Reducing the numbers of animals in scientific research

Fireflies to the rescue

ANZCCART | Ministry for Primary Industries

Reducing the numbers of animals in scientific research

Scientists are busy developing some really exciting high-tech methods to replace the use of many animals in scientific research, like organs-on-a-chip. But for those researchers who don't yet have an alternative, the principles of *reduction* and *refinement* are crucial.

reduction: *using the least number of animals possible while still getting useful, reliable data*
refinement: *minimising potential suffering and improving animal welfare*

What problem are scientists trying to solve?

Infectious diseases caused by bacteria and viruses kill millions of people all around the world every year. Here in New Zealand, 1 in 4 people who end up in hospital overnight are there because of an infectious microbe. Researchers are working hard to develop better antibiotics and vaccines to protect people from infectious diseases, but this still relies on the use of animals. These animals (usually mice) are infected with microbes and then groups of animals are euthanised at different times after infection so that the researchers can find out where the microbes have spread to, how many are there and whether experimental medicines and vaccines are able to stop the animals from getting sick.

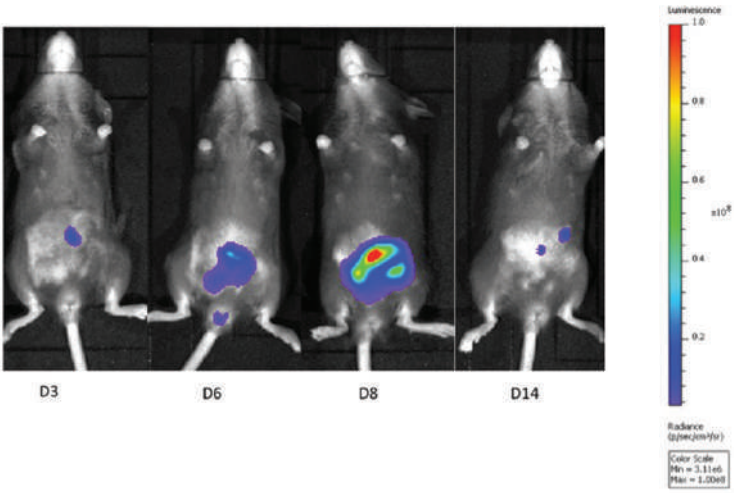
The solution

Making microbes glow-in-the-dark

Many creatures in nature glow in the dark. Some use their light to find food, like the anglerfish or the New Zealand glow worm. Others use their light to find a mate, like fireflies. This living light is called bioluminescence, and animals create it using a simple chemical reaction with the help of an enzyme called a luciferase.

How is it done?

The luciferase genes from fireflies and naturally glowing bacteria can be engineered into disease-creating bacteria to make them glow. The bioluminescence reaction needs energy so only living organisms glow. If the organisms die, their light goes out. Because light travels through flesh and skin, scientists can use sensitive cameras to watch these glow-in-the-dark bacteria inside animals without having to euthanise those animals. This means that the scientists can watch where the bacteria go over time, and how they change in number, within the same animals, instead of needing to euthanise different animals throughout their experiments.



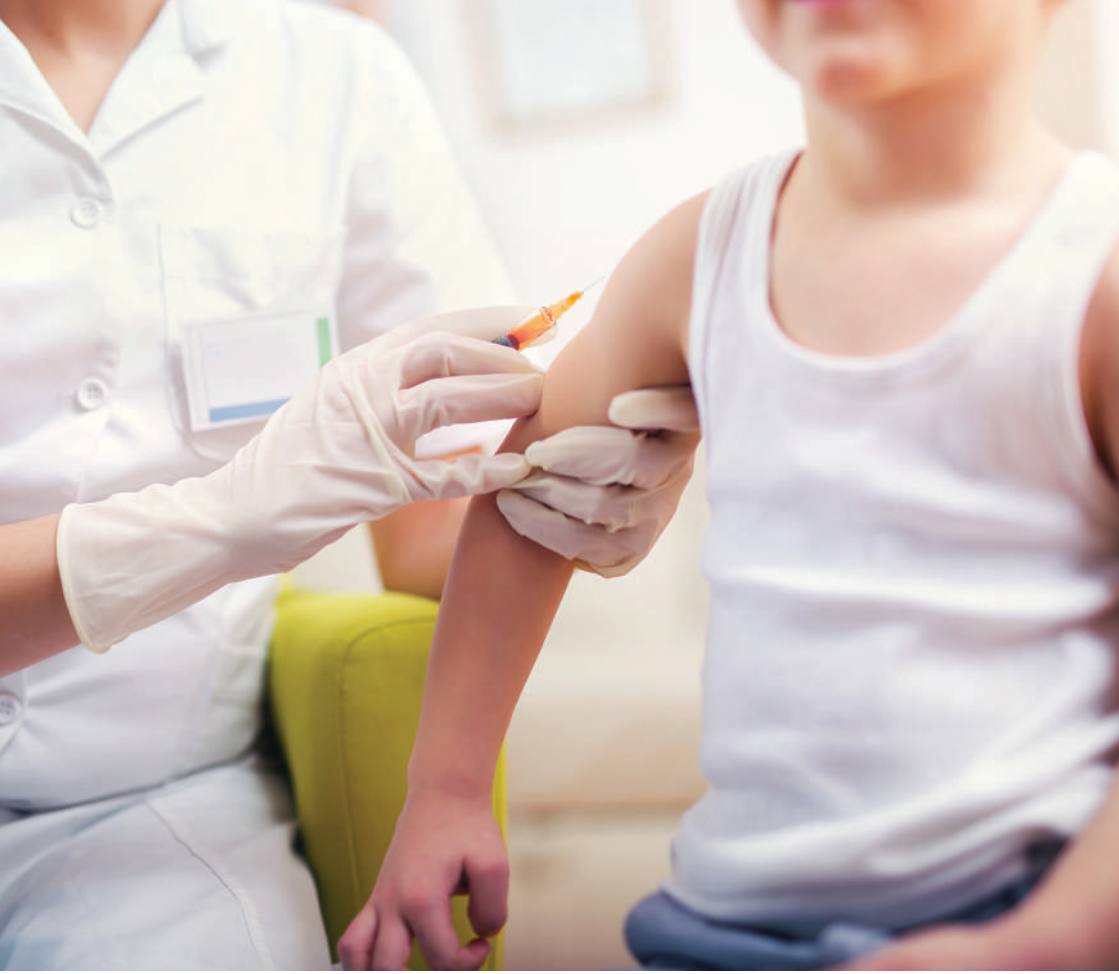
Left: Visualisation of bioluminescent bacteria from within an anaesthetised mouse taken over 14 days. First bacteria colonise the animal's caecal patch, appearing as a blue dot. Then the bacteria move to infect the colon and rectum. The animal's immune system responds and clears the infection and the bioluminescent bacteria begin to disappear.

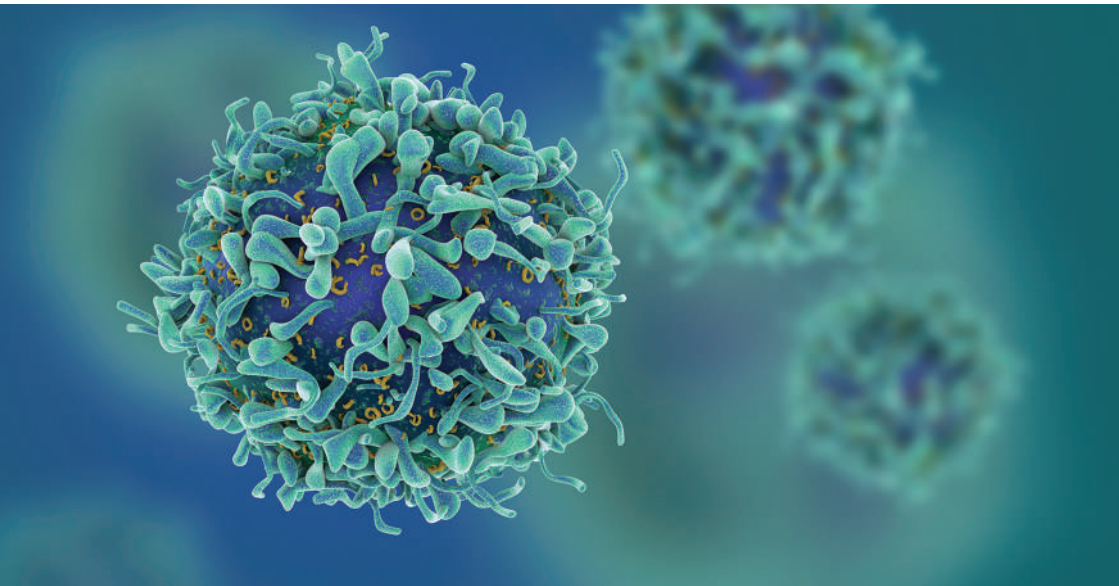
Advantages

- Fewer animals are used because the microbes can be tracked in the same group of animals over the whole experiment.
- Animals that do not respond to new antibiotics or vaccines can be euthanised before they show any symptoms of disease, preventing any suffering.
- The infection can be followed without needing to do invasive sampling procedures, such as collecting blood. This means a reduction in stress and discomfort/pain.
- Animals not properly infected can be identified and removed from the study.

Disadvantages

- Requires repeated handling and anaesthesia for imaging, although newer imaging systems can image freely moving animals.
- Engineering bioluminescent microbes can be difficult.





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Bioluminescent monitoring of in vivo colonization and clearance dynamics by light-emitting bacteria. Wiles S, Robertson BD, Frankel G and Kerton A (2009). *Methods in Molecular Biology* 574, 137–153.

Health Research Council (HRC) News, Issue 74, March 2012

www.hrc.govt.nz/sites/default/files/HRC%20News%20-%20March%202012.pdf

Helpful links

www.youtube.com/watch?v=kP_RaHo1Pmw

www.superbugslab.org/

www.nc3rs.org.uk/exploiting-bioluminescence-mouse-studies-bacterial-infection

For further information

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