0116. U.K. Becomes First Country to Approve a CRISPR Disease Treatment 英国成为第一个批准 CRISPR 疾病治疗方法的国家

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Sickle 镰刀-cell anaemia 贫血（症） is marked by **red blood cells** that are misshapen (a.)畸形的；扭曲变形的 and sticky 黏（性）的, affecting (v.) blood flow.
镰状细胞性贫血的特点, 是红细胞畸形且粘稠，影响血液流动。

In a world first, the UK **medicines regulator** has approved a therapy that uses (v.) CRISPR **gene editing** as a treatment for diseases.
英国药品监管机构批准了一种使用 CRISPR 基因编辑, 来治疗疾病的疗法，这在世界范围内尚属首次。

The therapy, called Casgevy, will treat (v.) the blood conditions（因不可能治愈而长期患有的）疾病 **sickle-cell disease** and **β-thalassaemia** 地中海贫血.
这种疗法称为Casgevy，将治疗"镰状细胞病"和"β地中海贫血"等血液疾病。

Sickle-cell disease, also known as **sickle-cell anaemia** 贫血（症）, can cause debilitating 虚弱 pain, and people with β-thalassaemia can require **regular blood transfusions** 输血; 追加投资；（资金的）注入.

镰状细胞病，也称为镰状细胞性贫血，可引起衰弱性疼痛，β-地中海贫血患者可能需要定期输血。

Example 1. 案例

debilitate

(v.) to make sb's body or mind weaker（使身心）衰弱，衰竭，虚弱

-→ de-, 不，非，使相反。-hab, 持，握，力量，词源同able, habit.

主 The approval by **the Medicines and Healthcare products 产品；制品 Regulatory (a.)（对工商业）具有监管权的，监管的 Agency** (MHRA) 谓 follows (v.) **promising 有希望的；有前途的 results** (n.) from **clinical trials**（对能力、质量、性能等的）试验，试用 that tested (v.) the one-time treatment, which is administered by **intravenous (a.)注入静脉的；静脉内 infusion**.

药物和医疗产品监管机构（MHRA）的批准, 是基于对经过临床试验的一次性治疗进行的有希望的结果，这种治疗是通过静脉输注进行的。

Example 2. 案例

intravenous

-→ intra-,在内，-ven,静脉，词源同vein,venous.

Researchers also tested the treatment for a severe form of β-thalassaemia, which is conventionally 照惯例，照常套 treated with **blood transfusions** roughly once a month.

研究人员还测试了针对严重β地中海贫血的治疗方法，传统上大约每月一次输血治疗这种贫血。

HOW DOES THE GENE THERAPY WORK (v.)?

基因疗法如何发挥作用？

Casgevy **relies on** the gene-editing tool CRISPR, the developers of which won the Nobel Prize in Chemistry in 2020.

Casgevy 依赖于基因编辑工具 CRISPR，该工具的开发者获得了 2020 年诺贝尔化学奖。

Sickle-cell disease and β-thalassaemia 地中海贫血 are caused by errors in **the DNA sequence** of genes that encode for haemoglobin 血红蛋白, a molecule 分子 that helps red blood cells to carry oxygen around the body.
镰状细胞病和β地中海贫血, 是由编码血红蛋白的基因DNA序列错误引起的，血红蛋白是一种帮助红细胞将氧气输送到全身的分子。

In sickle-cell disease, abnormal haemoglobin **makes** blood cells **misshapen and sticky**, causing them to form (v.) clumps **that can clog (v.) blood vessels**.
在镰状细胞病中，异常的血红蛋白使血细胞变形且粘稠，导致它们形成团块，从而堵塞血管。

These blockages reduce (v.) **the oxygen supply** to tissues（人、动植物细胞的）组织, which can cause periods of severe pain, **known as** pain crises.
这些阻塞会减少组织的氧气供应，从而导致一段时间的剧烈疼痛，称为疼痛危象。

β-thalassaemia occurs (v.) when 主 mutations in **the haemoglobin gene** 谓 lead to **deficient 缺乏的；缺少的；不足的; 有缺点的；有缺陷的 or absent levels** of the oxygen-carrying molecule in red blood cells, **low numbers** of red blood cells and symptoms **such as** fatigue, **shortness of breath** 呼吸短促 and **irregular heartbeats**.
当血红蛋白基因突变, 导致红细胞中携氧分子水平不足或缺失、红细胞数量减少以及疲劳、呼吸急促和心律不齐等症状时，就会发生β地中海贫血。

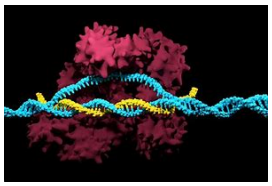
Clinicians ① **administer (v.)施行；执行 Casgevy** 疗法名 by taking blood-producing **stem cells** 干细胞 out of the **bone marrow** 髓，骨髓 of people with either disease and ② using CRISPR to edit (v.) **genes 后定 encoding (v.) for haemoglobin** in these cells.
临床医生通过从患有这两种疾病的人的骨髓中, 取出造血干细胞，并使用 CRISPR 编辑这些细胞中编码血红蛋白的基因, 来施用卡吉维。

The gene-editing tool ① an RNA molecule 后定 that **guides** (v.) the enzyme 酶 **to** the correct region of DNA and ② **a Cas9 enzyme** that cuts DNA.
基因编辑工具包括, 引导酶到达 DNA 正确区域的 RNA 分子, 和切割 DNA 的 Cas9 酶。

Once **the Cas9 enzyme** reaches (v.) the gene 后定 **targeted by Casgevy**, called BCL11A, it cuts (v.) both DNA strands（线、绳、金属线、毛发等的）股，缕.
一旦 Cas9 酶到达 Casgevy 靶向的基因（称为 BCL11A），它就会切割两条 DNA 链。

Example 3. 案例

Cas9 enzyme



BCL11A usually prevents (v.) **the production of a form of haemoglobin** that is made only in fetuses 胎儿.
BCL11A 通常会阻止一种仅在胎儿中产生的血红蛋白的产生。

By disrupting 妨碍; 扰乱 the BCL11A gene, Casgevy unleashes (v.)发泄；突然释放；使爆发 the production of **fetal haemoglobin**, which does not carry **the same abnormalities** (n.)异常 (尤指人的身体或行为中令人担忧或危险性的特征) 后定 as **adult haemoglobin** in people **with sickle cell or β-thalassaemia patients**.
通过破坏 BCL11A 基因，Casgevy 释放胎儿血红蛋白的产生，该胎儿血红蛋白不具有"与镰状细胞或β地中海贫血患者的成人血红蛋白相同的"异常。

Example 4. 案例

unleash

[VN] ~ **sth (on/upon sb/sth)** : to suddenly let a strong force, emotion, etc. be felt or have an effect 发泄；突然释放；使爆发

• The government's proposals **unleashed (v.) a storm of protest** in the press.
政府的提案引发了新闻界的抗议浪潮。

Before **the gene-edited cells** are infused (v.)使具有，注入（某特性）; 输注（药物等） back into the body, people must **undergo a treatment** that prepares (v.) the **bone marrow** to receive the edited cells.
在将基因编辑的细胞输回体内之前，人们必须接受治疗，使骨髓做好接受编辑的细胞的准备。

Once administered, the stem cells **give rise to** 导致,引起,使…产生 red blood cells 后定 containing (v.) fetal haemoglobin.
一旦施用，干细胞就会产生"含有胎儿血红蛋白的"红细胞。

After some time, **this relieves (v.) symptoms** by boosting **the oxygen supply** to tissues.
一段时间后，这会通过增加组织的氧气供应来缓解症状。

“Patients may need to **spend at least a month** in a hospital facility 设施；设备 while **the treated (a.)治疗的；已处理过的 cells** ① take up 开始从事;占用(时间、空间或精力) residence 居住；定居 in the **bone marrow** and ② start to make red blood cells with the stable form of haemoglobin,” the MHRA said in a **press release** （向媒体发布的）新闻稿.
MHRA 在一份新闻稿中表示：“患者可能需要在医院住院至少一个月，而接受治疗的细胞会在骨髓中驻扎, 并开始产生具有稳定形式血红蛋白的红细胞。”

HOW SAFE IS CASGEVY?
卡吉维有多安全？

主 Participants 后定 **involved in the trials** 试验, which are ongoing (a.)持续存在的；仍在进行的；不断发展的, 谓 experienced **side effects** 后定 including nausea (n.)恶心；作呕；反胃, fatigue, fever and **an increased risk of infection**, but no **significant safety concerns** were identified 确认；认出；鉴定.
参与正在进行的试验的参与者, 出现了副作用，包括恶心、疲劳、发烧和感染风险增加，但没有发现重大的安全问题。

Example 5. 案例

> *nausea*
> -→ 它来自希腊语naus（船）；词根naus-指“船”；后缀-ea是疾病后缀-ia的变形，再如insomnia（失眠）等；所以其本义就是“晕船”，后词义扩大为“恶心”。noise（噪声）是它的同源词，长期处于噪声环境中亦会引起诸如恶心等的不适感觉，体会此处元音音变。

The MHRA and manufacturer are monitoring 监视；检查；跟踪调查 the safety of the technology and will release further results.
MHRA 和制造商正在监测该技术的安全性，并将发布进一步的结果。

One concern surrounding the approach **is that** CRISPR can sometimes **make unintended 非计划的；无意的；无心的 genetic modifications** with unknown side effects.
围绕该方法的一个担忧是，CRISPR 有时会产生意想不到的基因修饰，并产生未知的副作用。

It is well known that CRISPR can **result in** spurious 虚假的；伪造的;建立在错误的观念（或思想方法）之上的；谬误的 genetic modifications **with unknown consequences** to **the treated cells**.
众所周知，CRISPR 可能会导致错误的基因修饰，对"被处理的细胞"产生未知的后果。

For now, the therapy is likely **to remain the reserve** 谨慎；保留; 预备役部队；后备部队 of rich nations 后定 **with developed 发达的；先进的；成熟的 health-care systems**.
目前，拥有发达医疗保健系统的富裕国家, 可能仍然将这种疗法作为后备的治疗选项(保持谨慎)。

“This treatment may not easily **scale up** 增加; 放大; 按比例增加 to be able to **provide treatments** in low- and middle-income countries, since it requires the technology **to obtain a patient’s blood stem cells**, **deliver** 递送；传送；交付；运载 the genetic editor **to** these stem cells, and then reinjection of these cells,”
“这种治疗方法可能不容易扩大规模，以便能够在低收入和中等收入国家提供治疗，因为它需要技术来获取患者的血液干细胞，将基因编辑器传递给这些干细胞，然后重新注射这些干细胞。细胞，”

“It is not **an ‘off the shelf’ 现成的 medicine** that can be readily injected or taken **in pill form**,”
“它不是一种可"以轻松注射, 或以药丸形式"服用的‘现成’药物，”

Example 6. 案例

> *off the shelf*
> 现成的：指产品或物品已经制造好, 并且可以立即购买和使用的，而不需要定制或特别制作。

HOW MUCH WILL IT COST (v.)?
它要花多少钱？

Even in places **where it win (v.) approval**, the high cost of Casgevy is likely to limit (v.) who can benefit from it.
即使在获得批准的地方，Casgevy 的高成本, 也可能会限制谁可以从中受益。

The challenge is that these therapies will be very expensive **so** a way of making these more accessible globally is key.
挑战在于这些疗法将非常昂贵，因此如何让这些疗法在全球范围内更容易获得是关键。

The treatment's price **has not yet been settled**（最终）决定，确定，安排好 in the United Kingdom, but **estimates suggest that** it could cost roughly US$2 million per patient, **in line with** 与…相似（或紧密相连） the pricing of other gene therapies.
英国尚未确定该疗法的价格，但估计每位患者的费用可能约为 200 万美元，与其他基因疗法的定价一致。

Example 7. 案例

in 'line with sth

similar to sth or so that one thing is closely connected with another 与…相似（或紧密相连）

• Annual pay increases **will be in line with inflation**. 每年加薪幅度将与通货膨胀挂钩。

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2. U.K. Becomes First Country to Approve a CRISPR Disease Treatment

Sickle-cell anaemia is marked by red blood cells that are misshapen and sticky, affecting blood flow.

In a world first, the UK medicines regulator has approved a therapy that uses CRISPR gene editing as a treatment for diseases.

The therapy, called Casgevy, will treat the the blood conditions sickle-cell disease and β-thalassaemia. Sickle-cell disease, also known as sickle-cell anaemia, can cause debilitating pain, and people with β-thalassaemia can require regular blood transfusions.

The approval by the Medicines and Healthcare products Regulatory Agency (MHRA) follows promising results from clinical trials that tested the one-time treatment, which is administered by intravenous infusion.

Researchers also tested the treatment for a severe form of β-thalassaemia, which is conventionally treated with blood transfusions roughly once a month.

HOW DOES THE GENE THERAPY WORK?

Casgevy relies on the gene-editing tool CRISPR, the developers of which won the Nobel Prize in Chemistry in 2020.

Sickle-cell disease and β-thalassaemia are caused by errors in the DNA sequence of genes that encode for haemoglobin, a molecule that helps red blood cells to carry oxygen around the body.

In sickle-cell disease, abnormal haemoglobin makes blood cells misshapen and sticky, causing them to form clumps that can clog blood vessels. These blockages reduce the oxygen supply to tissues, which can cause periods of severe pain, known as pain crises.

β-thalassaemia occurs when mutations in the haemoglobin gene lead to deficient or absent levels of the oxygen-carrying molecule in red blood cells, low numbers of red blood cells and symptoms such as fatigue, shortness of breath and irregular heartbeats.

Clinicians administer Casgevy by taking blood-producing stem cells out of the bone marrow of people with either disease and using CRISPR to edit genes encoding for haemoglobin in these cells. The gene-editing tool an RNA molecule that guides the enzyme to the correct region of DNA and a Cas9 enzyme that cuts DNA.

Once the Cas9 enzyme reaches the gene targeted by Casgevy, called BCL11A, it cuts both DNA strands. BCL11A usually prevents the production of a form of haemoglobin that is made only in fetuses. By disrupting the BCL11A gene, Casgevy unleashes the production of fetal haemoglobin, which does not carry the same abnormalities as adult haemoglobin in people with sickle cell or β-thalassaemia patients.

Before the gene-edited cells are infused back into the body, people must undergo a treatment that prepares the bone marrow to receive the edited cells. Once administered, the stem cells give rise to red blood cells containing fetal haemoglobin. After some time, this relieves symptoms by boosting the oxygen supply to tissues. “Patients may need to spend at least a month in a hospital facility while the treated cells take up residence in the bone marrow and start to make red blood cells with the stable form of haemoglobin,” the MHRA said in a press release.

HOW SAFE IS CASGEVY?

Participants involved in the trials, which are ongoing, experienced side effects including nausea, fatigue, fever and an increased risk of infection, but no significant safety concerns were identified. The MHRA and manufacturer are monitoring the safety of the technology and will release further results.

One concern surrounding the approach is that CRISPR can sometimes make unintended genetic modifications with unknown side effects.

It is well known that CRISPR can result in spurious genetic modifications with unknown consequences to the treated cells.

For now, the therapy is likely to remain the reserve of rich nations with developed health-care systems. “This treatment may not easily scale up to be able to provide treatments in low- and middle-income countries, since it requires the technology to obtain a patient’s blood stem cells, deliver the genetic editor to these stem cells, and then reinjection of these cells,”

“It is not an ‘off the shelf’ medicine that can be readily injected or taken in pill form,”

HOW MUCH WILL IT COST?

Even in places where it win approval, the high cost of Casgevy is likely to limit who can benefit from it.

The challenge is that these therapies will be very expensive so a way of making these more accessible globally is key.

The treatment's price has not yet been settled in the United Kingdom, but estimates suggest that it could cost roughly US$2 million per patient, in line with the pricing of other gene therapies.