

## DNA Repair in the Brain through Targeted Nanoparticle Delivery of NAD<sup>+</sup> Precursors

When brain cell DNA is damaged by disease, the cell's attempts to repair the DNA can dry up crucial resources needed to maintain the cell's energy, eventually leading to cell death. This technology aims to replenish these resources by using cost-effective, highly customizable nanopetoids to deliver building blocks for the needed resources and achieve the first effective method for targeted energy regeneration in the brain. This both aids the repair of DNA and helps to prevent cell death.



### What is the Problem?

Over 20% of the oxygen we breathe is used in the brain to produce energy for cells to use. When that process is impaired by DNA damage from neurological diseases, brain cells suffer from the lack of energy and eventually die. The root cause can be traced back to a depletion of NAD<sup>+</sup>, a vital chemical in the processes of both energy production and DNA repair.

Normally, NAD<sup>+</sup> is used inside cells in a cycle converting oxygen into useable energy. However, when a disease damages the DNA inside a cell, the cell responds by producing a different molecule acting as a "first responder" to repair DNA. This process uses up NAD<sup>+</sup>, resulting in the lack of energy production, and eventually leads to cell death.

Replenishing NAD<sup>+</sup> levels within a cell in case of DNA damage is challenging; it cannot be directly passed into a cell, and its production from precursors such as NAM is still not well understood. While nanomaterial-based drug delivery platforms have shown great promise,

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designing and manufacturing nanoparticles to carry NAD<sup>+</sup> or NAM into damaged cells has not yet been demonstrated. There is therefore an unmet need in the targeted restoration of cell energy inside the brain.

### **What is the Solution?**

In order to replenish energy specifically to cells suffering from DNA damage, this technology uses nanoscale peptoids as a platform to deliver NAD<sup>+</sup> or NAM. Peptoids are a highly customizable class of molecules, capable of being manipulated into various shapes and sizes, and have been used to reach hard-to-target organs such as the brain.

The use of this therapy would prevent the root cause of this form of cell death, and aid in repairing damaged DNA. In addition, this technology aims to provide fundamental understanding into targeted drug delivery to injured brain cells, and treatment of energy depletion-induced cell death.

### **What is the Competitive Advantage?**

Peptoid nanoparticles are both more economical and more effective as a drug delivery platform for this use case than other nanomaterials studied in literature. They are easy to manufacture and customize, with a variety of shapes and molecular structures that can be tuned to various drug molecules. In the present study, the stability of peptoids in a nanotube shape helps to prevent premature release of the intended drug.

The direct impact of the technology aims at underserved patient populations, namely victims of neonatal and pediatric brain disease. In addition, fundamental research has the potential to go beyond the brain. Through understanding nano-peptoid delivery of NAD<sup>+</sup> precursors and the subsequent role of those precursors in restoring energy levels within a cell, this can be extended to other energy depletion conditions such as COVID-19.