Division of Developmental Regulation
## Medical Cell Biology

# “Focus on EPIgenetics” Understanding how our life and disease are programmed Applying new findings to future medicine

Our body and mind function through gene control on the genome.
Epigenetics is the study of the “program of life.”
Changes in this program can lead to cancer, lifestyle disease, and aging.

Epigenetics: advanced research focused on the essence of life and disease

Professor
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### Profile

1985 Graduates from the School of Medicine, Shimane Medical University
1991 Receives Ph. D. from the Graduate School of Medicine, Kurume University
1992 Research associate, Howard Hughes Medical Institute, Baylor College of Medicine, USA
1995 Assistant and Associate professor, School of Medicine, Kumamoto University
2002 Professor, Institute of Molecular Embryology and Genetics (IMEG), Kumamoto University
2006-2008, 2010-2014 Director, IMEG, Kumamoto University

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## Epigenetics: mechanisms for regulating gene activity

Genome is the blueprint of our life. Human bodies are made up of more than 200 types of cells, and each of these cells contains, in principle, the same genome. So why is that, despite the genome being the identical, each cell is so distinctly unique? As Professor Nakao puts it, “There are around 25,000 genes in the human genome, of which about 10,000 genes are active in a single cell. The individual cell does not use the remaining genes. Essentially what this means is that genes are used selectively. The program—in other words, the selective use of genes—differs according to the cell type and the cell condition. This is what enables us to live every day.” He explains further: “To control the gene activity in the human genome, each gene is given marks. The epigenome is the modified genome where all genes are distinctively marked, and the epigenetics is the study of the biological significance of the epigenome. Put simply, epigenetic research tries to understand how gene activity is regulated in our life and disease.”

## Deciphering the epigenome: benefits for future medicine and healthcare

So what exactly are the “marks” on the epigenome? Marks are made either by DNA methylation or by histone modification, by complexes of DNA and protein (known as chromatin) or by intranuclear structure in the cell. The epigenome, actually, consists of many numbers of molecules binding with and marking the genome; stem cells, differentiated cells, cancer cells, and senescent cells all have their own distinct epigenome. “It has been established that epigenetic mechanisms determine how each gene is to be activated or to be inactivated in individual cell, and these cells together make up our body. On the other hand, in germ cells, this marking is temporarily erased, then to be rewritten with a parental origin-specific mark in the mother or the father. It’s a very amazing mechanism.”

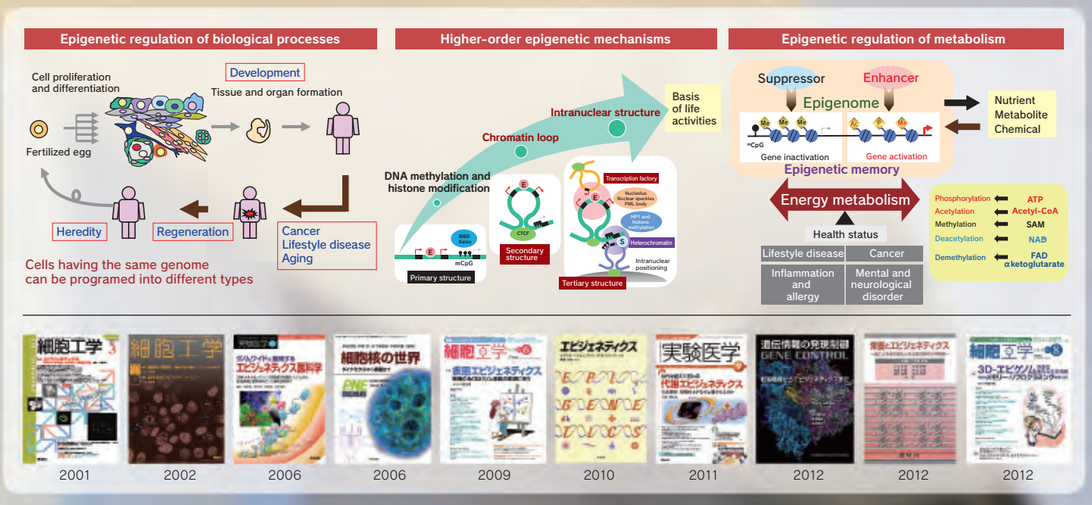
By examining the markings on the epigenome, we can know the nature of the cell. Dr. Nakao notes this ability to diagnose the “identity" of each cell has allowed us to make important discoveries for regenerative medicine, cancer therapies, and reproductive treatments.

## Epigenetic memory induced by life style and diet

In recent years, it has been reported that the epigenome can be affected by environmental factors such as diet and nutrition. The increasing researches focus on the links between the epigenome and lifestyle disease. As Dr. Nakao says, “It is quite evident that the marks on the epigenome may be affected by diet, exercise, and the environment in which we are brought up and are living every day. The marks on the epigenome change, and these changes will be maintained for a long time. This is what we refer to as ‘epigenetic memory’.”

A set of identical twins, for example, both came from the same fertilized egg, so they have exactly the same genome. After they grow older, they may become quite different. The greater the difference in life style and living environment, the more clear dissimilarities may emerge between the twins. “The more identical twins age, the greater the differences in DNA methylation and histone modification will appear. This has been made clear by research. Essentially, what they accumulate every day comes to affect their epigenomes. For example, we have found that, in the case of high fat diet–induced obesity, a new epigenetic mechanism by LSD1 is involved in the reprogram to store excessive energy.”

All cancer cells have epigenetic abnormalities such as the changes of DNA methylation, and these abnormalities are useful for the cell diagnosis. It would perhaps not be an exaggeration to say that human disease is caused by errors in the epigenetic program and epigenetic memory. Epigenetics research seeks to uncover the foundation of life and disease, and contributes to understanding the mechanism of the iPS cell induction and the production of the desired cells/tissues, and the pathogenesis of cancer and lifestyle disease. “This is a research field that will capture attention as we proceed further in the 21st century. There is so much potential to advance future medicine and new drug development.”







## Teaching Staff

Associate Professor

### Noriko Saitoh

Regulation of gene expression is important for almost all of biological activities, including development, regeneration, and diseases. My research focus is to understand how the cell nucleus, as a three-dimensional structure, controls genes. I would like to bring about a novel concept on genome organizations and functions. In IMEG, I would like to dedicate myself to helping students who explore scientific field, globally.

Assistant Professor

### Shinjiro Hino

My research is focused on the mechanisms through which environmental information, such as nutrition, is imprinted onto cells and individuals. I examine, from a molecular level, the biological flexibility that allows organisms to go beyond their “default” program, and ultimately hope that my findings can form the basis of further useful work in medicine and industry.