

It's won six Nobel prizes – so why the fascination with the fruit fly?

They might make a meal of your picnic, but drosophila share 60% of human DNA, making them perfect for genetics research that has led to vital strides in treating cancer, autism, diabetes and many other ills. As scientists in the field win yet another Nobel, science editor **Robin McKie** salutes the little beasts

*Am not I
A fly like thee?
Or art not thou
A man like me?*

With these lines, from *The Fly*, William Blake posed a question of unusual prescience for a poet writing 200 years ago. At first glance, there seem to be few similarities between *Homo sapiens* and airborne insects. Yet Blake was not so sure. He could see connections. And in recent years, science has found that he was probably correct. Fruit flies, it transpires, have common features with humans to a remarkable degree (we share 60% of the same DNA) – a point underlined last week when the Nobel committee awarded yet another prize to scientists who have used *Drosophila melanogaster* as the basis of groundbreaking research.

In this case, Jeffrey Hall, Michael Rosbash and Michael Young – all based in the US – were awarded the Nobel prize in physiology or medicine for their work on the molecular mechanisms that control circadian rhythms – in other words, the 24-hour body clock that controls lives throughout the animal kingdom. Crucially, this work was done largely by experimenting on fruit flies.

Nor was this a first for drosophila research. At least five other groups have received Nobels for their work using fruit flies to unpick the secrets of human physiology and biology in general. This Nobel love affair with drosophila began in the early 20th century, when US biologist Thomas Morgan used fruit flies to confirm that genes are located on chromosomes like beads on a string, and that some genes are linked – in other words they are inherited together. In doing so, Morgan established genetics as a modern science.

Ever since, the discipline has relied – to a startling degree – on fruit fly research, leading to breakthroughs

in a vast range of topics. Today, scientists believe that about 75% of known human disease genes have a recognisable match in fruit flies. These include Down's, Alzheimer's, autism, diabetes and cancers of all types. "It's almost as if they were designed to help scientists," says geneticist Steve Jones.

As their name suggests, fruit flies like to eat fruit – particularly the ripening variety – and appear in summer to settle on apples, pears and sweet drinks. (Hence Groucho Marx's observation that "time flies like an arrow but fruit flies like a banana".) They pose no threat to health but have a number of features that make them ideal laboratory fodder: drosophila have a life cycle of two weeks. They eat

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Andreas Prokop, cell biologist

cornmeal, yeast and sugar, and little else, and can be housed in tiny tubes.

"You put a male and female together, and a fortnight later you have a new generation of fruit flies to study," said Simon Collier, head of Cambridge University's Fly Facility. "That makes them a very powerful tool for studying mutations in genes."

On its own, that would be useful enough. However, the fruit fly possesses other key features that impress scientists. The drosophila genome has only four pairs of chromosomes. Humans have 23. That means it is much easier to manipulate and study the function of genes and understand how they interact. "In addition, fruit fly genes have very high mutation rates and that makes them very useful to study," says Jones. "The changes that these mutations

throw up can be traced quite easily on a relatively simple organism like drosophila. In more complex animals – like mice or men – these changes are much more difficult to trace."

As a result, the fruit fly has played a key role in unravelling biological processes for the last century. "Drosophila is now the best known organism on the planet because of this work," said Professor Andreas Prokop, of Manchester University. "Due to this knowledge, we can plan an experiment on a fruit fly and have the result in three weeks. In a mouse that could take a year. Fruit flies offer a cheap, fast pipeline to reach understanding of complex biological questions which can then be translated into medical applications."

In Prokop's case, the fruit fly has provided a new understanding of extensions of nerve cells known as axons. These degenerate as people age, but far more sharply if they suffer from Alzheimer's or other degenerative disease. "We can grow drosophila neurones in culture and use them to study axon development. That helps us get a new understanding of what causes neurodegenerative disease."

Another example is provided by work at the Institute of Cancer Research. "There is a biological process known as cell death which occurs in all living creatures – from worms to humans," said Professor Pascal Meier, head of the cell death and inflammation laboratory in the institute's breast cancer unit. "Essentially, it is a suicide mechanism that is fundamental to life, and key aspects were discovered first in fruit flies. When a cell becomes damaged, its death – a process known as apoptosis – is triggered and it is killed off, allowing organs to remain healthy."

In cancers, however, cell deaths are not triggered, and this aids the process by which tumours spread. "We now know, from fruit fly research, that molecules known as inhibitors of apoptosis proteins (IAPs) are involved," said Meier. "They act to

block cell deaths. In other words, if levels of IAPs are elevated, apoptosis is prevented and cancers spread."

As a result, scientists are now testing drugs that can inhibit IAPs in humans and so allow apoptosis to regain control of cells. "It is a very promising approach," said Meier. "However, the behaviour of IAPs in humans is more complex than it is in fruit flies and that complicates the hunt for drugs. Nevertheless, it is an avenue of cancer treatment that would not have existed today had we not made basic discoveries using fruit flies."

Today, fruit flies are a major undertaking at research centres. The Cambridge fly facility houses 60,000 tubes containing drosophila and provides carefully cross-bred

PRIZE WINNERS

Six Nobel prizes in physiology or medicine' have been awarded to a total of 10 scientists for their groundbreaking biological work based on fruit fly research:

1933 Thomas Hunt Morgan used drosophila to uncover the role played by chromosomes in heredity

1946 Hermann Joseph Muller used X-ray irradiation to increase mutation rates in fruit flies

1995 Edward B Lewis, Christiane Nüsslein-Volhard, and Eric F Wieschaus used drosophila to understand genetic control of embryonic development

2004 Richard Axel concentrated on odour receptors and the organisation of the olfactory system

2011 Jules A Hoffmann was given the award for his research on the activation of innate immunity

2017 Jeffrey C Hall, Michael Rosbash and Michael W Young won the prize for uncovering the molecular mechanisms that control circadian rhythms

flies for about 30 research groups. "The vast majority of these scientists are doing research either on human conditions or on general biological problems," said Collier. "Only one or two are involved on research on insects themselves. That shows you the usefulness of fruit fly research to biological research in general and to understanding how the human body works in particular."

Not everyone has been convinced about the value of fruit fly research, of course. In her 2008 election bid to be vice-president of the US, Sarah Palin – in an early policy speech – went out of her way to denounce drosophila experiments. "They really don't make a whole lot of sense and sometimes these dollars go to projects that have little or nothing to do with the public good. Things like fruit fly research. I kid you not," she announced.

Palin urged that more money be spent on particular research priorities, such as autism – remarks that were seized upon by infuriated scientists who pointed out that only a few years earlier, scientists had pinpointed a chemical called neurexin which in some forms appear to be a genetic risk factor for autism. And there are no prizes for guessing where neurexins were first identified: in fruit flies. As Richard Wolffe, the senior White House correspondent for *Newsweek*, remarked, this was "the most mindless, ignorant, uninformed comment we have seen from Governor Palin and there's been a lot of competition for that prize".

Fortunately, others have been more appreciative of the use of fruit flies in research – including Michael Rosbash, one of the recipients of last week's Nobel prize for medicine. He heard he had won the prize when the Nobel committee chair called him at 5am local time. "When the landline rings at that hour, normally it is because someone died," Rosbash said last week. Then he got the good news. "I am very pleased for the fruit fly," he replied.

