



Lawrence H. Thompson: A life of bikes, birds, and DNA repair (1941–2024)

Larry H. Thompson died on December 16th, 2024, in California, and he will be greatly missed by his friends and his colleagues. Larry was a “grandfather” in the field of genome integrity, and pioneer in the identification and cloning of DNA repair genes. Larry was born in Tyler, Texas in 1941, and developed an interest in science and nature from an early age, in high school. Larry was the best cell biologist I knew, with an almost intuitive understanding of cell growth and behaviour. Larry’s skills in cell biology were not innate, of course, but rather were hard-earned during his PhD in the laboratories of Bill Dewey, Ronald Humphrey, and Herman Suit in the Physics Department at MD Anderson in Houston. At that time, in the mid 1960’s, laminar flow hoods did not exist, and cell biology was an art form requiring immense patience and with a high rate of experimental loss to contamination. I remember as a new postdoc in Larry’s lab at Lawrence Livermore National Laboratory (LLNL) in 1991, being shown how to derive clonal isolates of cDNA transfectants in Chinese hamster ovary (CHO) cells, without the use of replica plating or a cloning ring. I recall, to this day, Larry removing the lid from a 10 cm plate, holding the plate up to the ceiling light to identify a colony of interest, and gently scaping the colony with a Gilson pipette while drawing up the dissociated cells into a pipette tip, all without the protection of the laminar flow hood! His cultures rarely became contaminated. I still occasionally demonstrate this technique to new students and postdocs in my own lab, but never with the confidence to do so outside of a hood.



Larry’s lab, 1991/1992

1. Mutants, genes, and DNA repair

Another skill of Larry’s was his imagination and ability to develop new innovative tools for research. For example, Larry’s PhD work in Herman Suit’s lab in the late 1960’s involved time lapse photography to follow the fate of individual cells following ionising and ultraviolet radiation, using a home-made microscope comprised of an aerial reconnaissance camera from World-War II and a dissection microscope. This technical adeptness likely reflects Larry’s childhood in Texas, during which he learned to repair lawnmowers and motorcycles. Larry’s undergraduate degree was in Physics, prompted by his childhood fascination with the Universe. However, Larry realised during a period of summer work with NASA engineers in Mountain View that his interest in physics was not enough to form the basis of a career. It was soon after that Larry heard about ongoing work in the Dewey and Humphrey laboratories on the effects on cells of UV and ionising radiation, and began what was to become a hugely influential career in DNA repair.

It was during four years of postdoctoral work with Gordon Whitmore at the Ontario Cancer Institute in Toronto that Larry began his groundbreaking work with mutagenized mammalian cells, creating temperature sensitive mutants in mouse and CHO cells. Following his subsequent recruitment to the LLNL in California in the mid 1970’s, by the then new Director Mort Mendelsohn, Larry continued to isolate TS sensitive CHO mutants. However, following a Keystone DNA Repair conference in 1978, Larry began what became the love of his scientific career; the creation, isolation, and characterisation of CHO cell mutants defective in DNA repair. In those days, a task which is now simple using CRISPR gene editing and dropout screening was immensely time consuming, requiring imaginative ways to identify clonal isolates of single cells that were sensitive to DNA damage. Larry’s understanding of cell behaviour served him well, and through collaborative work with David Busch and Don Glaser, and Herculean efforts in his own lab by himself and Kerry Brookman, sitting at the microscope (often at weekends) to identify genotoxin-sensitive cells under a microscope, he isolated an array of mutant CHO cells defective in different pathways of DNA repair. These mutant cells have been enormously influential in the DNA repair field, enabling the cloning and molecular characterisation of a number of human genes involved in nucleotide excision repair, base excision repair/single strand break repair, and homologous recombination. For example, in 1990, Kerry and Larry employed the CHO cell line EM9 to identify *XRCC1*, the first human gene involved in the repair of X-ray induced DNA damage to be cloned. This work was hugely influential in my own career. At that time, I was a PhD student in Penny Jeggo’s laboratory, located in Robin Holliday’s Genetics Division at the National Institute for Medical Research in London, characterising DNA repair

defects in different CHO cell mutants (including EM9). I had already decided that I wanted to work on the molecular biology of DNA repair and so, soon after completing my PhD in 1990, I moved to Larry's lab in California to purify and try to discover the role of XRCC1. This period in my life initiated a scientific fascination that has lasted thirty years, revealing XRCC1 to be a master regulator of single-strand break repair and a "Swiss army knife" that interacts with and regulates the DNA polymerase, DNA kinase, DNA phosphatase, and DNA ligase activities that catalyse this process.

Larry's mutant cells also had a large but serendipitous impact on the direction of the human genome project, which was in its infancy at LLNL in the early 1990s. Larry once told me that when asked by colleagues which chromosome he thought LLNL should begin mapping, he suggested chromosome 19, because he and his colleagues had located two of his favourite DNA repair genes (ERCC2 & XRCC1) on that chromosome! In 1995, chromosome 19 became the first human chromosome for which there was an integrated metric physical map, and its full sequence was published in 2004.

2. Birds, bikes, and beer

Larry's life was not just about science. Larry had a passion for motorcycles, which began in rural Texas at 12 years of age. Larry's favourite was the Honda Magna that he bought new in 1985, and was still riding in 2016. I remember an offer of a "piggy-back" on his bike around the streets of Livermore, which sadly (in retrospect) I didn't accept. He also had a passion for nature and conservation, which I first became aware of while living in Larry's house at the start of my postdoc, in 1990. Due to an administrative error, I was not officially employed at



Larry on his brand new Honda Magna, in 1985

In later life, after retirement, Larry was able to explore his passion for nature, full-time. Myself and many other colleagues would occasionally receive emails from Larry telling us of his latest trip and with links to photographs of birds from far-flung exotic places such as Colombia, Peru, and Ecuador. These photographs were exceptional and, to my eye at least, quite professional! A beautiful picture of a Hummingbird is included below, and this and many other of Larry's fabulous photos are available to view on the Discover Life website (<http://www.discoverlife.org>).



Calothorax lucifer, Lucifer Hummingbird (Larry Thompson)



Chlolophonia cyanea, Blue-naped Chlorophonia (Larry Thompson)

LLNL for several months, and was paid as a visiting scientist a token \$16, per day! Larry, kindly put me up for a few months while the paperwork was completed, which turned out to be a blessing in disguise because I got to know Larry very well. Larry liked nothing more than drinking a beer after work, with some almond or pistachio nuts, and watching National Geographic on the television, an activity I happily shared with him for a few months.

The quality of Larry's wild life photography is typical of the man. If he did something, he did it carefully, to the best of his ability, and with total conviction. In one of his emails Larry sent me an amusing photo of himself taken on a recent birding trip (see below). By way of explanation, he told me "I fell off the steep side of a trail in Ecuador, but fortunately was caught by the vegetation. I landed with my feet in the air and my head at

the bottom. I couldn't move but the guide pulled me up!". The photo says it all. Larry was a quiet and serious person, often lost in his own thoughts, but he also had a great sense of humour.



Larry in Ecuador, after a falling from a slope (2014)

In 2016, Larry came to stay with me and my family for a few days, at my home on the South Coast in Sussex, while on what he called a “*Birds and Beer*” trip to the UK. It was great to see him again, but he was suffering a little from the periodic insomnia that had plagued him for many years, and which sadly became much worse and chronic during the last year or two of his life. Larry leaves behind him not only seminal contributions to our understanding of mammalian DNA repair, but also very tangible contributions to our planet. Larry was immensely passionate about conservation, and during his retirement he worked closely with the guides and close friends that he met on his birding travels. Larry helped set up the conservation organisation *Birds Nepal* in 2020, with his friend and guide Seejan from an earlier trip to Nepal (<https://www.birdsnepal.org>). Larry also strongly supported Women For Conservation (<https://womenforconservation.org/>), an organisation established in Colombia by the mother of his “adopted” daughter, Isabella. One of my favourite quotations and “mantras” for life is “*live simply, and do serious things*” by Dorothy Hodgkin. That was Larry.

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