0117-science

**Cancer treatments boosted by immune-cell hacking**

**自译：癌症治疗通过免疫细胞攻击而爆发**

# 微软：免疫细胞黑客攻击促进癌症治疗

**Precision-controlled CAR-T-cell immunotherapies could be used to *tackle* a range of tumour types.**

自译：精确控制CAR-T细胞免疫疗法可能被应用于阻止肿瘤复制。

**微软：精确控制的CAR-T细胞免疫疗法可用于治疗一系列肿瘤类型。**

**Elaborately** **engineered** immune cells can not only recognize cancer cells, but also evade defences that **tumours** use to **fend off** **attacks**, researchers have found.

自译：研究者发现，精心地改变免疫细胞的基因不仅能识别癌症细胞，也能躲避肿瘤细胞防御自身的攻击。

**微软：研究人员发现，精心设计的免疫细胞不仅可以识别癌细胞，还可以逃避肿瘤用来抵御攻击的防御。**

Two studies published today in *Science* ***build on*** the success of **chimeric antigen receptor** (CAR)-T cancer therapies, which use genetically altered T cells to ***seek out* tumours** and mark them //for destruction. These treatments have the **potential** to lead to long-lasting remission, but are not successful for everyone, and have ***so far*** been effective *against* only a small number of cancers.

自译：今天《科学》杂志上发表了两项研究，依赖于(CAR)-T癌症疗法的成功，运用基因改造T细胞找出肿瘤细胞同时做标记以销毁。这些疗法有潜在的作用，**可引发长时间免疫，但是不能对每个人都成功，**同时只针对一小部分的癌症，离有效性很远。

**微软：今天发表在*《科学》*杂志上的两项研究，建立在嵌合抗原受体（CAR）-T癌症疗法成功的基础上，该疗法使用基因改变的T细胞来寻找肿瘤并标记它们以进行破坏。~~这些治疗有可能导致长期缓解，但并非对每个人都成功~~，到目前为止，仅对少数癌症有效。**

To bolster the power of CAR-T therapies, researchers have further engineered the cells to contain switches that allow control over when and where the cells are active. The **hacked** cells produce a protein that stimulates T cells, to **counteract** immunosuppressive **signals** that are often **released** by **tumours**.

自译：加强CAR-T therapies改善治疗的效力，研究者狠狠设计了细胞去控制//允许控制细胞活跃的时间和地点的//开关。黑客细胞产生蛋白质刺激T细胞，抵抗癌细胞释放的免疫抑制信号。

**微软：为了增强CAR-T疗法的力量，研究人员进一步设计了细胞，使其包含开关，可以控制细胞活跃的时间和地点。被黑客入侵的细胞产生一种刺激T细胞的蛋白质，以抵消通常由肿瘤释放的免疫抑制信号。**

Both studies are **a tour de force** in T-cell engineering and **highlight** the **direction** that researchers want to push CAR-T-cell therapy, says systems immunologist Grégoire Altan-Bonnet at the US National Cancer Institute. “We know a lot of the *parts*, now it’s being able to put them together and explore,” he says. “If we engineer the system *well*, we can really put the tumours into **checkmate**.”

自译：两项研究是T-细胞修饰的自传，和启发预防//研究者想要推进CAR-T细胞治疗，系统免疫学家xxx说“我们知道很多片段，现在能把他们放在一起探索。”他说，“如果我们改造系统顺利，我们能真正的将肿瘤细胞击破。”

**微软：这两项研究都是T细胞工程的一次巡回演出，并强调了研究人员希望推动CAR-T细胞疗法的方向，美国国家癌症研究所的系统免疫学家Grégoire Altan-Bonnet说。“我们知道很多零件，现在能够将它们放在一起并探索，”他说。“如果我们设计好系统，我们真的可以把肿瘤置于将死状态。**

## Engineered immune cells 改造肿瘤细胞

T cells **typically patrol** the body, looking for foreign proteins displayed on the surface of cells. Such cells could be **infected** with a virus, for example, or they could be tumour cells that are producing abnormal, cancer-associated proteins. A class of T cells called killer T cells can then destroy the abnormal cells.

自译：T细胞常常在体内巡逻，寻找排列在细胞表面的外源性蛋白质。一些细胞能够被病毒感染，比如，或者它们可能变成肿瘤细胞产生畸形，癌症组织蛋白。一类T细胞被称作杀手T细胞能够破坏不正常的细胞。

**微软：T细胞通常在体内巡逻，寻找细胞表面显示的外来蛋白质。例如，这些细胞可能感染了病毒，或者它们可能是产生异常癌症相关蛋白质的肿瘤细胞。一类称为杀伤性T细胞的T细胞可以破坏异常细胞。**

CAR-T therapies ***involve*** genetically engineering T cells from a person with cancer to produce CARs, which are proteins that recognize the proteins displayed by tumour cells.

自译：CAR-T疗法包括基因改造/来自癌症病人体内生产的CARs的/T细胞，识别排列在肿瘤细胞表面的蛋白质。

**微软：CAR-T疗法涉及对癌症患者的T细胞进行基因工程改造以产生CAR，CAR是识别肿瘤细胞显示的蛋白质的蛋白质。**

The **approach** has been **approved** to treat some leukaemias, lymphomas and myelomas. But researchers have been **pursuing** ways to make the treatments safer and more effective, and to expand their use to other diseases.

自译：这个成果取得了一些治疗白血病、淋巴瘤、骨髓瘤的的成果。但是研究者们追求更加安全有效的治疗，并扩大他们治疗疾病的范围。

**微软：该方法已被批准用于治疗一些白血病、淋巴瘤和骨髓瘤。但研究人员一直在寻求使治疗方法更安全、更有效的方法，并将其应用于其他疾病。**

In one of the new studies, Ahmad Khalil, a synthetic biologist at Boston University in Massachusetts, and his **colleagues** **wired** a *complex* system of 11 DNA **sequences** into CAR T cells. The resulting genetic circuits can be switched on and off using already-approved drugs, which allows researchers to control when and where the hacked T cells are active, as well as their production of a protein called IL-2, which stimulates immune responses.

自译：在一项新的研究中，人造生物学家xxxxx和他的团队在CAR T cells连接了一个含有11个DNA序列的系统。结果显示基因的循环能够通过被已批准的药物（控制）开关，这让研究者能够控制黑客T细胞何时随何的活跃度，同时它们蛋白质的产物称作IL-2，刺激免疫应答。

**微软：在其中一项新研究中，马萨诸塞州波士顿大学的合成生物学家Ahmad Khalil和他的同事将一个由11个DNA序列组成的复杂系统连接到CAR-T细胞中。由此产生的遗传回路可以使用已经批准的药物打开和关闭，这使得研究人员能够控制被黑客入侵的T细胞活跃的时间和地点，以及它们产生一种叫做IL-2的蛋白质，这种蛋白质刺激免疫反应。**

The other group of researchers, led by synthetic biologist Wendell Lim at the University of California, San Francisco, **programmed** CAR T cells to produce IL-2 only when the engineered T cell **encounters** a cancer cell. The team found that //this IL-2 production was most efficient at fighting tumours in mice with pancreatic cancer //when it was activated through a pathway//that was separate from the one used to recognize the cancer cell — a detail that could help in **shaping** future **therapies**, says Andrea Schietinger, a **tumour immunologist** at Memorial Sloan Kettering Cancer Center in New York City.

自译：其他研究团队，被xxxxx领导，建立了CAR T cells //仅仅在编码T细胞遇到癌细胞时//生产IL-2。团队找到了这种IL-2产物在患有胰腺癌的大鼠中是最有效的攻击肿瘤的物质。~~当它通过一个通道激活的时候//他和一个曾经识别到的细胞分开~~//一个能够帮助形成未来的疗法。Xxxx说

**微软：另一组研究人员由加州大学旧金山分校的合成生物学家Wendell Lim领导，他们编程CAR-T细胞仅在工程T细胞遇到癌细胞时才产生IL-2。研究小组发现，这种IL-2的产生在对抗胰腺癌小鼠的肿瘤方面最有效，当它通过与用于识别癌细胞的途径分开的途径被激活时 - 这一细节可能有助于塑造未来的治疗方法，纽约市纪念斯隆凯特琳癌症中心的肿瘤免疫学家Andrea Schietinger说。**

## Solid progress ~~固定项目~~ 坚实的进展

Both approaches could be particularly useful in **crafting** CAR-T therapies that can **target** **solid tumours**, Schietinger says. Solid tumours have posed a particular challenge to CAR-T approaches because the engineered cells have difficulty infiltrating the tumours and, **once there**, can be disabled by signals that cancer cells use to **suppress** the immune response. “These engineered T cells ***overcome*** both **roadblocks**,” she says. “They find their *way* in and then, ***once*** they’re in, get the signals in the right space and at the right time to be really effective in killing the cancer cell.”

自译：xxx说，一些方法可能有特殊的作用，在CAR-T免疫治疗中锚定固定的癌细胞。固定的癌细胞是CAR-T方法的挑战，因为修饰细胞很难渗入癌细胞，同时不能通过施压免疫回应标记癌症细胞。“这些修饰过的T细胞超过了两种路径。”她说，“它们找到了它们的路~~，（曾经它们在）~~然后在正确的空间和时间收到信号，真正有效的在杀死癌细胞。”

**微软：Schietinger说，这两种方法在制作可以靶向（锚定）实体瘤的CAR-T疗法方面都特别有用。实体瘤对CAR-T方法提出了特殊的挑战，因为工程细胞难以浸润肿瘤，一旦浸润肿瘤，就会被癌细胞用来抑制免疫反应的信号禁用。“这些工程T细胞克服了这两个障碍，”她说。“他们找到自己的方式，然后，一旦他们进入，在正确的空间和正确的时间获得信号，以真正有效地杀死癌细胞。**

The ability to turn the T cells on and off could also help to reduce a phenomenon called T-cell exhaustion, in which T cells become inactive after a **prolonged** period of stimulation, says Evan Weber, a cancer immunologist at the Children’s Hospital of Philadelphia in Pennsylvania. Some studies have found that giving T cells a ‘rest period’ can reduce T cell exhaustion and boost their overall effectiveness against tumours.

自译：开或者关T细胞的能力也能帮助减少T细胞耗竭的现象，在T细胞在//xx激活期后//处于不活跃的状态，xxx说，一个xxxxx的癌症免疫学家。一些研究发现给T细胞“休息期”能减少T细胞耗竭同时提升他们克服肿瘤的消极影响。

**微软：打开和关闭T细胞的能力也有助于减少一种称为T细胞衰竭的现象，其中T细胞在长时间刺激后变得无活性，宾夕法尼亚州费城儿童医院的癌症免疫学家Evan Weber说。一些研究发现，给T细胞一个“休息期”可以减少T细胞的衰竭，并提高它们对肿瘤的整体有效性。**

Lim plans to ***further*** develop the system for testing in clinical trials, and to tweak it to explore the effects of producing other **molecules** that, like IL-2, stimulate immune cells. There has been a growing realization that such molecules, called **cytokines**, could be **pivotal** to the success of CAR-T therapies, says Weber. “We know we need smarter ways of tapping into them,” he says, “***rather than*** just turning on a receptor all the time or **secreting** a cytokine **constitutively**.”

自译：在临床诊断中，极限计划远远提升了系统检测，同时稍微调整它探索//降低其他分子，比如IL-2,刺激免疫细胞//的效果。~~一个增长的识别比如~~小分子，细胞激素，会提升T-细胞疗法的成功性，xxx说。“我们需要更灵敏的方法去xx他们，比仅仅一直打开接收者和隐匿细胞激素的组成性有效。”

微软：Lim计划进一步开发用于临床试验测试的系统，并对其进行调整以探索产生其他分子（如IL-2）刺激免疫细胞的效果。Weber说，**人们越来越意识到**这种称为细胞因子的分子可能对CAR-T疗法的成功至关重要。“我们知道我们需要更聪明的方法来利用它们，”他说，“而不仅仅是一直打开受体或**分泌细胞因子**。

Khalil hopes that the system that he and his colleagues have *developed* will be usable in other cell types, including another type of immune cell called **macrophages**, which are better than T cells at **penetrating** solid tumours. His genetic circuits were **designed** with adaptability //in mind, so that researchers who *specialize* in cancer immunotherapies — or fields such as gene therapy or stem-cell biology — can **tweak** them to ***suit*** their needs. “I hope this will ***capture*** the imagination of a lot of researchers ***out*** there,” he says.

自译：xx希望他和他的同事发展/提升的系统在其他种类的系保障也会有用，包括另一种免疫细胞xx，比T细胞对肿瘤更有针对性。他的基因的循环被标记//用获得性物质在思维中，所以研究者//专业在癌症免疫学—或基因治疗的领域—细胞生物学—能够促使他们去塑造自己的需求。“我希望这能够采集这些研究者信息。”

**微软：Khalil希望他和他的同事开发的系统能够用于其他细胞类型，包括另一种称为巨噬细胞的免疫细胞，它在穿透实体瘤方面比T细胞更好。他的基因回路在设计时考虑到了适应性，因此专门研究癌症免疫疗法或基因治疗或干细胞生物学等领域的研究人员可以调整它们以满足他们的需求。“我希望这能吸引很多研究人员的想象力，”他说。**