

## NEWS &amp; COMMENTARIES

**The Rare Disease Innovation Hub**

<https://www.fda.gov/news-events/fda-voices/fda-rare-disease-innovation-hub-enhance-and-advance-outcomes-patients>

Patrizia Cavazzoni reported in the article above that more than 10,000 rare diseases impact over 30 million individuals in the U.S.—roughly one in ten people—about half of whom are children. Many of these rare illnesses can be life-threatening, and most lack approved treatments. A core objective of the U.S. Food and Drug Administration (FDA) is to engage with patients and caregivers to gain insights from their distinct perspectives and experiences, ensuring these considerations are prioritized during the review of medical products for those with rare diseases.



**Immatics**<sup>®</sup>

**TCER<sup>®</sup> IMA401 (MAGEA4/8)**

<https://immatics.com/overview/tcer-ima401/>

Immatics announced that the first proof-of-concept clinical data for the next-generation, half-life extended TCR Bispecific molecule, TCER<sup>®</sup> IMA401 (MAGEA4/8), Bispecific T cell engaging receptors (TCER<sup>®</sup>) are off-the-shelf biologics that leverage the body's immune system by redirecting and activating T cells towards cancer cells expressing specific tumor targets. The design of these novel biologics allows any T cell in the body to become activated and attack the tumor, regardless of the T cells' intrinsic specificity.

## SELECTED PUBLICATIONS

**Accidental Discovery In Science Magazine: Vitamin D Found to Boost Cancer Immunity Through the Microbiome:**

*Vitamin D regulates microbiome-dependent cancer immunity*

**Giampazolias et al., 2024.**

<https://doi.org/10.1126/science.adh7954>

History is filled with instances of serendipitous discoveries that have transformed our understanding of the world, and such moments continue to drive scientific progress in modern research. Recently, Caetano Reis e Sousa, an immunologist at The Francis

Crick Institute, and his team made a noteworthy discovery linking vitamin D to cancer via a bacterial ecosystem. They identified that vitamin D interacts with a binding protein, Gc globulin, and the gut-dwelling *Bacteroides fragilis* to enhance antitumor immunity in mice. These results represent the first evidence of a relationship between vitamin D metabolism, a specific microbiome species, and the immune response to cancer within a living organism.



## What happens to the brain during pregnancy?

Maxwell, 2024

<https://doi.org/10.1172/JCI183888>

Embodying the true essence of any MD/PhD student, the moment Maxwell noticed that second pink line on her pregnancy test early one Saturday morning, Maxwell immediately began researching. In addition to the typical "new mom" inquiries (Prenatal genetic testing? Choline? Doula?), Maxwell dug out her embryology textbook from medical school to provide her husband with unsolicited daily updates on their fetus's exact developmental stage. Maxwell delved into Williams Obstetrics to familiarize her with perinatal clinical care and even studied placental physiology. Generally, Maxwell discovered ample information about her fetus's growth and learned all there was to know—both the desirable and the undesirable—about the mechanics of childbirth, including the fetoplacental unit. However, Maxwell struggled to find any information concerning my body above the neck.....

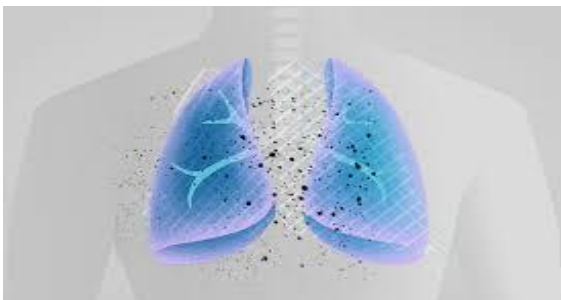


## Novel delivery systems for controlled release of bacterial therapeutics

Zaragoza et al., 2024

<https://doi.org/10.1016/j.tibtech.2024.01.002>

Recent progress in synthetic biology has opened up possibilities for the use of bacteria as biotherapeutics; however, these systems face limitations due to formulation issues. Significant improvements in materials development have led to precise delivery of small-molecule drugs. Additionally, cost-effective and user-friendly analytical techniques have facilitated the creation of microbial products. In the 21st century, microbial therapeutics could be as groundbreaking as antibiotics were in the previous century, provided there are further advancements in materials science, chemistry, and synthetic biology. As knowledge about the advantages of microbes increases, their potential for disease prevention and treatment is growing. Compared to traditional molecular drugs, microbial therapeutics tend to be less costly and easier to produce while often demonstrating greater efficacy.....



## Anti-inflammatory therapy with nebulised dornase alfa in patients with severe COVID-19 pneumonia A Randomised Clinical Trial

Porter et al., 2024

<https://doi.org/10.7554/eLife.87030.1>

In this proof-of-concept study involving patients with severe COVID-19 pneumonia, the administration of nebulised dornase alfa significantly lowered inflammation levels, markers of immune pathology, and shortened the duration until hospital discharge. Further research into the efficacy of dornase alfa in individuals experiencing acute respiratory infections and inflammation is warranted through larger clinical trials. Published in eLife, Porter et al study revealed that dornase alfa effectively mitigated hyper-inflammation in COVID-19 patients, a condition in which the immune system overly reacts, potentially leading to tissue damage and fatality.....



## Using AI in medical decision-making: a friend or a foe ?

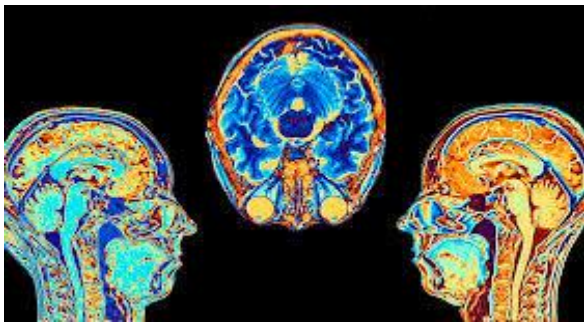
*Hidden flaws behind expert-level accuracy of multimodal GPT-4 vision in medicine.*

**Jin et al., 2024.**

<https://doi.org/10.1038/s41746-024-01185-7>

The GPT-4V AI model frequently erred in both its interpretations of medical images and its rationale for diagnoses, even when it arrived at the correct conclusion, according to NIH/NLM research. Jin et al study assessed how effectively the GPT-4V model could be integrated into medical decision-

making. In a quiz aimed at healthcare professionals, the AI exhibited strong accuracy in diagnosing clinical images, often surpassing the performance of physicians in a closed-book environment. Nonetheless, it often faltered in articulating its thought process and describing the images accurately, even when it correctly identified diagnoses. Furthermore, physicians outperformed the AI on more complex questions, particularly when they had access to external resources. These results emphasize the AI's potential contributions in clinical contexts while also pointing out its limitations and the necessity for continued research to facilitate precise and trustworthy use in the healthcare field.



## Robust and interpretable AI-guided marker for early dementia prediction in real-world clinical settings

**Lee et al., 2024**

<https://doi.org/10.1016/j.eclinm.2024.102725>

Artificial intelligence demonstrates superior capability compared to traditional clinical tests in forecasting the advancement of Alzheimer's disease. Researchers from the University of Cambridge have created a machine learning model that utilizes

non-invasive, cost-effective data such as cognitive assessments and MRI scans to predict the disease's progression. This model surpasses existing diagnostic techniques, achieving accurate predictions of Alzheimer's onset in 82% of instances and non-progression in 81%. The algorithm is able to distinguish between stable mild cognitive impairment and those at risk of progressing to Alzheimer's within three years, as well as categorize patients based on the rate of disease progression. This breakthrough has the potential to lessen the reliance on expensive and invasive diagnostic procedures, reduce the chances of misdiagnosis, and aid in the personalization of early interventions, which could enhance patient outcomes. Supported by various research institutions, the study showcases the model's practical applications in real-world clinical contexts and aspires to expand its use to address other forms of dementia.

## FOCUS ON AGING



### Type 2 cytokine signaling in macrophages protects from cellular senescence and organismal aging

Zhou et al., 2024

<https://doi.org/10.1016/j.immuni.2024.01.001>

The build-up of senescent cells in tissues and organs is a defining characteristic of aging and is associated with a range of age-related diseases. While it is recognized that immune dysfunction related to aging, often referred to as immunosenescence, plays a role in this process, the precise mechanisms still remain unclear. The study, Zhou et al. reveal that a deficiency in type 2 cytokine signaling accelerates the aging process. Conversely, the interleukin-4 (IL-4)-STAT6 signaling pathway offers protection to macrophages against senescence. Mechanistically, activated STAT6 enhances the expression of genes related to DNA repair through both homologous recombination and Fanconi anemia pathways. In contrast, a lack of STAT6 results in the release of nuclear DNA into the cytoplasm, which contributes to tissue inflammation and accelerates aging in the organism. Notably, Zhou et al. findings show that treating with IL-4 not only inhibits macrophage senescence but also enhances the health span of aged mice, achieving results comparable to senolytic treatments, with additional benefits when both methods are combined. Together, Zhou et al. findings support that type 2 cytokine signaling protects macrophages from immunosenescence and thus hold therapeutic potential for improving healthy aging.



### Aging and Inflammation

Singh et al., 2024

<https://doi.org/10.1101/cshperspect.a041197>

Aging can be understood as the gradual imbalance between the accumulation of random damage and the resilience mechanisms that work to repair that damage. This imbalance ultimately contributes to the onset of chronic diseases, frailty, and mortality. The immune system plays a key role in these resilience mechanisms. In fact, aging is characterized by a persistent activation of the immune response, indicated by elevated levels of inflammatory markers in circulation and the activation of immune cells both in the bloodstream and within tissues. This condition is referred to as "inflammaging." Similar to aging itself, inflammaging is linked to an increased risk of various age-related diseases, disabilities, frailty, and mortality. In this discussion, Singh et al. explore recent progress in understanding the mechanisms that lead to inflammaging and the intrinsic dysregulation of immune function associated with aging. Singh et al. particularly emphasize the mechanisms underlying chronic inflammation, focusing on the role of NF- $\kappa$ B and recent studies that target pro-inflammatory pathways.



## Meningeal lymphatic vessel crosstalk with central nervous system immune cells in aging and neurodegenerative diseases

Gao et al., 2024

<https://doi.org/10.4103/NRR.NRR-D-23-01595>

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## The human gut microbiome and aging

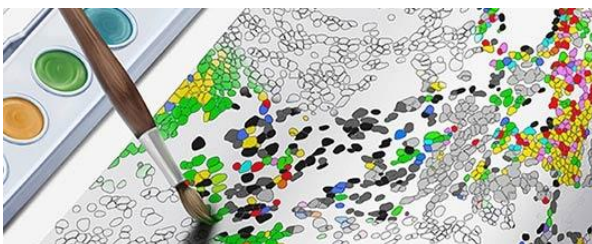
Bradley and Haran 2024

<https://doi.org/10.1080/19490976.2024.2359677>

It has been noted that an individual's gut microbiome changes throughout the course of their lifetime. It is affected by various elements right from birth, including the way the body is delivered, food, environmental exposures, location, usage of medications, and aging naturally. This review offers a thorough account of the gut microbiome's alterations over the lifetime

with a particular focus on how it affects human aging and age-related disorders. This review will examine the formation of the gut microbiome, draw attention to its correlations with many life phases disorders, and underscore its possible deleterious impact on the process of healthy aging. A varied microbiome that includes microorganisms known to generate anti-inflammatory metabolites, such as short-chain fatty acids, has been associated with good aging throughout life, but especially in old age. These results have shown remarkable global consistency, indicating that they may represent characteristics of healthy aging common to many cultures and genetic backgrounds.

## RECOMMENDED EVENTS



### Cell Symposia: Hallmarks of cancer

In partnership with Sun Yat-sen University Cancer Center and Guangdong Provincial Anticancer Association

November 7–9, 2024, Guangzhou, China

<https://www.cell-symposia.com/hallmarksofcancer-2024/index.html>



Apply today for the inaugural Prize for Innovations in Women's Health

**Deadline: November 1, 2024**

The BII & Science Translational Medicine Prize for Innovations in Women's Health aims to recognize researchers who have developed innovative advances with translational potential to impact women's health globally.

**The winner will:**

- ❖ have their essay published in Science Translational Medicine;
- ❖ receive a cash reward of USD \$25,000;
- ❖ be invited to BII headquarters in Copenhagen, Denmark, for the grand award ceremony

<https://www.science.org/content/page/bioinnovation-institute-science-translational-medicine-prize-innovations>



**2024 Dinner Short Courses\* (In-Person Only)**

**MONDAY, SEPTEMBER 30, 2024 5:00 - 7:30 PM**

<https://www.discoveryontarget.com/short-courses>

- **SC1:** Protein Degradation: A Focus on PROTACs from an ADME-Tox Perspective
- **SC2:** Fragment-Based Drug Design: Advancing Tools and Technologies
- **SC3:** DNA-Encoded Libraries
- **SC4:** Best Practices for Targeting GPCRs, Ion Channels, and Transporters with Monoclonal Antibodies
- **SC5:** Developing Physiologically Relevant 3D Models
- **SC6:** Protein Degradation: A Focus on PROTACs from a Beyond Rule of Five Space Perspective
- **SC7:** Chemical Biology for Covalent Discovery, Phenotypic Screening, and Target Deconvolution
- **SC8:** Biophysical Approaches for GPCRs
- **SC9:** Fundamentals of Generative AI for Drug Discovery

**Jobs Corner**



You can search exact phrases by using quotation marks, for example "Research Associate" will match jobs on this exact phrase only.

<https://jobs.biospace.com/searchjobs/>