTrials.gov





On 21st June, Mark Lloyd of the Alpha-1
Organisation Australia will be organising "Winter
Trails of Manly Dam" for the second year
running. This scenic yet challenging trail run
doubles as a fundraising opportunity for
Alpha-1, helping to raise awareness and support
for our charity.

As part of the event, participants can choose to make a donation when registering. The race features an 8km trail loop with three distance options: 8km, 16km, and 24km—perfect for both seasoned trail runners and those looking to take on their first off-road adventure.

Learn more here: https://alphatrailevents.com.au/upcoming-events/manly-dam-trail-event/

You can also donate here:

Go to our *TryBooking* account - https://www.trybooking.com/BJWTS or transferring directly to our bank account:

Bank – Westpac Account Name – Alpha-1 Organisation Australia Inc BSB – 036069 Account Number – 072007









Advances in Gene Therapy for Alpha-1 Antitrypsin Deficiency

BEAM Therapeutics, Wave Life Sciences, and Korro Bio are all in the process of developing genetic treatments for Alpha-1 Antitrypsin Deficiency (AATD). Each company has recently announced early success in their current clinical trial.

While BEAM-302 is the only base-editing candidate in the clinic for AATD, Wave Life Sciences is advancing an RNA-editing oligonucleotide WVE-006 through clinical trials in AATD (Phase 1 and Phase 1/2 trials ongoing) and Korro Bio received regulatory clearance in Australia late in 2024 to initiate a Phase 1/2 trial of its ADAR candidate KRRO-110 in patients with AATD. Boston- and Germany-based biotech startup AIRNA is also preparing to bring an ADAR candidate for AATD into the clinic in 2025.

Beam Therapeutics

Scientists have successfully corrected the AATD gene mutation using a single infusion, restoring it to its normal state, marking a significant advancement in gene therapy.

A small study involving nine patients demonstrated the ability to precisely target and correct the mutated gene with a single infusion.

The study involved fixing a "spelling error" in the DNA sequence. BEAM-302 is designed to make a single A-to-G correction of the PiZZ mutation in the SERPINA1 gene. BEAM-302 corrects the mutation directly, allowing natural protein production. Beam Therapeutics plans to continue and expand the trial to include patients with liver disease later in 2025.

In patients with alpha-1 antitrypsin deficiency, a single treatment of BEAM-302 increased the levels of healthy protein and reduced harmful mutated protein by up to 78%, with only mild side effects reported.

Korro Bio

Their goal is to create a clinically differentiated, disease-modifying treatment to address both lung and liver manifestations of AATD.

REWRITE is a two-part single and multiple dose-escalating study that will evaluate the safety and tolerability of KRRO-110 in up to 64 participants, including healthy adults and clinically stable AATD patients with the PiZZ genotype.

KRRO-110 is the first RNA editing oligonucleotide product candidate from Korro's proprietary RNA editing platform, Oligonucleotide Promoted Editing of RNA (OPERA™).

KRRO-110 is designed to co-opt an endogenous enzyme, Adenosine Deaminase Acting on RNA (ADAR), to edit the "A" variant on SERPINA1 RNA, repair an amino acid codon, and restore secretion of normal AAT protein. This repair of the endogenous protein has the potential to clear protein aggregates from within liver cells to create a potentially clinically differentiated benefit for liver function and to preserve lung function by providing an adequate amount of normal AAT protein.

Preclinical data demonstrates rapid restoration of functional AAT protein levels and durable editing.

Korro is currently recruiting in Melbourne.

Nucleus Network Pty Ltd

Contact: Nucleus Network, Melbourne

61 1-800-243-733 melbourne@nucleusnetwork.com

Contact: Ofer Gonen, MD, PhD, FRACP



Wave Life Sciences

The study has received positive proof-of-mechanism data from the ongoing Phase 1b/2a RestorAATion-2 study of WVE-006 in alpha-1 antitrypsin deficiency (AATD). WVE-006 is a GalNAcconjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that was developed with Wave's oligonucleotide chemistry platform. It is designed to address AATD-related lung disease, liver disease, or both.

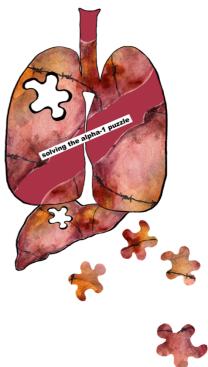
The level of mRNA editing observed with a single dose exceeded their expectations and they expect M-AAT levels to continue to increase with repeat dosing, based on preclinical data.

Wave's RNA platform uses their PRISM® technology, to combine multiple modalities with chemistry innovation.

YouTube Videos to Watch

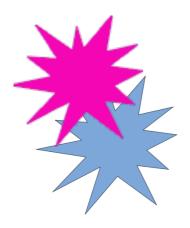
BEAM Therapeutics has released several videos about living with Alpha-1 as well as updates on their genetic breakthrough with base editing (more on this below).

> Don't forget to check out our YouTube channel where you'll find lots of informative videos! https://www.youtube.com/@alpha-1organisationaustral421









Not joined the A1OA charity yet?

We'd love to have you with us.

Consider joining the Alpha-1 Organisation Australia; membership is open to individuals and organisations large and small.

Membership is just \$20/year. You can join by going to our *TryBooking* account

- https://www.trybooking.com/BJWTS

or by transferring the fee to our bank account:

Bank – Westpac Account Name – Alpha-1 Organisation Australia Inc BSB – 036069 Account Number – 072007

Please quote your surname as a reference, and email <u>member.a1oa@gmail.com</u> to let us know you've joined.

Your membership will help us to provide support and advocacy, and to participate in research into novel treatments, you'll also get access to resources such as our monthly peer support group meeting.

Thank you!

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