Sociedade Brasileira de Bioquímica e Biologia Molecular - SBBq

Edital de Seleção PMBqBM 01/2025

Prova B: Suficiência em Língua Inglesa

Candidato (nome legível):

_____

CPF: _____

Orientações para a Prova de Suficiência em Língua Inglesa

1. Duração e Formato da Prova

- A prova tem duração máxima de **2 horas** e é composta por questões de interpretação de texto.
- A prova é presencial e possui caráter eliminatório, com resultado de "aprovado" (percentagem de acertos igual ou superior a 50%) ou "reprovado" (caso não atinja o percentual mínimo).
- As questões discursivas podem ser respondidas em português.

2. Regras de Consulta

- É permitido o uso de **dicionário impresso** apenas, sendo vedada a consulta a qualquer outro tipo de material, mídias ou anotações pessoais.

3. Uso de Equipamentos Eletrônicos

- Todos os aparelhos eletrônicos, incluindo celulares e dispositivos digitais, devem ser **desligados** e **guardados** antes do início da prova.

4. Preenchimento do Gabarito

- Preencha a **folha de gabarito** com atenção e sem rasuras. Respostas rasuradas ou duplas não serão consideradas.

5. Devolução dos Materiais

- Ao término da prova, devolva tanto o caderno de prova quanto o gabarito ao responsável. O caderno de prova poderá ser levado após **1 hora do início da prova.**

6. Finalização e Saída da Sala

- Ao finalizar, informe o responsável pela prova e permaneça no seu lugar até que receba orientações para a saída.

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FOLHA GABARITO

Preencha com X a alternativa correta.

1	A	B	C	D
2	A	B	C	D
3	A	B	C	D
4	A	B	C	D
7	A	B	C	D
8	A	B	C	D
9	A	B	C	D
10	A	B	C	D

Questões discursivas

5. Although the team didn't feel it could ethically do a risky liver biopsy to prove the base editor repaired KJ's cells, indirect evidence suggests it worked. After three doses, KJ can consume more protein and needs less medication to control his blood ammonia levels, the team reported this week at the annual meeting of the American Society of Gene & Cell Therapy in New Orleans and in its NEJM paper. He's had two viral infections without experiencing the ammonia crisis they would normally trigger.
6. A combination that could effectively repair a patient's mutated gene. The Penn Medicine team and collaborators first practiced on mice with various mutations for a metabolic disorder called phenylketonuria. By streamlining steps such as inserting the disease gene into cultured cells, they pared down the time needed to make a custom base editor from 1 to 2 years to months and showed they could cure the mice.
11. Mice that lacked the PrP gene remained healthy and showed no major abnormalities. This suggested that the normal prion protein's physiological function is still unknown.
12. Because prions do not contain nucleic acids (DNA or RNA), unlike viruses and other infectious agents. They are composed only of protein, which was a radical idea at the time.

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TEXT 1

Gene-editing therapy made just 6 months helps baby life-threatening disease (2025, May 15). *Science*. Retrieved June 16, 2025,<https://www.science.org/content/article/gene-editing-therapy-made-just-6-months-helps-baby-life-threatening-disease>

In a world first, researchers report easing the symptoms of a baby boy with a rare, life-threatening disease by giving him a version of the CRISPR gene editor tailored to a mutation he carries. The boy, first treated in February at just 7 months old, still needs a special diet and medication; the experimental therapy alone isn't enough to prevent a dangerous buildup of ammonia in his blood caused by a faulty gene for a key liver enzyme. Still, the swift development of a gene editor that appears to have repaired the defect in some of his liver cells is a landmark demonstration of a personalized approach that has tantalized rare disease researchers.

"It's a heroic effort and a really nice proof of principle," says neurologist Timothy Yu of Boston Children's Hospital, who leads a collaborative of teams developing personalized treatments for rare genetic disorders. The boy's case is reported today in The New England Journal of Medicine (NEJM) and at a gene therapy meeting. His treatment relies on a base editor, a variation on the better known CRISPR. With CRISPR, an enzyme fully cuts DNA at a specific site in the genome determined by a strand of guide RNA. In base editors, CRISPR's enzyme is altered so it only nicks one of DNA's double strands. A second enzyme then swaps out a DNA base, correcting a single "letter" misspelling. Base editors infused into a body to edit liver cells have shown success at treating adults with a high cholesterol disease and another genetic disorder.

Cardiologist Kiran Musunuru of the University of Pennsylvania Perelman School of Medicine, who helped develop one such treatment, and Rebecca Ahrens-Nicklas, a physician-scientist at Penn Medicine and the Children's Hospital of Philadelphia (CHOP) who treats metabolic diseases, wanted to move on to a bigger challenge. They set their sights on quickly designing base editors customized for young patients born with diseases called urea cycle disorders, who might avoid organ damage and other complications if treated very early in life. These conditions involve defects—often a single-base change—in genes encoding enzymes the liver needs to create harmless urea from the body's ammonia. Ammonia, produced by the breakdown of proteins, accumulates in the blood, where it can cause lethargy, coma, and brain damage.

The idea was to develop a pipeline to rapidly test various base-editing enzyme components and guide RNAs to find a combination that could effectively repair a patient's mutated gene. The Penn Medicine team and collaborators first practiced on mice with various mutations for a metabolic disorder called phenylketonuria. By streamlining steps such as inserting the disease gene into cultured cells, they pared down the time needed to make a custom base editor from 1 to 2 years to months and showed they could cure the mice.

In August 2024, they found an ideal human test case, a baby whose urea acid disorder would likely become so severe the potential benefits of treating him outweighed the risks. The infant, nicknamed KJ by his family, was diagnosed soon after birth with severe carbamoyl phosphate synthetase 1 (CPS1) deficiency, a disease that occurs in just one in 1 million births. Doctors immediately controlled KJ's ammonia levels with a low-protein diet and nitrogen-scavenging drugs, but he was likely going to need a risky liver transplant.

The CHOP/Penn Medicine team and collaborators raced to develop and test a base editor to correct one of KJ's broken copies of the CPS1 gene in just 6 months. After safety testing in lab animals, they got regulatory approval to infuse microscopic balls of fats, known as lipid nanoparticles, carrying messenger RNA encoding the editing tools into the bloodstream of the nearly 7-month-old.

Although the team didn't feel it could ethically do a risky liver biopsy to prove the base editor repaired KJ's cells, indirect evidence suggests it worked. After three doses, KJ can consume more protein and needs less medication to control his blood ammonia levels, the team reported this week at the annual meeting of the American Society of Gene & Cell Therapy in New Orleans and in its NEJM paper. He's had two viral infections without experiencing the ammonia crisis they would normally trigger.

The study's approval only allowed KJ to get three doses of the base editor, and he's clearly not cured. But his doctors hope he can avoid a liver transplant—and could in theory get more doses of the base editor as he grows. He is reaching developmental milestones and his father, Kyle Muldoon, said in a press call, "We're very, very happy with the results." He will soon go home from the hospital.

The treatment caused levels of certain liver enzymes to rise, signaling an immune response to the nanoparticles or their cargo, but they soon returned to normal. As with CRISPR, base editors have a theoretical risk of changing unintended DNA sequences—indeed, tests of KJ's base editor on cells revealed an off-target change, but not one likely to cause harm. "We're thrilled," Ahrens-Nicklas says. "This seems to be safe. … There's some early signs that this is going to benefit [KJ]." Musunuru adds, "Our hope is that this will be the start of something that many, many others around the world will pick up on."

The base editors complement efforts begun 7 years ago when Yu developed a tailor made RNA-based drug to treat a girl with a severe neurological disorder. That approach, which has now been tested in about 30 children, works best for neurological disorders, Yu notes, whereas base editors appear promising for diseases that involve the liver, which readily sops up nanoparticles carrying the editing tools. Another promising approach relies on a CRISPR-like tool not to repair a gene, but to insert a whole working version at a specific site in the genome. A baby who received this treatment for a different urea cycle disorder, ornithine transcarbamylase (OTC), is now off all special diet and medication, a company reported in

January and in recent scientific meeting presentations. The gene insertion strategy is delivered with a virus, however, which carries its own risks. It can only be given once for now and is much more expensive to manufacture than base editors. Medical geneticist Cary Harding of Oregon Health & Science University, who is consulting on the trial for OTC, welcomes a diversity of strategies to treat these rare but devastating conditions. "At this stage, it's all experimental and all [approaches] deserve to be explored."

Use Text 1 to answer the questions below (1 to 6)

1. Why is KJ still required to maintain a special diet and medication despite the treatment?
A) The therapy failed to reach the target gene.
B) The gene editing had no impact on his condition.
C) He developed immunity to the treatment.
D) The therapy alone isn't sufficient to stop ammonia accumulation.

2. What is the role of lipid nanoparticles in the therapy?
A) To remove excess ammonia from the blood.
B) To deliver the gene editing tools into liver cells.
C) To stabilize the enzyme after gene correction.
D) To reverse the immune response caused by CRISPR.

3. What evidence suggests that the base editing therapy may have worked in KJ?
A) His genetic sequence was fully mapped.
B) He experienced increased ammonia levels.
C) He can tolerate more protein and uses fewer medications.
D) He underwent a successful liver biopsy.

4. What is a theoretical concern associated with CRISPR and base editors?
A) Inability to edit liver tissue
B) Off-target genetic changes
C) Immune rejection of healthy cells
D) Rapid degradation of mRNA

5. What evidence suggests that the gene editing therapy was effective in KJ?
R:

- Although the team didn't feel it could ethically do a risky liver biopsy to prove the base editor repaired KJ's cells, indirect evidence suggests it worked. After three doses, KJ can consume more protein and needs less medication to control his blood ammonia levels, the team reported this week at the annual meeting of the American Society of Gene & Cell Therapy in New Orleans and in its NEJM paper. He's had two viral infections without experiencing the ammonia crisis they would normally trigger.

6. Describe the strategy used by the researchers to reduce the development time of personalized gene editors.

combination that could effectively repair a patient's mutated gene. The Penn Medicine team and collaborators first practiced on mice with various mutations for a metabolic disorder called phenylketonuria. By streamlining steps such as inserting the disease gene into cultured cells, they pared down the time needed to make a custom base editor from 1 to 2 years to months and showed they could cure the mice.

TEXT 2

Prions – a new biological principle of infection

Adapted from Press release. NobelPrize.org. Nobel Prize Outreach 2025. Tue. 17 Jun 2025. <https://www.nobelprize.org/prizes/medicine/1997/press-release/>

Summary

The 1997 Nobel Prize in Physiology or Medicine was awarded to Stanley Prusiner for discovering a new class of disease-causing agents: prions. Unlike bacteria, viruses, fungi, or parasites, prions are normal cellular proteins capable of transforming into highly stable, harmful conformations that cause fatal brain diseases in humans and animals. Prion diseases can be inherited, transmitted, or occur spontaneously. Affected brains develop a spongy, porous appearancedue to extensive nerve cell death, leading to symptoms like impaired motor control, memory loss, mental decline, and insomnia. Prusiner's work provides crucial insight into the mechanisms of other dementia-related diseases, such as Alzheimer's, and offers a foundation for future treatments and drug development.

In 1972 Stanley Prusiner began his work after one of his patients died of dementia resulting from Creutzfeldt-Jakob disease (CJD). It had previously been shown that CJD, kuru, and scrapie, a similar disease affecting sheep, could be transmitted through extracts of diseased brains. There were many theories regarding the nature of the infectious agent, including one that postulated that the infectious agent lacked nucleic acid, a sensational hypothesis since at the time all known infectious agents contained the hereditary material DNA or RNA. Prusiner took up the challenge to precisely identify the infectious agent and ten years later in 1982 he and his colleagues successfully produced a preparation derived from diseased hamster brains that contained a single infectious agent. All experimental evidence indicated that the infectious agent was comprised of a single protein, and Prusiner named this protein a prion, an acronym derived from "proteinaceous infectious particle." It should be noted that the scientific community greeted this discovery with great skepticism, however, an unwavering Prusiner continued the arduous task to define the precise nature of this novel infectious agent.

The infectious prion particle forms within the body

The prion protein, designated PrP, could fold into two distinct conformations, one that resulted in disease (scrapie PrP = PrPSc) and the other normal (PrP = PrPc). It was subsequently shown that the disease-causing prion protein had infectious properties and could initiate a chain reaction so that normal PrPc protein is converted into the more stabile PrPSc form. The PrPSc prion protein is extremely stabile and is resistant to proteolysis, organic solvents and high temperatures (even greater than 100o C). With time, non-symptomatic incubation periods vary from months to years, the disease-causing PrPSc can accumulate to levels that result in brain

tissue damage. In analogy to a well known literary work, the normal PrPc can be compared to the friendly Dr. Jekyll and the disease causing PrPSc to the dangerous Mr. Hyde, the same entity but in two different manifestations.

Mutations in the prion gene cause hereditary brain diseases

The long incubation time of prion diseases initially hindered protein purification, requiring Prusiner to use many mice and wait about 200 days per experiment. This process improved when scrapie was adapted to hamsters, which had shorter incubation periods. Prusiner, with collaborators, cloned the prion gene and showed that the normal protein is present in various tissues, especially on neuron surfaces and in white blood cells. He demonstrated that hereditary prion diseases like CJD and GSS are caused by mutations in the prion gene, confirmed when mutant genes induced disease in transgenic mice. In 1992, researchers created prion knock-out mice, which were completely resistant to infection, but regained susceptibility when the prion gene was reintroduced. Strangely enough, mice lacking the prion gene are apparently healthy, suggesting that the normal prion protein is not an essential protein in mice, its role in the nervous system remains a mystery.

Structural variant disease-causing prions accumulate in different regions of the brain

Specific mutations within the prion gene give rise to structurally variant disease-causing prion proteins. These structural prion variants accumulate in different regions of the brain. Dependent upon the region of the brain that becomes infected, different symptoms, typical for the particular type of disease are evident. When the cerebellum is infected the ability to coordinate body movements declines. Memory and mental acuity are affected if the cerebral cortex is infected. Thalamus specific prions disturb sleep leading to insomnia, and prions infecting the brain stem primarily affect body movement.

Intrinsic defense mechanisms do not exist against prions

Prions are much smaller than viruses. The immune response does not react to prions since they are present as natural proteins from birth. They are not poisonous, but rather become deleterious only by converting into a structure that enables disease causing prion proteins to interact with one another forming thread-like structures and aggregates that ultimately destroy nerve cells. The mechanistic basis underlying prion protein aggregation and their cummulative destructive mechanism is still not well understood. In contrast to other infectious agents, prion particles are proteins and lack nucleic acid. The ability to transmit a prion infection from one species to another varies considerably and is dependent upon what is known as a species barrier. This barrier reflects how structurally related the prions of different species are.

Prion diseases in animals and man

All known prion diseases are universally fatal, though incubation periods and disease progression vary. This variability is illustrated by several well-documented cases in both animals and humans. Scrapie, affecting sheep since the 18th century, later spread to Scotland and also affects animals like mink, cats, deer, and moose. Bovine Spongiform Encephalopathy (BSE), or mad cow disease, emerged in England via contaminated cattle feed and peaked in 1992 with around 37,000 cases. Kuru, among the Fore people in New Guinea, was linked to cannibalistic rituals, with disease lasting 3-12 months. Gertsmann-Sträussler-Scheinker (GSS) is a hereditary dementia caused by prion gene mutations, affecting ~50 families, with a course of 2-6 years. Fatal Familial Insomnia (FFI), also hereditary, leads to death in about one year, affecting nine known families. Creutzfeldt-Jakob Disease (CJD) occurs mostly spontaneously (85–90%), with 10–15% hereditary and a few cases from infections like contaminated growth hormone or transplants. The disease affects ~1 in a million people, with death usually within one year. A variant CJD, likely from BSE, appeared in 1995, characterized by psychiatric symptoms, muscle spasms, and mobility issues.

Use Text 1 to answer the questions below (7 a 12)

7. What makes Prusiner's discovery particularly relevant beyond prion diseases themselves?
A. It revealed that all infectious diseases are caused by protein malfunctions.
B. It suggested that protein misfolding may also play a role in other neurodegenerative diseases.
C. It demonstrated that prion diseases are the only type of dementia affecting humans.
D. It proved that memory loss is exclusively linked to infectious brain diseases.

8. Why are prion diseases typically not detected by the immune system?
A. Prions are always too small to trigger immunity.
B. Prions carry no viral DNA.
C. Prions have built-in immune suppression.
D. Prions are identical to harmless proteins and thus ignored.

9. Which statement about species transmission is correct according to the text?
A. Transmission depends on the similarity of prion structure between species.
B. All prion diseases spread easily between species.
C. Only spontaneous cases occur, not interspecies transfers.
D. Immune systems prevent any cross-species transmission.

10. About prion diseases in animals and humans, choose the correct alternative:
A. Kuru, observed among the Fore people of Papua New Guinea, is a genetic disease associated with a mutation in the prion protein gene.
B. Bovine Spongiform Encephalopathy (BSE), also known as "mad cow disease," originally appeared in cows infected through direct contact with contaminated animals.
C. Creutzfeldt-Jakob Disease (CJD) occurs exclusively through infectious transmission, such as organ transplants or the use of contaminated biological products.

D. Fatal Familial Insomnia (FFI) is caused by a mutation in the human prion protein gene and typically leads to death within approximately one year after the onset of symptoms.

11. What was observed in mice that lacked the PrP gene, and what conclusion was drawn from this experiment?

R: Mice that lacked the PrP gene remained healthy and showed no major abnormalities. This suggested that the normal prion protein's physiological function is still unknown.

12. Why were prions not considered viruses or typical infectious agents?

R: Because prions do not contain nucleic acids (DNA or RNA), unlike viruses and other infectious agents. They are composed only of protein, which was a radical idea at the time.