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The epigenetic origin of retinoblastoma

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As an emerging new scientific approach linking the genome to the environment, Epigenetic, as applied to the interpretation of clinical, epidemiological and biological data in retinoblastoma, can not only explain the inconsistencies of the mutational ("two hit") model, but also open new outstanding scenarios in the fields of diagnosis, treatment and prevention of this eye tumor. This work on retinoblastoma epigenetic is both a collection of literature data arguing against the role of the mutational ("two hit") model in the genesis of retinoblastoma, and an evaluation of how the Epigenetic, rather than the genetic model fit the variegated phenotypic expression of the disease. The epigenetic model in the genesis of retinoblastoma, proposed herein, emphasizes the role of environment and the interaction of the environment with the genome, in generating retinoblastoma in young children. Environmental toxicants, including radiations, wrong diets, and infectious diseases, among others, all play a major role in conditioning the degree of DNA methylation in embryos and fetuses during pregnancy, thus leading to stable, functional alterations of the genome, which, on the other hand, can be also transmitted from one generation to another, thus mimicking a hereditary disease. An accurate analysis of the currently available literature on both retinoblastoma and Epigenetic, coupled with the knowledge of the variegated phenotypic expression of the disease, can easily lead to the conclusion that retinoblastoma is an epigenetic, rather than a genetic.

Biography

Domenico Mastrangelo, medical doctor, specialist in haematology, oncology, clinical pharmacology, and ophthalmology. From 1985 to1992 researcher, responsible of clinical pharmacology and clinical trials at the Instituto Sieroterapico e Vaccinogeno Sclavo of Siena. For the National Research Council (CNR), he worked in the research laboratory of the Montreal Branch of the Ludwig Institute for Cancer Research on a project on retinoblastoma, an experience that allowed him to make a decisive contribution to the establishment of a laboratory of genetics and molecular biology, for pre-symptomatic and prenatal diagnosis of retinoblastoma and other tumors of the eye in the Department of Ophthalmological Sciences of the University of Siena. Since 1991, member and founder of the Center for Interdepartmental Research for the Study of Tumoral and Pseudotumoral Ophthalmological Disorders in Childhood and in the Adult, directed by Renato Frezzotti. From January to September 1992, he attended, as "International Research Scholar", the Research Department of the Wills Eye Hospital (Director: prof Larry Donoso) and the Research Laboratory of the Jefferson Cancer Center (Director: prof. Carlo Croce) in Philadelphia, where he completed a refresher course on biology investigations and molecular genetics applied to the study of childhood eye cancer (retinoblastoma). Within the Department of Ophthalmological Sciences of 'University of Siena he set up a laboratory, unique in Italy, for genetic counseling and prenatal diagnosis of retinoblastoma. He is currently working on the hypothesis that retinoblastoma is an epigenetic disease, and it can be effectively treated with drugs which modulate the epigentic landscape of cancer cells. He, more recently tested the effects of ascorbate on retinoblastoma cell lines and found that ascorbate can be an excellent anticancer drug for retinoblastoma, if administered in high doses, by intravenous injection. He is presently working as a Senior Scientist in the research laboratory of the Department of Medical, Surgical, and Neurological Sciences of the University of Siena (Italy).

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