Using plant-derived nanothylakoid units to induce anabolism in mammals to reduce disease progression

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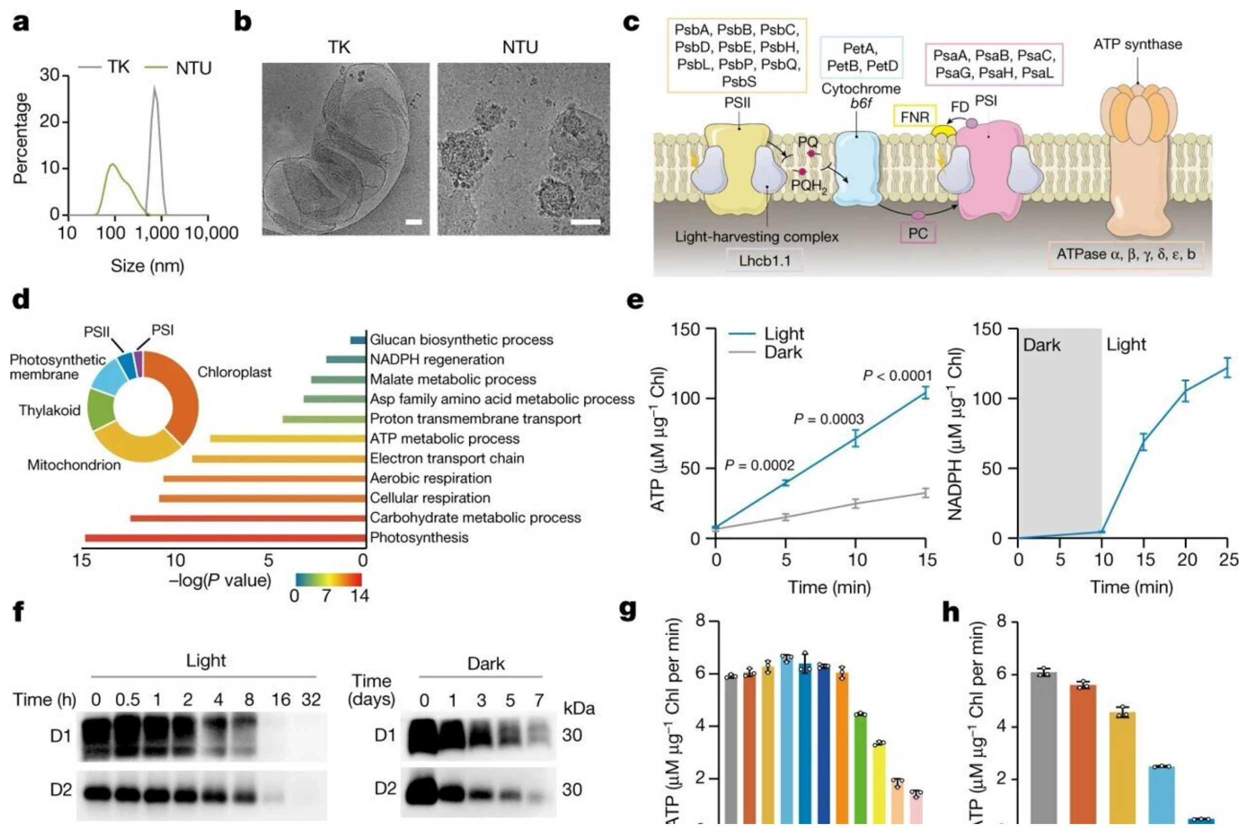

Preparation and characterization of CM-NTUs. **a**, Diameters of thylakoid (TK) organelles and NTUs. **b**, Cryo-TEM images of thylakoid organelles and NTUs. **c**, Schematic illustration of photosynthesis light reaction-associated proteins and the photosynthetic electron transport chain in NTUs. FD, ferredoxin; PC, plastocyanin; PSI, photosystem I; PSII, photosystem II; PQ, plastoquinone. **d**, Proteomics analysis of NTUs. The identified proteins were classified according to their cellular components and biological processes and analyzed using protein analysis through evolutionary relationships (PANTHER) overrepresentation test with Fisher's exact test for significance. **e**, ATP and NADPH production capacity of NTUs in vitro ($n = 3$, mean ± s.d.). **f**, Immunodetection of D1 and D2 abundance in NTUs under light illumination for 0–32 h (80 µmol photons m^{-2} s^{-1}) or darkness for 0–7 days (at room temperature). Similar results were obtained from three biologically independent samples. **g**,**h**, ATP production of NTUs was measured under light illumination (**g**) for 0–32 h (80 µmol photons m^{-2} s^{-1}) or in the dark (**h**) for 0–7 days (at room temperature) ($n = 3$, mean ± s.d.). **i**, Proteomics analysis of CM. The identified proteins were classified according to their cellular components. **j**, Content and categories of proteins in the CM involved in vesicle targeting and membrane fusion. **k**, Western blot analysis of Na^+/K^+-ATPase and β-tubulin in CM and cytoplasm. Na^+/K^+-ATPase was significantly enriched, and β-tubulin was present at low levels on the CM. **l**, Diameters of NTUs, CM, LNP-NTUs and CM-NTUs. **m**, Zeta potential of NTUs, CM, LNP-NTUs and CM-NTUs ($n = 3$, mean ± s.d.). **n**, Cryo-TEM images of LNPs, LNP-NTUs, CM and CM-NTUs. *n* represents the number of biologically independent samples. *P* values are indicated on the graph and were determined using two-tailed *t*-test (**e**). Scale bars, 50 nm (**n**) or 100 nm (**b**). Credit: *Nature* (2022). DOI: 10.1038/s41586-022-05499-y

A team of researchers at Zhejiang University School of Medicine has developed a way to use photosynthetic cells from plants when treating osteoarthritis in mice.

In their paper published in the journal *Nature*, the group describes how they created nanoscale thylakoid structures, called nanothylakoid units, in plants and delivered them into animal cells as a way to slow or stop disease progression. Two of the team members, Pengfei Chen and Xianfeng Lin have also published a Research Briefing outlining their work in the same journal issue.

Prior research has shown that in some progressive diseases, such as osteoarthritis, cells lack the amount of energy they need to function properly due to insufficient anabolism (where simple molecules are converted to complex molecules). Prior research has also shown that the compound ATP provides the energy needed by mammalian cells.

Prior research has also shown that the molecule NADPH plays an important role in allowing cells to use ATP. And finally, prior research has also shown that both ATP and NADHP are produced in plants during photosynthesis. The researchers therefore wondered if it might be possible to deliver some of the plant machinery into a mammalian cell where it could be used to produce ATP and NADPH for use by the mammalian cells when a light was applied, instigating the photosynthetic process.

To find out, the researchers created structures called nanothylakoid units (NTUs) from plant chloroplasts. They then covered them with mouse cells to prevent the mouse immune system from attacking when the NTUs were injected into the knee joints of mice with osteoarthritis.

Next, they shined a light on the joints to incite the photosynthetic process and thus the production of ATP and NADPH. Testing showed that the technique led to improved anabolism in the mouse cells, which in turn led to reducing the progression of the disease (slowed cartilage degeneration) in the test mice.

The researchers suggest their initial experiments show that their approach holds promise as a therapeutic approach to treating progressive diseases. They also note that the same approach could be used to metabolize cells as part of a process to create biofuels and perhaps other useful chemicals.

More information: Pengfei Chen et al, A plant-derived natural photosynthetic system for improving cell anabolism, *Nature* (2022).

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Plant-cell machinery for making metabolites transferred to mammalian cells, *Nature* (2022). DOI: 10.1038/d41586-022-03629-0