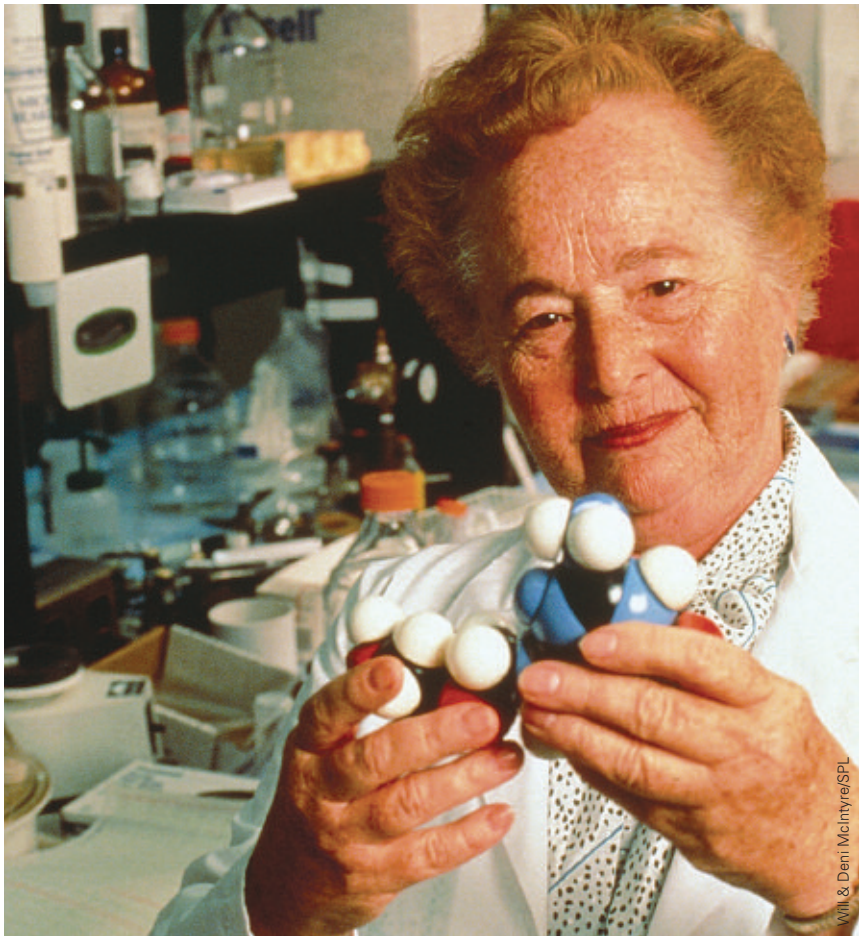
A life in science

Gertrude (Trudy) Belle Elion (1918–99) was an exceptional team player. She cared more about getting something useful from her work than making a name for herself. People are alive today because of her research, and the knowledge that her work made a difference to people's lives was important to Trudy.

'It's amazing how much you can accomplish when you don't care who gets the credit'

(Gertrude Belle Elion)



Will & Deni McIntyre/SPL

Gertrude B. Elion

Trudy was born in New York in 1918. Her parents were immigrants from Eastern Europe. Trudy did so well at school that she was accelerated ahead of her classmates. Her grandfather, who was a scholarly watchmaker, encouraged Trudy in her studies.

Two events then happened which were to shape Trudy's future life:

- Her grandfather died from stomach cancer — this prompted Trudy to decide that she wanted to find a cure for cancer.
- Her family lost their savings in the Depression — this meant that although her parents valued education for girls they could not afford to educate Trudy beyond school.

Trudy's parents were teenagers when they emigrated and had to educate themselves as well as work.

Education

Trudy got a place at Hunter College, New York, where tuition was free. She studied chemistry there — an unusual choice even in an all-girl college — and graduated with distinction. However, although universities would take her to do a PhD, Trudy could not get the necessary financial assistance. So she looked for a scientific job instead.

At the time, most people thought it was a waste to educate girls beyond school.

Finding work

Despite her qualifications, Trudy could not find any scientific work. Employers did not want 'distracting' women in laboratories. She did a series of temporary and part-time jobs to gain experience. Trudy saved her wages to pay for a Master's degree and 18 months later enrolled at New York University. She worked on her degree in the evenings and at the weekends, graduating as the only woman in her class in 1941.

During this time Trudy met Leonard Canter, a young mathematician. They planned to marry, but Leonard died of a bacterial infection. His death reinforced Trudy's ideas about using science to develop drugs. She never married — in those days people thought that married women should not work.

Hitchings and Burroughs Wellcome

The Second World War gave Trudy the chance she was waiting for. Many scientifically qualified men were fighting in the war so women were allowed to work as technicians. She came across a drug company, Burroughs Wellcome, and asked about work.

Box 1 New research methodology

Hitchings and Elion's approach to developing drugs was ground-breaking. Other researchers tested chemicals randomly in the hope that something would be effective. Hitchings was more logical. He knew that sulphonamide drugs interfered with bacterial metabolism so there must be other substances that also interfered with cell processes.

Hitchings and Elion used knowledge of cell biochemistry to design molecules that would interfere with cellular activities. They knew cells needed nucleic acids to reproduce, so they searched for substances to interfere with DNA synthesis in cancer cells and bacteria. Ideally a drug would interfere with processes in the harmful cells but not affect normal cells.

This approach, based on cell biology and differences between healthy and diseased cells, is the standard research method used today.

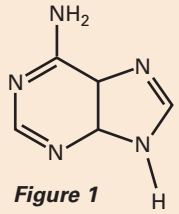


Figure 1 *Adenine*

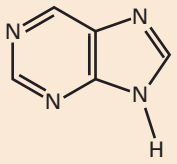


Figure 2 *A general purine structure*

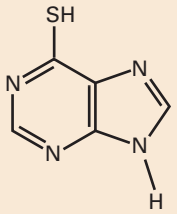


Figure 3 *6-mercaptopurine (6-MP). This molecule interferes with DNA synthesis because it is so similar to the adenine that cells need*

Box 2 Purines

Purines (Figure 1 and 2) are a group of widely occurring substances, including caffeine. Adenine (A) and guanine (G) in DNA are purines. They have a two-ringed structure containing carbon and nitrogen.

In 1944 Trudy joined the research lab at Burroughs Wellcome and began a life-long collaboration with her boss, Dr George Hitchings. The lab was looking for new drugs, but Hitchings took a different line from the usual methodology (Box 1). They worked on the chemicals in DNA. Trudy worked on purines (Box 2), synthesising molecules that might interfere with DNA duplication.

Trudy also started a PhD, but she had to give up after 2 years because the college did not like the fact that she only worked in the evenings. She was unhappy about her lack of proper qualifications. However, Dr Hitchings encouraged all his research assistants to publish their research so Trudy Elion began to make a name for herself.

Breakthrough

Trudy created and investigated hundreds of purine compounds. It took years to find di-aminopurine, which stopped mouse leukaemia cells reproducing. Unfortunately, it was too damaging to healthy cells for use in medicine, but it showed that Hitchings and Elion's theory was sound.

A similar molecule — 6-mercaptopurine (6-MP) — helped some leukaemia patients, but it wasn't a cure (Figure 3). More research led to a better version which boosted patient survival rate to 50% — and the drug is still in use today. Another 6-MP derivative was found to reduce uric acid production and it is used to treat gout.

6-MP also reduces immune system activity. The research group developed a similar compound — azathioprine — that depressed the immune system. The potential of this substance for helping transplants was spotted. After successful trials using dogs, it was tried on humans. Azathioprine (Imuran) enabled the first successful kidney transplant between unrelated people in 1961.

Anti-viral drugs

Early on in her research, Trudy observed that some compounds affected viruses but were too toxic to be useful. When more had been learned about viral reproduction she went back to her earlier work and focused on chemicals that could target bacterial and viral nucleic acids. The result was trimethoprim, for treating meningitis, septicaemia and other infections, and pyramethamine, for malaria.

Unless drugs are given to supress the immune system a transplant is rejected because the patient's immune system attacks it.

Trudy Elion became head of the research lab after Dr Hitchings retired. In the 1970s, the lab released Acyclovir which was the first effective anti-viral medicine. Later, the team developed AZT — this anti-HIV drug was released a year after Trudy had retired in 1984.

As for the PhD — Trudy was awarded an honorary doctorate by George Washington University to recognise the work she had done. It was the first of many.

The Nobel prize

In 1988 Elion and Hitchings were awarded the Nobel prize in physiology or medicine. This came so long after their research that it was quite a surprise. Trudy's award was also unusual as she had no PhD, worked in the drug industry and was female. When she and Hitchings were nominated there were concerns about her contribution. However, Trudy's publication record and the work done after Hitchings' retirement soon showed how much she was involved in the discoveries.

When Trudy began her research at Burroughs Wellcome, no one knew the structure of DNA, but its components had been identified.

Retirement

After retiring Trudy Elion remained active in science. She communicated the excitement of science to many others, and gained pleasure from feeling that she had made a difference to people's lives, and had encouraged young people, especially women, to follow their interest.

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