

Interview with Scarlet Therapeutics

DARPA awards grant to UK biotech for defense

In the US and elsewhere, programmes financed by governments for national defense can take many forms – including to support basic science. The Defense Advanced Research Projects Agency (DARPA) of the US, originally founded in the late 1950s to develop satellite technology, has in recent years branched out into computers and vaccines. On 23 September, DARPA stepped deeper into biology with the award of a research grant of up to \$14 million to a consortium led by Scarlet Therapeutics Ltd of the UK to develop engineered, laboratory-produced red blood cells for defense. Besides Scarlet, the consortium includes the University of Bristol and Unicorn Biotechnologies Ltd of the UK and Northwestern University of the US.

In an interview, Alistair Irvine, Scarlet's chief executive, said DARPA is looking for red blood cells that could enhance the body's natural capabilities to improve performance and survivability in challenging conditions. "They are basically looking for something that is going to help people survive and cope better under extreme conditions, whether that be extreme exertion or extreme altitude and therefore low oxygen availability. It's really about helping people survive," he said.

According to DARPA, the first phase of the project will involve demonstrating the feasibility of engineering red blood cells with these enhanced capabilities, while the second will focus on testing functional prototypes. The programme focuses on engineering cells that are potentially safer and more effective in extreme environments.

Red blood cells are small disc-shaped cells that are produced in the bone marrow and carry oxygen from the lungs to the rest of the body. However a deficiency in these cells can impair the body's ability to carry oxygen to body

tissues and, depending on the severity, can be treated with iron supplements or red blood cell transfusions. Transfusions are common but require donors, collection centres, and processing to purify the cells to make sure they are safe.

Scarlet was founded in 2022 by two professors at the University of Bristol, initially to address rare blood shortages in the UK and elsewhere. In the process, the scientists discovered that synthetic biology could be used to generate therapeutic red blood cells to treat rare metabolic diseases. In May the company raised £3.2 million in seed funding to progress this work.

In the interview, Dr Irvine said the company's development of treatments for metabolic diseases, including hyperammonemia and hyperoxaluria, will continue. The DARPA project is an expansion of the company's existing activities. "What the work with DARPA is about is taking the sort of work that we have already done of modifying red blood cells and actually taking it a step further...so they have additional functionality that is switched on and off dependent on physiological conditions," he said.

Scarlet's technology platform is based on engineered red blood cells with a potential for delivering therapeutic proteins *in vivo* to humans. The proteins remain inside the red blood cell membrane and therefore are not recognised by the immune system. The laboratory-grown cells have been designed without standard blood group antigens which means that they do not need donor matching and can be used as transfusions for a large group of patients. They are long-acting which means they can continuously clean the blood. Finally, they are expected to be able to deliver complex therapies for a variety of metabolic disorders.

– By Victoria English

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