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THE CONVERSATION

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Of mice and men: role of mice in biomedical research questioned

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[A study recently published](#) in the peer-reviewed journal [PNAS](#) (Proceedings of the National of Academy Sciences) shows that mice are poor models for human inflammatory diseases. The paper, which focused on [sepsis](#), burns and trauma, raises questions about the fundamental role of mice in biomedical research.

Bodily responses to burn injuries and acute infections look similar in mice and humans, but the study authors found they're driven by fundamentally different genetic and molecular mechanisms. They spent ten years examining which genes in human white blood cells are activated during infection. Data from 167 patients suggested there are particular patterns of genomic change associated with acute inflammation.

After having their paper rejected by several journals, the researchers decided to redesign their study. Apparently, one objection from [reviewers](#) was that the results had not been validated by mouse studies. But when the researchers looked at the genomic response to different forms of inflammation in mice, they made a number of startling discoveries:

1. The relatively uniform gene changes found in human patients were not found in mice.
2. Genomic changes in mice were completely different to humans, and there was no discernible pattern of gene modification.
3. None of the mouse models for sepsis, bacterial blood poisoning, trauma or burns predicted the magnitude or direction of inflammation in humans.

These findings have significant ramifications.

There have been almost 150 clinical trials of drugs designed to block immune responses to acute sepsis in humans. These trials were all based on research in mice and have all failed to produce a positive result.

Clinical trials are expensive. The costs of a failed trial include financial losses and opportunity costs (other things that could have been done with the resources used). These

opportunity costs are both scientific, and in terms of the health and well-being of human participants.

As specified by the [Declaration of Helsinki](#), which governs the ethics of research involving people, before a candidate drug can be given to humans, it must first be tested on at least two different animal models. So the drugs used in human trials were run through standardised mouse models, and each model was designed specifically to replicate human inflammatory responses.

The authors of the PNAS study make clear their findings don't invalidate mouse models of other human diseases. But they do think their experience raises important questions about how biomedicine is researched, particularly, the central role of animal models.

In an interview in the [New York Times](#), one of the authors said,

They were so used to doing mouse studies that they thought that was how you validate things. They are so ingrained in trying to cure mice that they forget we are trying to cure humans.

The study also highlights a problem for researchers who study animal models to better understand and treat human diseases. The practice depends on the assumption that some properties of humans and non-human animals are both functionally and causally similar. But to assume that the first leads to the second is to commit what some [philosophers of science](#) describe as the “modeller’s functional fallacy”.

Digital watches and sundials can both tell the time, for instance, but they do this in completely different ways. A cloudy day obscures the time on the sundial but it doesn't have the same effect on the digital watch. Similar functions can clearly have different causes.

Other biomedical researchers are beginning to take a [different approach](#) to devising therapies. They advocate a comparative strategy that prioritises the study of naturally occurring human and animal disease. They believe this form of “[translational research](#)” could solve many of the quandaries raised by this and [other examples](#) of research where animal models have been poor predictors of human disease.

Public support for animal experimentation rests on its purported value to human health. But [arguments against the practice](#) are increasingly based on examples of how it has misled medicine. Unfortunately, however, so much is invested in current research models that it's unlikely to see significant change anytime soon