Twenty-six years at the Cancer Research Institute of Sapporo Medical University

Kei Fujinaga
Professor Emeritus, Sapporo Medical University

The more we learn, the more we realize that we still have to learn.
No sooner do we reach one summit than the next appears before us.

It was April 1971 when I moved from Aichi Cancer Center Research Institute (Nagoya), where I had served as section head in the Laboratory of Viral Oncology, to the Cancer Research Institute (CRI) of Sapporo Medical College, and started my career as a professor at the newly established Department of Molecular Biology. Since then, twenty-six years passed very quickly until my retirement from the position in March 1997. During my tenure at CRI, over one hundred graduate and postdoctoral students and scientists from Japan and abroad spent time in our laboratory to learn and conduct their research on viral infections and the molecular biology of carcinogenesis.

The core research projects in our laboratory were molecular biological analyses of viral carcinogenesis, cancer-related viral and cellular genes, and viral infections. I suppose most, if not all, of the molecular biological studies, especially analyses of viral genetic information flow and the mechanism of DNA tumor virus carcinogenesis, originated from our early discovery with Dr. Maurice Green in St Louis University that viral-specific genetic information (mRNA) exists in virus-free tumors and transformed cells induced by adenovirus (Fujinaga and Green 1966, PNAS 55:1567). Formerly, it had already been demonstrated that highly oncogenic adenovirus type 12 and type 18 induce malignant tumors in new-born hamsters (Trentin, Yabe and Taylor 1962, Science 137:835). However, there is no virus detected in these tumors. It was therefore a puzzling fact that the virus disappears from tumors and transformed cells induced by adenovirus and other DNA tumor viruses such as polyomavirus and SV40. With the limited molecular biology tools and techniques available at that time, it was a challenge to find even where to begin in order to analyse these tumors and cells. Therefore, the molecular mechanism of DNA tumor virus carcinogenesis was completely unknown. In 1966, by utilizing a newly improved membrane DNA-RNA hybridization technique, we could detect for the first time adenovirus mRNAs as viral-specific genetic information present in virus-induced tumors and transformed cells.

At CRI, we extensively investigated the adenoviral genome, its transforming gene (the viral oncogene), and its genetic information detected in virus-induced tumors and transformed cells. We identified and determined the primary structure (the nucleotide sequence) of the highly oncogenic adenovirus type 12 transforming gene, and characterized its integration and mRNA transcription in tumors and transformed cells (Fujinaga, et al. 1980 CSH Symp. Quant. Biol. 44:519, Sugisaki et al. 1980 Cell 20:777). To initially conduct this research, we had to isolate and purify restriction endonucleases from bacte-

To whom correspondence should be addressed :
Kei Fujinaga, Asahiga-oka 5 chōme 6-25, Sapporo 064-0941, Japan

ria by ourselves in order to carry out the essential genome analysis, because unlike now these enzymes were not commercially available at that time. We employed several newly developed techniques or techniques under development such as Southern and Northern blotting, S1 mapping, and thereafter polymerase chain reaction (PCR), which turned out to be very useful and powerful. Results from the above-mentioned core research projects and utilization of newly developed techniques used in these projects opened vast possibilities for our molecular research and led to several other research projects. These projects include characterization of human papillomavirus transforming genes in cervical, penile and tongue carcinomas, investigations and characterizations of viral and cellular oncogenes and tumor suppressor genes in tumors and transformed cells, genomic analysis of various DNA viruses, and molecular epidemiological analysis of viral infections. Studies on transcription factors associated with the function of adenovirus transforming genes resulted in the isolation and cloning of one of the human ets family genes, E1AF, for the first time, which was later demonstrated by us to be involved in tumor invasiveness. Our results were published in more than three hundred articles (the entire list of publications can be found in the commemorative booklet "A Collection of Academic Papers in Commemoration of Professor Kei Fujinaga's Retirement" published in 1997; as of 2010, the sum of the impact factors of these articles is 571 and the total number of citations is 3715). Particularly in Tumor Res., we reported many restriction endonuclease cleavage maps of several viral genomes and transforming genes. As I look back over the events of these past 26 years, I cannot help feeling how fast time flies.

A research team made up of scientists in different disciplines offers great potential.
Interdisciplinary conversations frequently bring out original and creative ideas.
The introduction of new technology is often the door to a new research field.

Acknowledgements

I would like to thank our staff members (Particularly, Y. Sawada, K. Yoshida, and T. Yamashita) of the Department of Molecular Biology, Sapporo, Medical University Cancer Research Institute, and all of our collaborators in and out of Japan. Without their excellent work, none of the aforementioned research would have been accomplished. I am indebted to F. Higashino for his help in calculating the impact factor and the citation index of our publications. I would also like to thank Koh and Antonia Fujinaga and Iain Fraser for editing this manuscript.

(Accepted for publication, Dec. 27, 2010)