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The Discovery of Reverse Transcriptase:

A Summary

The Discovery of Reverse Transcriptase, written by John Coffin and Hung Fan and published in the Annual Review of Biology, begins its story in 1970, with some contextual events — the Vietnam War protests, the US invasion of Cambodia, and the bombing of the University of Wisconsin's Sterling Hall. This series of events certainly paints a picture of unrest, war, and strained hope, in sharp contrast to what was happening in laboratories at the UW and MIT at the same time. Simultaneously, these two institutions had discovered for the first time the existence of RNA-dependent DNA polymerase, soon to be renamed "reverse transcriptase".

Reverse transcriptase is an enzyme which, after the successful transcription of information from DNA to a messenger RNA molecule, can use that new mRNA molecule to synthesize a new, duplicate strand of the original DNA sequence. This discovery opened many new doors for research into cancer, virus replication, and our understanding of how our own genes replicate and carry information about our unique biological selves.

The next section covers the discovery of retroviruses, first discovered in 1907 in the form of avian leukosis. The discovery was made that retroviruses, unlike other viruses, propagate their genomes using RNA — other viruses, and indeed most organisms, rely on DNA to reproduce and grow. Authors John M. Coffin and Hung Fan, representatives of the Molecular Biology

departments of the University of California Irvine and the University of Wisconsin respectively, dive deep into the background of the field during the 50s and 60s that kicked off with the discovery of the helical DNA structure. This discovery, in turn, allowed scientists to blaze new trails with regard to nucleotide structure and chemical forms, as well as the newly termed Central Dogma of molecular biology — the idea that genetic information always starts with DNA and is transferred to RNA, then translated into proteins.

The discovery of RNA-dependent DNA polymerase in 1970, however, put a dent in this dogma. Coffin and Fan present the background of molecular biologist Howard Temin, who found through a series of experiments that viruses relying on single-stranded RNA as their genetic material were somehow able to copy their genome into *DNA*, which was then incorporated permanently into the genome of the infected cell, serving as a template for further viral RNA synthesis. Unfortunately for Temin, another biologist, David Baltimore, made the same discovery independently at the same time — their papers were published back-to-back, and Baltimore's was first. Despite this, Temin's experiments and findings cemented his position as a founder of molecular retrovirology and molecular cancer research, paving the way for others to build upon his explorations.

Baltimore, before the publication of his paper, was invited to attend the 1970 Cold Spring Harbor Symposium on Transcription and present the results of his experiments — this was met with immediate enthusiasm, including one scientist who left right away to his laboratory and returned shortly after with news that he had been able to recreate Baltimore's experiment with the same results. The discovery of reverse transcriptase opened many new opportunities for research into the fundamentals of viral reproduction and into cancer treatments, at a time when cancer research was stalled and little new was being discovered.

The article follows up with a short summary of the process of reverse transcription and a figure displaying each step, then goes into more detail about each of its founding fathers and their lives after this discovery: Temin took hold of his new fame and gladly used it to advocate for social causes, including bringing scientific literature to oppressed Jewish scientists in the USSR, for over twenty years before succumbing to metastatic lung cancer in 1994; Baltimore dove further into his studies in animal virology, and even today pursues an interest in using viruses to fight disease in both animals and humans.

Works Cited:

1. Coffin J, Fan H. The discovery of reverse transcriptase. *Annu. Rev. Virol.* 2016.3:29-51