Federal Headship of Carcinogenesis – Hereditary & Environmental Cancer –

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Cancer in its early stages are approximately 1 cm. Actually, we can now detect cancers as small as 0.5 cm, and it is safe to say that almost all cancers up to 1 cm can be completely and effectively treated. The weight of a 1-cm cancer is 1 gram. The size of a single cancer cell is about 20 microns. This means that it takes about $10^9$ cancer cells to make up a 1-cm cancer. In a time where a cancer with $10^9$ cells can be treated 100%, you can imagine how silly it is for a scientist to be desperately looking for a single cell of cancer. It is said to take about 20 years for a clinical cancer to develop. If someone discovers cancer at the age of 40, it means that cancer budged when the patient was 20 years old. In fact, only one in thousands of cancer buds fully blossoms. Not very many do, and the same could be said about humans.

**Key words:** environmental cancer, hereditary cancer, Yamagiwa, Yoshida, Knudson


We, in researching hereditary kidney cancer in rats (Knudson’s 2 hit model), found that the product of the gene ErC, which appears with high frequency in simultaneous progressive process cancer, is secreted in the bloodstream, thereby providing a possible method for blood diagnosis. Because the ErC gene exists in the mesothelium, this could possibly be used to diagnose mesothelioma. Mesothelioma is an aggressive malignant tumor, which initially progresses along the surfaces of the pleura and peritoneum and is chiefly attributed to asbestos exposure. X-rays are commonly used for the assessment of a tumor in populations at risk for developing the cancer. However, currently there are no effective and curative treatments except for surgery. Since, early diagnosis for mesothelioma is important for prognosis. We reported that N-ERC/mesothelin could be a useful serum tumor marker for mesothelioma and have developed an ELISA kit (IBL Co., Ltd. Gunma, Japan). Indeed, this is a real-life example of translational research.

‘Environmental carcinogens’ came to light in 1775 when the British surgeon Percival Pott reported scrotal cancer associated with chimney sweeps in ‘cancer stimulated by chimney soot.’ One hundred years later, bladder cancer caused by aniline pigment factories, among others, were reported in Europe. Industrialization following the Industrial Revolution of the latter half of the 18th century witnessed the introduction of environmental pollutants. This introduction created the tragic reality of environmental carcinogens in which the public was forcefully exposed to these substances without their
knowledge. In 1915, Katsusaburo Yamagiwa (1863-1930) achieved a pioneering work in chemical (coal tar)-induced carcinogenesis by formative stimulation following the hypothesis of Virchow (1821-1902).

The media in Japan has taken up and reported on widescale ‘mesothelioma caused by asbestos.’ This is truly ironic as Japan was a pioneering nation in chemical-induced carcinogenesis. How, then, should we approach such a critical problem? What lessons must we learn from these past mistakes in order that we do not make the same kind of mistakes in the future? Concerning asbestos, our preventative measures and practical responses are decades behind, despite the fact that there has been pathological and epidemiological evidence pointing to 'risk.' ‘Carcinogenic’ research for the future must include risk evaluation along with risk management, as well as well-ventilated communication. In reality, the length and amount of exposure deemed 'dangerous' to cause cancer involves some degree of vagueness. The fact that carcinoma from exposure takes long periods of time to develop (20-30 years) contributes to this vagueness. This will be an era in which the ability of professionals to predict the future will be challenged.

The World Organization’s International Agency for Research on Cancer (IARC) pointed out the higher risk of lung cancer and mesothelioma for laborers in asbestos mines. In addition, in 1987 the IARC classified asbestos as a group I carcinogen, defined as ‘exposure circumstance entails exposures that are carcinogenic’ based on literature that found an increased risk of lung cancer for laborers working at asbestos product production factories. Ironically, however, asbestos import reached its peak in Japan in 1974 and only in 1995 was the most carcinogenic blue asbestos banned for production and use. By this time, however, many mesothelioma patients were already emerging. Japan’s asbestos tragedy was multiplied by factors including the inadequacy of communicating the risks associated with asbestos production factories, the inadequacy of researchers to communicate relevant information to third parties, and the government’s delayed management and organization. In order to avoid these mistakes in the future, there must be an approach that includes exchange, evaluation and management of risk information. For this, not only the government, but also the academy, industry and labor as well as consumer groups must be brought together to form a specified non-profit organization like the Chemical Biological Integrated Management Society.

In 2003, I was immersed in the 100th anniversary event of the worldly renowned cancer pathologist Tomizo Yoshida, who paved the way in unveiling the mechanism of cancer.

Tomizo Yoshida preached the individuality and diversity of cancer. He said that it is important to find out the common or most fundamental traits of cancer cells. Yoshida boldly stated that we humans play up the future—a sign of our inner desire to avoid reality. Apart from being a cancer pathologist, Tomizo Yoshida was also a thinker who eloquently used analogies of cancer to explain his outlook on life.

Cancer is a heritable disorder of somatic cells. The environment and heredity both operate in the origin of human cancer. The accumulation of mutations, which are likely to occur during continuous cycles of cell division, may eventually transform some cells through a multi-stage process. These conditions may be designated as the ‘hypercarcinogenic state’. This reminds us of the formative stimulation of Yamagiwa’s carcinogenesis. Our goal, then, should be directed to the reversion of the ‘hypercarcinogenic state’ to the ‘normo- or hypocarcinogenic state’ so as to hopefully prevent or at least postpone the development of cancers. The point is ‘From an era of making cancer to an era of intervening cancer’.

Unfortunately, it is impossible to wipe out cancer from the face of this earth. As long as humans live with a normal temperature of 37℃, there is a set probability that DNA will be damaged. Therefore, to live is like walking along a path towards cancer. The present goal of cancer research is to deliberately slow the growth process of cancer. If a patient’s life expectancy is 40 years, it is the researcher’s goal to prolong that expectancy, by slowing the onset and growth of cancer, to 80 years old. Preferably, one should live through to their maximum lifespan, and then die of cancer. In other words, one should not die of cancer unless they have reached their maximum lifespan. At autopsy, physicians should find out for the first time that their patient had cancer. "Lifetime cancer" can
really be true only if we can realize a life where people do not die of cancer—the ultimate goal of cancer research. In fact, we are seeing some light. More than 20% of thyroid and/or prostate cancer patients die with no showing symptoms. They die of another natural cause; this is particularly true in prostate cancer patients. It would be nice if a patient had a kind of cancer where doctors discovered it after the patient died. The type of cancer where a patient happened to have it, but died of natural causes—a "lifetime cancer"—is a coexisting one.

Humans first originate from one fertilized egg. Then, through repeated cell division, an adult human is said to have about 60 trillion cells, with each cell containing DNA. One cell is about 20 microns. Inside a cell is a nucleus, in which there are chromosomes, on which the DNA lies.

Think of a cell as the earth we live in. Chromosomes would be countries. DNA would be cities. And the bases would be individual people.

Pick up a "strand" of DNA from a single cell, and you will find that the strand would be about 2 meters. So when strands from 60 trillion cells are connected together, it will be 120 million kilometers long. The diameter of the sun is about 10 billion kilometers; so actually, humans sort of already do encompass the universe.

Many counterparts co-exist inside a living organism. In the cell, there is the oncogene and the anti-oncogene (tumor suppressor gene) that balance each other out. There is also the sympathetic nerve that counters the parasympathetic nerve, where the former activates and the latter suppresses. Like so, two opposites constitute a fine balance to maintain stability in an organism. It is necessary for a healthy living system to be an oval with two fixed point observations. The neoplasia of single-cloned cells is like a concentric circle and is typical of cancer. Kanzo Uchimura had a keen insight when he said that the truth is not in the circle, but rather in the oval.