ALZET Special Delivery™ Newsletter

September 2026

Hypothyroidism can be induced by obesity

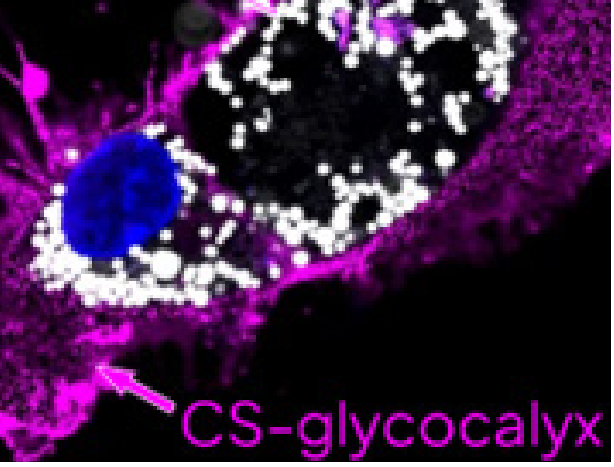
It has been long established that thyroid hormones stimulate energy expenditure (EE), while hypothyroidism reduces EE. In the context of comorbidities including obesity and hypothyroidism, obesity is typically secondary. However, there is increasing evidence that obesity can induce hypothyroidism. In a new research paper from The Journal of Clinical Investigation, Rampy et. al use a mouse model of diet-induced obesity to further investigate thyroid hormone action and overall thyroid function.

With ALZET® Osmotic Pumps, the researchers performed a metabolic cage experiment to investigate the effects of overnutrition on deiodinase and thyroid hormone activity. ALZET Model 2001 pumps containing T3, T4, or vehicle were implanted subcutaneously. After recovery, energy expenditure was measured over two 24-hour time periods. Notably, all mice receiving thyroid hormones via osmotic minipumps increased their EE. It was found that overnutrition impaired the conversion of T4 to T3 and effectively reduced EE, likely due to decreased D2 activity. Overall, overnutrition was shown to decrease local activation of T4 and slow down metabolic rate.

Rampy et al's findings are the latest example of continuous and controlled delivery of peptide hormones playing a pertinent role in obesity research. Their work especially provides a compelling argument to include deeper analysis of thyroid hormones in studies involving mouse models of diet-induced obesity. There is also potential for their work to provide a foundation for clinical approaches to improving thyroid function and treating obesity in humans.

Read the full publication: Rampy, Jessica et al. "Overnutrition in mice impairs thyroid hormone biosynthesis and utilization, causing hypothyroidism, despite remarkable thyroidal adaptations." *The Journal of clinical investigation* doi:10.1172/JCI194207

alzet® OSMOTIC PUMPS



Tumour acidosis remodels the glycocalyx to control lipid scavenging and ferroptosis

Glioblastomas are heavily associated with lipid droplet (LD) accumulation, and increasing evidence points to LDs promoting tumor survival under hostile conditions; however, the mechanisms involving LD formation, uptake, and storage are still not clearly understood. In a new Nature article, Bång-Rudenstam et al. sought to elucidate these molecular mechanisms within the tumor microenvironment. They focused on acidosis as a tumor stressor and identified that LD accumulation was linked to the formation of a chondroitin sulfate (CS)-enriched glycocalyx (a cell coat made of glycoconjugates).

Note: Featured image from Bång-Rudenstam et al. reveals CS-glycocalyx encapsulation is an adaptive response to tumour acidosis.

For in-vivo targeting, ALZET® Osmotic Pumps were used for delivery of a CSPG inhibitor (blocks CS-glycocalyx formation) and DGAT1 inhibitor (blocks LD formation) to the cerebellum. ALZET Pumps were chosen specifically considering the chemical properties of the CSPG inhibitor and would allow for it to cross the blood-brain barrier.

Process

1. Xenograft mouse models were generated by injecting PDX U3054MG cells, CDX U87MG7.4/NA cells, or CDX 6.4/AA cells into the brains of female NSG mice at 5-7 weeks.
2. ALZET Pump Models 1007D or 1002 containing the CSPG inhibitor or DGAT1 inhibitor were then implanted subcutaneously into the anesthetized mice.
3. Catheters were connected to the pumps to allow for direct intratumoral delivery of compounds to the brain.
4. Treatment continued for 7 or 14 days, after which the pumps were removed, and the mice were monitored for neurological distress.
5. Conclusion

Notably, treatment with these inhibitors prolonged survival in xenografted mice. From this, the researchers identified that tumor acidosis adaptation involves:

1. LDs buffering toxic lipids
2. CS-rich glycocalyx acting as a shield to limit lipid particle uptake and ferroptosis

This research is important because it points to a glycosylation process involving lipid uptake, storage, and survival in acidic tumors. The glycocalyx, acting as a shield in these acidic tumor environments, can thus be a potential therapeutic target. This process, coupled with intratumoral delivery capable with ALZET Pumps, researchers continue to reveal promising findings for cancer therapeutics and treatments.

Read the full publication: Bång-Rudenstam, Anna et al. “Tumour acidosis remodels the glycocalyx to control lipid scavenging and ferroptosis.” *Nature cell biology* doi:10.1038/s41556-026-01879-y

Importance of grey–white matter interactions in neurodegenerative diseases

As neurodegenerative conditions progress with age, focal white matter lesions in the brain accumulate and often lead to mental and physical impairment. There are other symptoms such as grey matter microgliosis, as well as loss of synaptic and neuronal function, though they are generally considered independent of lesions despite all of them eventually leading to neurodegeneration. In a new Nature publication, de Faria Jr et al. sought to understand the relationship and elucidate the effects of focal white matter lesions on neuronal function and grey matter inflammation. To do this, they induced a focal white matter lesion within a clinically relevant and well-defined neuronal circuit, common in neurodegenerative orders such as Alzheimer's disease, dementia, and Parkinson's disease.

The researchers bilaterally injected EtBr (ethidium bromide) into the CCP (caudal cerebellar peduncle) of 9-12 week old Sprague-Dawley rats to induce focal white matter lesions. A predicted series of events occurred after this, some of which included oligodendrocyte damage and demyelination, followed by OPC (oligodendrocyte precursor cell) recruitment. As part of the series of experiments to map this neuronal circuit, ALZET Osmotic Pumps were used to generate a model of failed myelin regeneration. Following local delivery of EtBr, the pumps delivered EdU (5-ethynyl-2'-deoxyuridine) above the lesioned areas. Incidentally, OPC's are responsible for myelination and sensitive to EdU. Minipump delivery of EdU resulted in "myelin regeneration failure without affecting macrophages or myelin clearance." Additionally, the researchers wanted to see the effects of failed myelin regeneration on the IO (inferior olive) microglia response. The ALZET Pumps were also used to deliver PLX5622 (potent inhibitor of CSF1R microglial survival factor). It was observed that local microglial density decreased and neuronal activity remained unchanged.

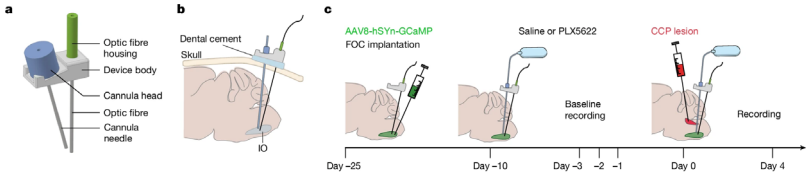


Figure 4A-C: Custom probe and experimental design for activity recording and pump-mediated delivery of PLX5622

Why is all this important? Grey matter microglia suppress neuronal activity and need to respond to trigger white matter myelin regeneration. Failure of white matter myelin regeneration subsequently leads to chronic microgliosis in grey matter. With the help of the ALZET Osmotic Pumps, the researchers were able to map a well defined neural circuit and highlight a form of neural plasticity related to grey-white matter interactions. These are important considerations for myelin regenerative therapies, but also expand the scope for further research in neurodegenerative disease models.

Read the full publication: de Faria, Omar Jr et al. "Focal white matter lesions drive grey matter inflammation and synapse loss." *Nature* doi:10.1038/s41586-026-10414-w

Ethiqa XR Warning

We have found that Ethiqa XR long-acting analgesia, which contains MCT oil, is not compatible with ALZET Pumps or iPRECIO Pumps. The use of Ethiqa XR as analgesic has been found to cause pump cracking. We recommend not using Ethiqa XR or any analgesic formulations containing oils. If the use of Ethiqa XR is important, please contact ALZET LLC.

It is with great sadness that we announce the departure of Clarisa Peer. Clarisa's tenure with ALZET spanned over half of its lifetime. She began as a Technical Information Associate and eventually became the General Manager of the business. Clarisa brought many insights from her time in school and years in industry. She utilized these perspectives while writing for and editing this publication, the ALZET Special Delivery™. Clarisa's critical eye has been imperative in establishing ALZET into the brand it is today. The ALZET team is commited to continue the legacy left by Clarisa, and we wish her the best with her future endeavors.

Clarisa's departure from ALZET ends a significant chapter for the company. As we look forward to the next chapter and to celebrating turning 50, we are evaluating what the next 50 years should look like. The majority of the Special Delivery Newsletters have been in Clarisa's voice. It only feels right to close this chapter with her departure. As such, this will be the final edition of the Special Delivery as you have come to know it.

To continue to see publication reviews and other company news, follow us on LinkedIn: https://www.linkedin.com/company/alzet

Do you have an upcoming research publication where you used ALZET products? Are you presenting ALZET research at a conference? Be sure to tag us on LinkedIn so that we can share the your accomplishments with the rest of the ALZET community.

Lafayette Life Science

In November 2024, ALZET was aquired by Lafayette Instrument Company and became part of Lafayette Life Science. Lafayette Life Science also includes: Actimetrics, Aurora Scientific, Avisoft, Campden Instruments, Lafayette Instrument, and Sutter Instrument. Lafayette Life Science is dedicated to manufacturing instruments that fit the way researchers actually work. If you are interested in learning more about products from Lafayette Life Science, please visit www.lafayettelifescience.com.

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