During the 1920s, mutation research was put on a firm basis by H. J. Muller, who developed the concept of “mutation rate” and devised quantitative techniques for its measurement. These techniques allowed the discovery of the mutagenic action of ionizing radiation and paved the way for the pioneering work of C. Auerbach on chemical testing, starting with mustard gas. Since that time the recognition of the multitude of possible sources of mutagenic insults promoted the development of the science of environmental mutagenesis. Today the mechanisms by which chemicals induce mutation and the role of genetic susceptibility in the response to environmental mutagens have been largely explored. Moreover, a battery of test methods is available for regulatory purposes. What are the current challenges in environmental mutagenesis? New techniques for mutation research have been developed. The “omics” technologies such as whole genome sequencing, epigenetic profiling, transcriptomics, proteomics and metabolomics have provided a snapshot on the effects of genetic polymorphisms, gene regulation, protein synthesis and stability, metabolic pathways in the control of cell function. This presentation will describe: 1) the successful identification of the mutagenic environmental agents underlying certain types of cancer by using whole genome sequencing; ii) the evidence that epigenetic alterations mediate toxicity from environmental chemicals and, iii) the use of the exposome approach, that comprises all environmental exposures that a person experiences from conception throughout the life course, to unravel complex gene environment interactions that affect disease risk.