Chapter 10

Anti-aging Genes and Thrifty Genes May Change Your Life

The genes which help to prolong our life and stave off aging have been found out. The thrifty genes which make you fat or genes which make you get less fat also have been found.

10.1 Anti-aging genes prolong the life

The anti-aging gene was discovered as *Sir2* from yeast, *Saccharomyces cerevisiae*[*1]. When the yeast cells were grown under the poor nutritious conditions, the expression of this gene was stimulated and their lives were prolonged about 1.3 times. Their lives were shortened up to 50% when the gene was deleted. You should not be disappointed to hear about the result from the experiment with yeast, because the experiment is not on a human body.

It is needless to say that you ought to recognize the importance of yeast. The basic mechanisms of life are almost the same with any living organs because we have been evolved from *Archaea* (Fig. 1.1). We can explain it from the fact that basic information of genes DNA and RNA we know now were discovered by the experiments of a bacterium, *Escherichia coli*. The secret of life of higher animals and plants, which was not revealed by the experiments by using *E. coli*, was revealed by the research of yeast. It is because like human cells, yeast has a nucleus and histones which wrap the chromosomal DNA in them, whereas *E. coli* doesn't have a nucleus in its cell. These living organisms which have nucleus are called *Eukaryote*, whereas bacteria like *E. coli* are called *Prokaryote*. The term of nucleus in the cells of living organisms is the same with the use of nuclear weapons. However, the use of this word, 'nucleus' is much older than that of nuclear weapons. The nucleus of weapons comes from atomic nucleus.

It has been found out that mammals have 7 kinds of the *Sir* genes, called 'Sirtuin'. It has also been found out that those genes have influences on restriction of calories, lowering of blood sugar and cholesterol levels, increase of neurons, activation of mitochondria, structures of ribosome and so on.

Except for these *Sir* genes, it has been known that telomere at the termination of DNA structure on the edge of chromosome gets shorter as we get older. Telomere is needed to protect the structure of DNA; in human bodies, telomere has 2500 times' repetitions of TTAGGG or similar sequences. About 50 to 200 base pairs of telomere are lost at each cell division. In stem cells, an enzyme telomerase works to replenish these lost base pairs. When we put the telomerase gene into human cultural cells, the cells become euthanasia[*2]. Although most of normal cells do not have this enzyme, most of cancer cells have this enzyme and repeat cell division.

The results of these researches would not lead to practical use for human beings soon. That is to say, we cannot lengthen our span of life with ease. However, if we believe in the results of experiments of the *Sirtuin* genes in yeast, we will be able to lengthen our life longer than now by taking less nutrient foods. On the other hand, there is a recent epidemiological research that very thin old people live shorter than stout people of BM1 25~30. It may mean that we should take moderate and nutritious food rather than poor meal.

10.2 How to calculate your BMI

The BMI is a statistical measure that is indicative of fat in the body in correlation between height and weight of a person. The BMI of a person is used as a simple method to assess whether he is underweight, normal, overweight, or obese (Fig. 10.1). The BMI of healthy men and women falls between 20 and 25.

If your fatness belongs to subcutaneous ones, BMI 30 may be the permissible level.

$$\text{BMI} = \text{Weight (kg)} \div \text{Height (m)}^2$$

Fig. 10.1 *Body Mass Index (BMI).*

BMI is an important index to judge fatness. By suggestion of WHO, 18.5 to 25 BMI are normal range of healthy men and women.

BMI is an abbreviation of Body Mass Index and calculates the next equation:

$$\text{BMI} = \text{kg body weight} / (\text{m body height})^2.$$

Fig. 10.2 *A Confucian, Ekiken KAIBARA (1630~1714).*

(Photo quoted from ja.wikipedia.org.)

The BMI of moderate Japanese men and women is 25, but 30 for Americans and Europeans. When I think about moderate food we should take, I recall that there was a great Japanese Confucian, named *Ekiken Kaibara*, in Edo-era (1603~1868) (Fig. 10.2), who persuaded us to live moderately, and left us a

saying, "*Hara-hachibu ni isha irazu*", "A moderate meal (80% of full stomach) keeps the doctor away". This old maxim is fit to the finding of the *Sir* genes in which the cells express them more under the low calories or nutrition.

10.3 Even Japanese foods make you fat if you eat them too much

One of the reasons why Japanese foods are popular in many countries is that they contain less fatty foods and have smaller calories, and as a result they don't make us fat.

Generally speaking, fatness is caused when ingested energies get over consumed energies. To continue eating without moderate exercise is a good example of it. Once, *natto*, fermented soybeans, shown in Chapter 8, were completely sold out from the Japanese markets because of the TV reports that they protect us from becoming fat, although it was a faking report by the TV station. We don't become less fat if we don't consume more energies than we get. Foods or supplementary foods which make us less fat even when we don't do exercise must be harmful to our bodies. There are, however, some people who don't become fat even when they eat much food, and there are some fat people even when they don't eat much food. Recently it came to be known that obesity is sometimes caused by hereditary factors.

Now, more than 80 genes which are related to obesity have been discovered. These genes are called 'thrifty genes'. Speaking of thrift, when we travel in the USA, we sometimes find stores called thrift shops, where they receive articles which people give them and sell them and get profits. They donate the money to nursing homes or hospitals. We often find good small articles, good clothing

and wonderful antiques. The meaning of thrift concerned with this will be understood in the next paragraph.

10.4 Human beings have had genes which can conquer their hunger

In the primitive ages, human beings had often had no food and had been hungry for a few weeks. It is now thought that they kept motionless in the caves and kept their bodies warm. We can surmise now that the genes concerned with consumption of energies had been conserved. This gene was named 'thrifty gene'. Even now, mammals which hibernate have the thrifty gene in their adipose tissues and they keep body heats from going down. We, human beings, also have the thrifty genes now, a trace of old days, which is sometimes called obesity gene or starvation one and now some people get fat because of these genes. Therefore, we must not blame such people for their fatness, saying that they are lazy or weak-willed. There are some people among them who can use received energies very efficiently.

Fig. 10.3 *Obesity has two types.*

Although *sumo* wrestlers are quite fat, they are mostly obese by subcutaneous fats rather than visceral fats. The latter case of obesity has a tendency to generate metabolic diseases.

Obesity is divided into two categories, subcutaneous fats and visceral fats. Although *sumo* wrestlers are quite fat as seen in Figure 10.3, they are mostly obese by subcutaneous fats rather than visceral fats. The latter case of obesity has a tendency to generate metabolic diseases.

We should not forget that there are more than one-fourth of people on the earth who are hungry or starving, whereas many people can enjoy plentiful foods. The meaning of *sapiens* of *Homo sapiens* is to be wise, so we should distribute food and conquer the hunger of the unfortunate people by our political wisdom in the world.

10.5 The *leptin* gene can make us get less fat

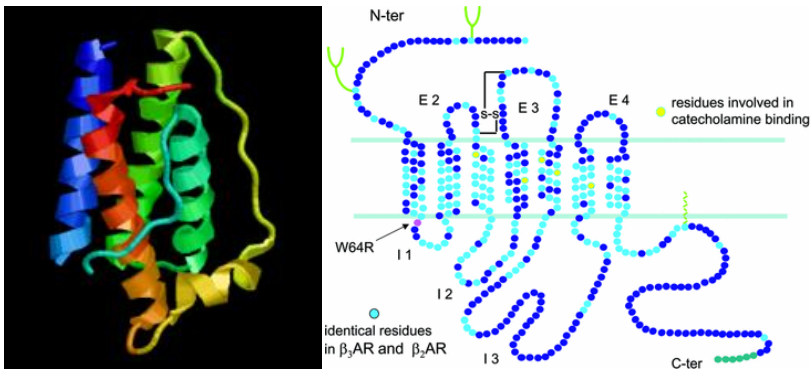

Fig. 10.4 *Structures of Leptin protein (left) and β3-adrenergic receptor protein (right).*

These proteins were found as the gene products related to the obesity. (Left figure source: ja.wikipedia.org.; right figure source: biochemsoctrans.org.)

One of genes well known as a thrifty gene is β3 adrenalin receptor protein[*3] (Fig. 10.4). This gene was discovered among the groups of the races who suffer from the second type of diabetes (II type). The gene is expressed in the internal adipose organs or brown adipose tissues and it is involved in the generation of

heat in our body caused by the impulse of the sympathetic nerve. The gene of the groups was mutated and differed from that of normal people and as a result, the basal metabolic rate decreased. That is to say, they keep energy efficiency highly under the present world where they can get enough food and as a result they become fat.

The most typical genes which make us less fat is the *leptin* gene[*4] (Fig. 10.4). This *leptin* gene is expressed in adipose tissues and produces Leptin protein and spoils our appetite by giving some influences to the hypothalamic part of the brain. This is one of hormones which can make us feel a full stomach and stop eating. A mouse whose *leptin* gene was broken continued eating and grew to be a giant mouse.

10.6 Fatness invites danger of developing cancers

It was well known epidemiologically that fatness caused by eating fatty food develops danger of cancers as well as several metabolic syndromes such as diabetes, high blood pressure and lipidosis. The recent study by Japanese scientists show that the causes of cancer developing are promoted by the complex action in our body, that is, a bacterial metabolite, deoxicolic acid made by the intake of high fatty food, promotes growth of carcinogenic bacteria or pathogenic bacteria. The conclusion is that Japanese food containing less fat lessens the risk of cancer developing as well as metabolic syndromes.

The new field of study, in which scholars are trying to solve the relation between nutrition and genomes, has started and it is named 'nutritional genomics'. There are some academic societies in the USA, where scholars are studying about the field.

10.7 Summary

More than 80 genes which are related to obesity have been discovered. These genes are called 'thrifty genes' which are concerned with the efficient energy consumption. We have this thrifty gene now as a trace of old days and some people get fat because of these genes. One of the genes which make us less fat is leptin. Visceral fat caused by eating fatty food could develop danger of cancers as well as several metabolic syndromes such as diabetes, high blood pressure and lipidosis. The BMI of healthy men and women falls between 20 and 25. If your obesity belongs to subcutaneous fat, BMI 30 may be the permissible level. The old maxim, "A moderate meal keeps the doctor away", would be the same as finding an anti-aging gene, the *Sir* genes, which is expressed under the poor nutrition.

[*1] Frye, R., Phylogenetic Classification of Prokaryotic and Eukaryotic Sir2-like Proteins. Biochemical and Biophysical Research Communications. 273: 793–798 (2000).

[*2] Bodnar, A. G., M. Ouellette, M. Frolkis, S. E. Holt, C. P. Chiu, G. B. Morin, C. B. Harley, J. W. Shay, S. Lichtsteiner, and W. E. Wright. 1998. Extension of life-span by introduction of telomerase into normal human cells. Science 279:349–352.

[*3] Clement, K., Vaisse, C., Manning, B. S. J., Basdevant, A., Guy-Grand, B., Ruiz, J., Silver, K. D., Shuldiner, A. R., Froguel, P., Strosberg, A. D., Genetic variation in the beta-3-adrenergic receptor and an increased capacity to gain weight in patients with morbid obesity. New Engineering Journal of Medicine 333: 352-354 (1995).

[*4] Zhang, Y., Proenca, R., Maffei, Balone, M., Leopold, L., and Friedman, J. M., Positional cloning of the mouse obese gene and its human homologue. Nature 372:425-432 (1994).