

From metabolism and epigenetics, to genome stability

Susan M. Gasser, Friedrich Miescher Institute for Biomedical Research, and Professor of Molecular Biology, University of Basel.

Prof. Susan M. Gasser is a swiss molecular biologist and is currently the Director of the Friedrich Miescher Institute for biomedical research. She studied biology and biophysics at the University of Chicago, and completed her PhD at the University of Basel in Biochemistry, under the direction of Prof. Gottfried Schatz. She was thereafter a research associate with Prof. Ulrich Laemmli in the Department of Molecular Biology of the University of Geneva, where she studied mammalian and fly chromosome structure. She began her own research on chromatin and chromosome organization in budding yeast, combining genetics, microscopy and biochemical approaches, at the Swiss Institute for Experimental Cancer Research in Epalinges/Lausanne, in 1986. After 15 years leading a productive research team in Epalinges, she returned to the University of Geneva as Professor of Molecular Biology and, in 2004, she was recruited as Director of the Friedrich Miescher Institute for Biomedical Research in Basel. In Basel, she also holds the chair of Professor of Molecular Biology at the University, and has also been a visiting professor at Osaka University in Japan.

Starting with the discovery that the enzyme topoisomerase II plays a structural role in the organization of metaphase chromosomes, Susan Gasser has explored how nuclear and chromosomal context establishes and maintains heritable patterns of gene expression. From the telomere position effect in yeast, to the inheritance of repressed tissue-specific genes in *C. elegans*, her studies have examined how the clustering and spatial organization of heterochromatin in the nucleus contribute to heritable gene silencing. Using genetic approaches she showed that histone modifications are directly instructive for the spatial organization of chromatin, and that the positioning of heterochromatin at the nuclear envelope can contribute to stable inheritance of gene expression states. Chromatin tethering at the nuclear lamina helps stabilize differentiated cell type in *C. elegans*, by ensuring that inappropriate genes are switched off. This is a fundamental process that contributes to tissue identity and integrity in all species, for when the subnuclear organization of chromatin is perturbed, it generates degenerative disease in man.

In parallel to these studies, Susan Gasser optimized live imaging techniques to pioneer the analysis of chromatin dynamics with time-lapse fluorescence imaging. By analyzing chromatin movement in living yeast cells, her laboratory showed that chromatin has constant near-random motion in the nucleus, which becomes reduced after chromosome replication, when the two sisters are tethered together. She showed that in yeast, as in other organisms, DNA damage and double-strand breaks increase chromatin movement in a checkpoint kinase- and chromatin remodeler-dependent manner. The increased random-walk movement of chromatin results from reduced nucleosomal occupancy and promotes the search for homologous template for repair, while directed motion towards nuclear pores ensues when repair by homologous recombination is not possible. Generally her work demonstrated how chromatin structure responds to environmental insult, with changes in long-range chromatin organization reflecting alterations on the level of the nucleosome.

Susan Gasser brought quantitative live fluorescence imaging, genetics, and genome-wide analyses to the field of nuclear organization. Her important insight was that chromatin domains have reproducible patterns of organisation and that the genetic perturbation of proteins that maintain chromatin organization, leads to compromised function. Most profoundly affected are telomere length maintenance, double-strand break repair, replication fork integrity in yeast, and in *C. elegans*, the stability of repetitive DNA.

Professor Gasser has authored more than 250 primary articles and reviews, and has received a number of awards for her work, including election to the Académie de France, EMBO and the Swiss Academy of Medical Sciences. She received the INSERM International Prize in 2011, the FEBS | EMBO Women in Science Award in 2012, the Otto Naegeli Award and Gregor Mendel Medal in 2006, and the Weizmann Institute Women in Science award in 2013, as well as an honorary doctorate from the University of Lausanne. She has been a member of many scientific review panels for institutes across Europe, including the Swiss National Research Council, the EC Presidents Science and Technology Advisory Council, and the EMBO Council, which she chaired from 2002 -2004. During this time she ensured that deserving applications from Czech scientists would be funded for EMBO meetings and workshops, and that Czech postdocs would be eligible for EMBO fellowships to work abroad. She has encouraged the nomination of Czech scientists as EMBO members, and scientifically she has interacted with a number of Czech researchers. Susan Gasser currently leads a Human Frontiers Science program grant that includes Professor Pavel Hozak of Charles University. For many years, particularly in the early days of her career, she extended help and friendship to Czech scientists in Switzerland and abroad, which is reflected both in joint publications and in continued exchange.