Philip D. Lawley laid the foundation for the idea that cancer is a genetic disease. He provided the first convincing evidence that DNA is the key target for chemicals that cause cancer and identified a major DNA repair mechanism that counters the assault of carcinogens on DNA.

Lawley, who died on 18 December 2011, was born in 1927 in the village of Abbots Bromley in Staffordshire to two teachers. He obtained a degree in chemistry in 1949 at Oxford University and moved to Nottingham University, where he studied the physicochemical properties of DNA (before its double-helical structure was revealed by James Watson and Francis Crick). His graduate work included the first investigation of what later became known as DNA denaturation (the separation of the macromolecule into two strands).

After gaining a PhD in 1953, Lawley took up a post at the Chester Beatty Research Institute (now the Institute of Cancer Research) in London, where he investigated the interaction of alkylating anticancer drugs with DNA. By 1957, he had demonstrated that these could bond covalently with DNA to produce stable products (adducts), a radical view at a time when it was believed that such interactions were weak or reversible.

With chemist Peter Brookes, in the late 1950s, Lawley carried out seminal studies on the binding of mutagens and carcinogens to DNA in living organisms. The Radiochemical Centre in Amersham, Buckinghamshire, had just begun producing radioactively labelled chemicals, including mustard gas, which had been used as a chemical weapon in the First World War. Ironically, Lawley’s father had been exposed to it while serving in the trenches. Mustard gas was already known to be a mutagen and later it was found to cause lung cancer. It was the archetype of difunctional anticancer drugs, such as melphalan and chlorambucil, which were developed during the 1950s at the Chester Beatty Research Institute.

To conduct these potentially hazardous studies, Lawley and Brookes moved out of London to the Institute’s Pollards Wood Research Station, which was set in 60 acres of woodland and conveniently close to the Radiochemical Centre. In these leafy and peaceful surroundings, they produced their seminal work on the binding of mutagens and carcinogens to DNA. In 1960, they reported that mustard gas formed adducts with guanine in DNA, in viruses, bacteria, cultured mouse cancer cells and cancers in mice.

The adduct hindered DNA replication and cell division by cross-linking the strands of the DNA helix, thus explaining mustard gas’s extraordinary toxicity to cells. They demonstrated that bacteria resistant to mustard gas used enzymes to remove those crosslinks, but sensitive bacteria did not. This was the first convincing evidence for the repair of DNA adducts in a living organism. It is now clear, 50 years on, that many of the genes mutated in human cancer are involved in DNA repair.

In a second landmark paper in 1964, Lawley and Brookes reported in ‘Nature’ a correlation between carcinogenicity and DNA binding, using radioactively labelled polycyclic aromatic hydrocarbons applied to mouse skin. These ubiquitous products of incomplete combustion (found, e.g. in tobacco smoke) are chemically inert, but many are potent carcinogens when metabolically activated. Lawley and Brookes found that the amount of binding to DNA, but not to protein or RNA, was positively correlated with the carcinogenic potency of the polycyclic aromatic hydrocarbons. This discovery overturned the prevailing view that proteins were the critical cellular targets for carcinogens and changed the course of cancer research.

Lawley went on to show how point mutations are induced when potent alkylating mutagens, such as N-methyl-N-nitrosourea, react with those atoms in DNA that determine base pairing during DNA replication. Point mutations are now known to occur frequently in a variety of human cancer genes. He also discovered the 6-methyltransferase DNA repair system that selectively removes such modified DNA bases.

Beneath his shy exterior, Lawley was a man of piercing intellect, prodigious memory, wry humour, deep scholarship, liberal views and iron-clad integrity. He did not follow scientific fashion and was happiest working at the bench. He wrote concisely and elegantly, in long hand, standing at tables piled with papers, moving from table to table until his manuscript was completed.

He took great pleasure in conversation, enriched by his passions for jazz, painting, reading, dogs and old trams. He often engaged in protracted and sometimes heated debate with whoever happened to be around—usually a scientific colleague but occasionally an innocent bystander—sometimes losing track of time. At Pollards Wood, these conversations would often continue al fresco in the copiced beechwoods, frequently in the company of Lawley’s whippet.

Lawley retired in 1992 but continued to work in the Institute of Cancer Research laboratories at Sutton in south London for many more years, enhancing the lives of those who worked alongside him with his knowledge, congeniality and wit. In January 2003, the Institute of Cancer Research honoured Brookes and Lawley by naming a £21 million laboratory in Sutton after them.

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