Large High Altitude Air Shower Observatory Formally Kicks Off

The Large High Altitude Air Shower Observatory (LHAASO), a major project as part of China's national scientific and technological infrastructure, passed the national acceptance assessment and formally went into operation on May 10.

Dedicated to cosmic ray observation and research, the design of LHAASO was approved by the national authorities on December 31, 2015. Jointly sponsored by the Chinese Academy of Sciences (CAS) and the People's Government of Sichuan Province, the construction of the principal part of the facility began in 2017 and was completed in 2021. The project then underwent the assessment by five expert panels organized by CAS, each focusing on different aspects. In April 2019, a quarter of the facility's devices were put into trial operation, and then in July 2021 the whole facility. The overall performance is now assessed as reliable, and capable of long-term stable scientific operation. The evaluation panel concluded that the performance of LHAASO is up to or better than the preset standard; and its formal operation will promote the exploration and original innovation on the frontiers of particle astrophysics research, as well as basic research in many related fields such as cosmology, astronomy, and particle physics.

Taking advantage of the high altitude on the Roof of the World, LHAASO can capture and record the signals from the high-energy cosmic rays before they vanish in their collisions with gaseous molecules in the atmosphere. With its smart design, advanced technology and powerful performance, it has become the most sensitive detector in the world for ultra-high-energy gamma rays, and the most sensitive survey telescope in the world for high-energy gamma-ray wide-field-of-view surveys. In addition, it is an advanced compound stereoscopic measuring system with the widest energy coverage in the world for cosmic rays of the "knee energy region" (the knee-shape bend in cosmic-ray spectra at around 10^{15} eV). With its completion and operation, LHAASO has become one of the three major international experimental facilities for particle astrophysics.

LHAASO is located on Mt. Haizi in Daocheng County, Sichuan Province, and covers an area of about 1.36 km^2. It consists of three arrays: a shower particle detector array composed of 5,216 electromagnetic particle detectors and 1,188 ground-installed muon detectors spreading 1 km^2 in area; a water Cherenkov detector array covering an area of 78,000 m^2; and an array of 18 wide-field-of-view Cherenkov telescopes.

A view of LHAASO (Image by IHEP)

Powered with these three arrays and state-of-the-art technologies, LHAASO is able to measure gamma rays and cosmic rays generated by high-energy celestial objects omnidirectionally in multiple variables, hence will help scientists understand the physical process corresponding to the cosmic rays of "knee region" energies.

Thanks to its high detection sensitivity, LHAASO had already made significant scientific breakthroughs even during its trial operations. For example, LHAASO discovered many ultra-high-energy cosmic accelerator candidates in the Milky Way and detected the highest energy photon ever recorded, thus heralding an era of "ultra-high-energy gamma astronomy". LHAASO also accurately measured the luminosity of the "standard candle" in the ultra-high-energy band and discovered gamma rays with energies over one quadrillion electron volts, which challenges the theoretical limit and hits the "knee region".

According to incomplete statistics, about 215 journal papers and 156 conference papers have been published based on the observational data obtained by LHAASO.

After the national acceptance, LHAASO will become an international center for cosmic ray research, with China as the central hub and participation from multiple countries. At present, 28 astrophysical research institutions have joined the international collaboration centered on LHAASO.

Clammy Hinges: Mussels' Secret to Avoiding Fatigue

Researchers from the University of Science and Technology of China (USTC) uncovered the secret behind mussel shells' incredible resistance to fatigue damage after repeated opening and closing (doi:10.1126/science.ade2038).

Using a combination of mechanical testing, microscopy and computational modeling, the researchers reported in *Science* on June 22 that the hinge connecting the two halves of mussel shells contains stiff mineral components strategically arranged to enable flexibility without fracture. The hinge has a folding fan-shaped region of radially aligned brittle nanowires embedded within a soft organic matrix. This design translates stresses into circumferential deformations and prevents failures. The study reveals nature's ingenious solution for combining deformability and fatigue resistance. The findings could inspire the engineering of flexible, damage-tolerant materials.

Mussels are appreciated as delicious seafood, but their shells hide an ingenious mechanical design. The hinge connecting the two shell halves withstands countless opening and closing motions without fatigue over the mussel's lifetime (Credit: *Pexel*)

So, the next time you slurp down a mussel, you may appreciate the exquisite natural engineering that allows it to open and close its shell for countless times over its lifetime.

New Study Uncovers How Immune Tolerance to Food Is Maintained

Eating a meal normally doesn't trigger an inflammatory immune reaction, but how the body

maintains tolerance to food has been unclear. Now, a new study published in *Cell* (doi:10.1016/j.cell.2023.05.027) by scientists at the University of Science and Technology of China (USTC) and Yale University School of Medicine reveals an unexpected role of a protein called gasdermin D (GSDMD) in inducing immune tolerance to food in the small intestine.

GSDMD usually acts as an alarm protein that signals cells to self-destruct to fight foreign invaders. But the study found it also takes on a tolerance-inducing role in intestinal cells in response to dietary proteins. When GSDMD is activated by digestive enzymes, it generates a fragmentation that travels to the nucleus and switches on genes involved in immune tolerance. Mice engineered to lack the GSDMD food-tolerance pathway couldn't properly develop regulatory T cells to maintain immune balance. This led to inflammatory overreactions to food, mimicking food allergy.

"A deeper understanding of these processes should facilitate the development of treatments against infection, inflammation, and allergy conditions in the intestine," noted the authors in the article. Uncovering GSDMD's peacekeeping role may ultimately open doors to new therapies for calming inflammatory conditions in the gut.

Food contains antigens that could trigger immune reactions, yet we maintain tolerance. New research reveals how. (Image by *Pixabay*)

Mapping Genes and Chromatin in the Developing Brain

Our brains begin as a simple sheet of cells that then grow and fold into the awe-inspiringly complex organ that makes us who we are. Now, researchers have created molecular atlases that reveal, in unprecedented detail, how specific genes are activated in coordination with changes to chromatin – the scaffolding that packages DNA – across the developing fetal mouse brain.

Using a new technique called MISAR-seq, Dr. PENG Guandun at the CAS Guangzhou Institutes of Biomedicine and Health and his coworkers simultaneously mapped the expression patterns of genes and the accessibility of chromatin throughout mouse brain samples at different developmental stages, and reported their results in *Nature Methods* on May 25, 2023 (doi:10.1038/s41592-023-01884-1).

By integrating both spatial transcriptomics and epigenetics data, the team gained crucial insights into the regulatory mechanisms governing brain development. The analyses exposed master regulators of neural development and predicted core gene networks that direct cell identity and function in key brain structures.

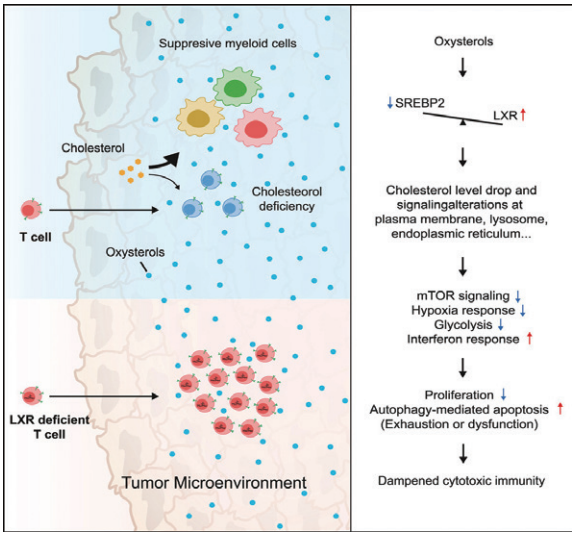
The researchers describe the methodology as "adding another layer of omics information directly to the spatial context." This extra dimension empowers the researchers to trace chromatin remodeling and correlated gene activation across the precise anatomical coordinates of the brain. Their findings underscore how dynamic changes in chromatin accessibility can prime, permit or restrict gene expression in certain cells as the brain develops.

Boosting T Cells to Beat Cancer by Normalizing Cholesterol

In a study appeared in *Cancer cell* on May 26 (doi:10.1016/j.ccell.2023.04.016), a research team jointly led by Dr. SONG Baoliang from Wuhan University and Dr. XU Chenqi from the Shanghai Institute of Biochemistry and Cell Biology (SIBCB) of the Chinese Academy of Sciences reveals an unexpected vulnerability – cholesterol deficiency in T cells that infiltrate tumors.

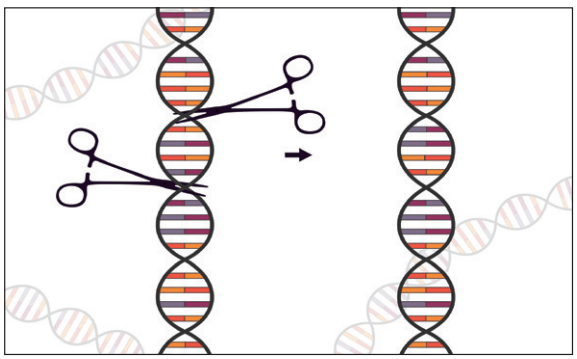
These vital immune cells normally rely on adequate cholesterol levels to mount an attack against cancer; but within tumors, T cells experience a form of cholesterol starvation. As a result, their activity falters, enabling cancer survival. The culprits are oxysterols – cholesterol breakdown products. Via complex signaling, oxysterols deprive T cells of cholesterol while allowing tumor cells to hog it for themselves.

Fortunately, the research team discovered a workaround. By genetically blocking one oxysterol receptor in T cells, they prevented the cholesterol imbalance. With their cholesterol normalized, souped-up T cells could proliferate and kill cancers more effectively in mouse models.



Exhaustion-associated cholesterol deficiency dampens the cytotoxic activity of T cells that infiltrate tumors. (Credit: Cancer Cell)

Potent and Miniature Genome Editors Discovered



Two highly compact and efficient DNA-editing tools are added to the toolbox of gene editors. (Image by Pixabay)

XIANG Guanghai et al. from the Institute of Zoology and the Institute for Stem Cell and Regeneration, both under CAS, systematically characterized a large set of RNA-guided DNA endonucleases called TnpB and identified two highly compact and efficient ones for genome editing applications. They reported their results in *Nature Biotechnology* on June 29 (doi:10.1038/s41587-023-01857-x).

By screening 78 TnpB proteins encoded by insertion sequences, the team found 33 hits that function in E. coli, including five candidates that also work in human cells. The smallest variants, ISAam1 (369 amino acids) and ISYmu1 (382 amino acids), demonstrated robust editing performance comparable to or better than commonly used CRISPR nucleases (1,368 amino acids).

The study establishes an effective framework to mine the extensive TnpB family for new compact genome-editing tools. It also highlights the remarkable diversity generated through natural selection, echoing Dobzhansky's famous words – "Nothing in biology makes sense except in the light of evolution."