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A Medical Enigma: Persons with Down Syndrome Do Not Develop MedulloblastomaD. Satgé^a, C.H. Rickert^b,^aLaboratoire d'Anatomie Pathologique, Centre Hospitalier, Tulle, France; ^bDepartment of Anatomical Pathology, Melbourne, Australia

Although medulloblastoma is the most common brain malignancy in children with an incidence of 0.6 per 100,000 person-years in children [1], it has never been reported in a fetus, an infant, a child, or an adult with Down syndrome (DS). DS is a condition identified more than 140 years ago by John Langdon Down, and is due to a supernumerary chromosome 21 [2]. The world population of persons with DS is estimated at around 5,000,000 individuals. A review of published cases of cerebral neoplasms in DS 8 years ago yielded 38 tumors [3]. Since that time, a close follow-up of the literature of clinical reports and epidemiological studies on neoplasms in DS from fetal life [4] to adulthood provided various types of benign and malignant intracranial neoplasms. These are mainly glial cell tumors and germ cell tumors, without medulloblastoma or any kind of neural cell neoplasm. Theoretically, we should observe around 30 new cases of medulloblastoma every year on the basis of the world population of persons with DS (5,000,000) and the incidence of the tumor (0.6/100,000 person-years) if the incidence of medulloblastoma is similar in DS and in the general population.

The etiology of medulloblastoma remains poorly understood. No environmental factor has been clearly implicated. Genetic conditions such as Gorlin's syndrome (nevoid basal cell carcinoma syndrome) and Turcot's syndrome importantly increase the risk of developing a medulloblastoma. Molecular studies focusing on these associations allowed to unveil the role of Hedgehog and Wingless pathways in the development of the tumor [5, 6]. Indeed, these observations lead to encouraging therapeutic results [7]. We suggest that it should as well be possible to learn more about this neoplasm by studying a condition, such as DS, which seems to strongly inhibit its development. Since it has been shown that DS also protects against another frequent embryonal neural tumor, i.e. neuroblastoma [8], we wonder whether this genetic condition could also have a protective action against neural (non-glial) neoplasms. This epidemiological observation may be related with a study on transchromosomal teratomas using mouse embryonal stem cells with a supernumerary human chromosome 21. These trisomic teratomas showed a threefold lower percentage of neuroectodermal tissue compared to euploid teratomas. According to

the authors, this demonstrates that supernumerary chromosome 21 inhibits the neuroectodermal differentiation of pluripotent embryonal stem cells [9].

As biological studies must rely on clearly established facts, we would like to strongly encourage epidemiological studies to document as precisely as possible the negative link between DS and medulloblastoma.

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