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This Week's Citation Classic

Kondo S, Ichikawa H, Iwo K & Kato T. Base-change mutagenesis and prophage induction in strains of *Escherichia coli* with different DNA repair capacities. *Genetics* **66**:187-217, 1970. [Dept. Fundamental Radiol., Fac. Med., Osaka Univ., Kita-ku, Osaka, Japan]

Three types of repairless mutant strains of *E. coli* were tested for mutability by seven representative mutagens. One strain turned out more mutable than the wild type or non-mutable depending on the repair deficiency and the mutagen. This paper describes a simple method for obtaining information on the mechanism of mutation induction by various mutagens such as environmental ones. [The *SCI*® indicates that this paper has been cited over 230 times since 1970.]

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" 'Incredibly small groups of atoms, much too small to display exact statistical laws, do play a dominating role in the very orderly events within a living organism.' This statement of E. Schrödinger in his famous book *What Is Life?*[1] had been a challenge to me. An idea occurred to me that the seemingly orderly events may be ascribed to self-controlled mechanisms which suppress the 'errors' in reactions of biomolecules which otherwise arise from statistical-mechanical fluctuations. Therefore, when I was offered the chair of the present professorship in the spring of 1963, I decided to switch from radiation physics to radiation biology to make a search for the biological mechanisms that correct genetic errors.

"In the fall of 1963, I was invited to work at the Oak Ridge National Laboratory, Tennessee, and started my first biological work on ultraviolet (UV) mutagenesis using E. *coli* strains isolated by E.M. Witkin. In the fall of 1964, on my way back to Japan, I visited Witkin in New York and learned a lot about the mutation work After discussions with her, I thought that if we could isolate repairless mutants from her strains, they must be invaluable for elucidating the error-correction mechanisms. After some painstaking work, T. Kato was able to isolate various mutants. I decided to pick up three repairless (now known to be excisionless, DNA polymeraseless, recombinationless) mutants from them for detailed studies of mutagenesis by seven mutagens: UV and X rays, 4-nitroquinoline 1-oxide (4NQO), mitomycin C (MMC), ethylmethanesulfonate (EMS), methylmethanesulfonate (MMS), and nitrosoguanidine (NG). Haruko Ichikawa worked hard and produced a major part of the mutation data. Kazuhiro Iwo, then a postgraduate student, worked on prophage induction.

"In 1964, H. Endo, Kyushu University, generously gave me a water-soluble chemical carcinogen, 4NQO, discovered in Japan. To my surprise, 4NQO turned out remarkably UV mimetic in the sense that the excisionless strain is about 30 times more sensitive than the wild type to both killing and mutation by 4NQO as well as by UV. It turned out that the recombinationless strain is nonmutable by UV, 4NQO, X rays, and MMS but mutable by EMS and NG, even though, when compared with the wild type, it is similarly sensitive to killing by EMS, MMS, NC, and X rays. Those results demonstrate that induction of mutation depends on the biological factor in addition to physicochemical alteration of DNA and that lethal damage to DNA is not necessarily identical to mutagenic damage. We also obtained suggestive evidence that prophage induction shares some common steps with induction of mutation.

"Our paper was one of the earliest ones in which various chemicals in addition to UV were tested for their differential mutagenicities between repairless mutants and the wild type Shortly after publication of our paper, environmental mutagens became the social concern, leading to the finding that carcinogens are mostly mutagenic in bacteria This may be the reason for the frequent citation of our paper. More recent work in the field is reported by Witkin. "[2]

1. **Schrödinger** E. *What is life? The physical aspect of the living cell.* Cambridge, England: Cambridge University Press, 1944. 91 p.
2. **Witkin E M.** Ultraviolet mutagenesis and inducible DNA repair in *Escherichia coli Bacterial. Rev* **40:**869-907. 1976.