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JÉRÔME LEJEUNE (1926-1994): FATHER OF MODERN GENETICS

JÉRÔME LEJEUNE (1926.–1994.), OTAC MODERNE GENETIKE

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Summary

Jérôme Lejeune's greatest achievement was the discovery of the genetic basis of Down's syndrome, which he named trisomy 21. His important research in human genetics, as well as his humanitarian spirit and fight against therapeutic abortion, rightly led to his recognition as the founder of modern genetics.

Key words: *Jérôme Lejeune, Down's syndrome, trisomy 21, anti-abortion movement*

Introduction

Down's syndrome was considered to be a racial defect for over one hundred years. Scientists presupposed the regression of certain typical features of a race towards race. Due to these presuppositions, Down's syndrome was viewed with indifference or contempt by the scientific community. The general public held the parents of affected children responsi-

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ble, accusing them of being alcoholics or suffering from syphilis. Ten years after the Nazi concentration camps and ten years before the first manipulations on embryos, Jérôme Lejeune revolutionized this scientific field. Not only was he the first to recognize that Down's syndrome was linked to a chromosomal aberration, but more importantly, he revived the Hippocratic medical ethics, supporting that man does not belong to a race that declines when he becomes sick.

Life, career, and distinctions

Jérôme Lejeune was born on June 13, 1926 in Montrouge, just outside Paris. He studied medicine in Paris and received his diploma in 1951. In 1952, he joined C.N.R.S. (National Center for Scientific Research) as director of research and a French delegate for atomic radiation [1] (Fig. 1). On June 24, 1960, Lejeune received his doctoral degree in science with a thesis entitled "*Le mongolisme*" [2] and in 1964, he was appointed professor of fundamental genetics. He is the first and only French geneticist who received the Kennedy Prize from the president of the United States John F. Kennedy as the highest scientific distinction for his groundbreaking research in 1962. In 1969, he received the Memorial Allen Award Medal and in 1993 the Leopold Griffuel Prize for his pioneering research on chromosomal abnormalities in cancer.

Jérôme Lejeune was a member of the Pontifical Academy of Sciences (1974), the Academy of Moral and Political Sciences in Paris (1981), the National French Academy of Medicine, the American Academy of Arts and Sciences, the Academies of Sweden, Argentina, and Chile, and presided over the Pontifical Academy of Life (1994). He was a friend and close collaborator of Pope John Paul II in opposing abortion. Lejeune died of lung cancer on April 3, 1994. A state-approved Jérôme Lejeune Foundation for research into the genetics of mental retardation and the care of the mentally ill has been named in his honor [3], [4]. On June 28, 2007 the cause for canonization of Jérôme Lejeune was introduced, acknowledging the heroic soul of this pro-life geneticist [5].

The "trisomy 21 ": Leujene's leading discovery

The stigma of Down's or "Mongolian" children goes way back in history. The physical resemblance of Down's syndrome patients to Mongolians (individuals of the Mongolian race) led to this association. In 1866, Sir John Langdon Haydon Down [6] described the so called "Mongolian idi-

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ocy". However, later investigations in medical history proved that this syndrome was not originally described by Down, but rather by Jean Etienne Dominique Esquirol in 1838 [7] and by Edouard Seguin in 1846 [8].

The idea that Down's syndrome might be due to a chromosomal anomaly had been proposed repeatedly through the works of Turpin and Alexandre Caratzali in 1937 [9], Penrose [10] and Fanconi [11] in 1939, and Ursula Mittwoch [12] in 1952. However, it was Lejeune who first demonstrated the presence of a supernumerary chromosome in these patients.

In 1953, Jérôme Lejeune and his teacher Raymond-Alexandre Turpin (1895-1988), who had long been interested in the disease, demonstrated the connection between dermatoglyphics and the physical and psychic characteristics of the patients [14]. Lejeune then proceeded to study the factors implicated in Down's syndrome pathogenesis. He recorded its frequency at birth (1 in 600) and observed that immaturity as well as ageing coul lead to the production of abnormal gametes. In a study of 144 cases of twins, he included at least one case with Down's syndrome and he concluded that it was a condition unrelated to the uterine environment or potential fetal trauma [15]. Summarizing his findings, Lejeune concluded that Down's syndrome was a constitutional disease arising at the time of embryo formation, was influenced by non hereditary factors, and was a genetic entity: "the only hypothesis that can explain its occurrence is the case of a 'chromosomal accident ', concerning a large number of genes." [15]. To prove his hypothesis, in 1958 Lejeune began culturing tissues from children with Down's syndrome in order to observe their chromosomes and established an original technique of chromosomal examination. He confirmed experimentally the fundamental concept first described in 1956 that the number of chromosomes in healthy human cells is 46 [16]. His in-depth chromosomal studies revealed for the first time in 1958 the presence of an additional small 47th chromosome in one of the Down's syndrome cases he was investigating. At that time, staining techniques could not identify the chromosomal origin of this 47th chromosome, which led him to consider two possibilities; either this was one chromosome in excess or a chromosome that broke in two.

At the end of January 26, 1959, Lejeune reported his findings to the Academy of Sciences journal under the title *Les chromosomes humains en culture de tissus* [13]. On March 16, 1959, with another communication entitled *L'étude des chromosomes somatiques de neuf enfants mongoliens* [17] he provided evidence to support that this 47th chromosome was morphologically identical to chromosome 21. The presence of three copies of the same chromosome led to the use of the term "trisomy", arising from the Greek treis (three) and soma (body), and since this involved the chromosome pair 21, Lejeune named the disease "trisomy 21".

During the same year, Lejeune presented his findings to the French Academy of Sciences. He began his speech by regretting that this disease was not originally described by an Asian doctor, who would have avoided attributing racial connotations to Down's syndrome. He then summarized the physical and mental characteristics of these patients with the following words: "The face is flat and broad and destitute of prominence. The cheeks are roundish and extended laterally. The eyes are obliquely placed and the internal canthi more than normally distant from one another. The palpebral fissure is very narrow. […] The lips are large and thick with transverse fissures. The tongue is long, thick and much roughened. The nose is small." [13]. He clarified that Down's syndrome was seen in individuals of all races and that its specific phenotypic characteristics would modify with age, resulting in distinct malformations that were however, unrelated to the Mongolian or any other race [13]. Concerning the mental disabilities that accompany the syndrome, Lejeune described a handicap towards the understanding of abstract notions and a decline in IQ with age, contrary to unaffected individuals, while the process of memory appeared to be less affected. He further added that these patients had a very loving nature and a cheerful character [13].

Lejeune's discovery of a chromosomal abnormality as the cause of a human disease represents a hallmark in human medical genetics, which contributed to the birth of clinical cytogenetics and opened the way to a new era towards deciphering human pathology.

Lejeune's controversial fight against therapeutic abortion

In his later years, Jérôme Lejeune became an outspoken defender of human life, speaking frequently against abortion. Noticing a high tendency of physicians to recommend therapeutic abortion to prevent the

birth of children with Down's syndrome and considering embryo as a person, in 1971, Lejeune initiated an antiabortion movement named "Laissez-les vivre" (Let Them Live) [18]. In one of his speeches, Lejeune says: "From the fertilized egg to adult life, a man is the same human being that matures and dies… There are his peculiarities that make him irreplaceable…. As medicine assists in the care at the end of life?, so it has to protect its beginning" and he continues "in face of distress caused by a diagnosis of a disease, the physician must assist the mother and the child. So deliberate interruption of a pregnancy for reasons of eugenics or for resolving a moral, economic or social issue is not for a doctor to perform?" [19], [20]. This famous text received support of at least 20,000 doctors and shed new light on the question of abortion. Lejeune was the indisputable leader of the opponents against the legalization of abortion, as he considered that the life of an individual was valuable as early as his time in the uterus. Furthermore, he asked for fetuses to be legally recognized as "people" right from their conception. This position enticed opposition to his scientific work and led to a series of public insults, media attacks, criticism of his research from 1982 onwards, and finally to destroying his chances to get the Nobel Prize for his groundbreaking discovery.

In the meantime, as a member of the Pontifical Council for Health Care Workers and the President of the Pontifical Academy of Life, he was appointed to study the relationships between biomedicine and Christian morals [4], [18].

Conclusion

Lejeune's work demonstrated the clear distinction between Down's syndrome and race, revolutionized our understanding of chromosomal contribution to disease pathogenesis, and set the foundations for clinical cytogenetics and medical genetics. Jérôme Leujene truly led the way to a new era in human genetics.

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Sažetak

Najveće postignuće Jérômea Lejeunea bilo je otkriće genetske osnove Downova sindroma, koju je nazvao trisomija 21. Zahvaljujući važnim humanim genetičkim istraživanjima, humanitarnome duhu i borbi protiv terapijskoga pobačaja, s pravom je priznat kao utemeljitelj moderne genetike.

Ključne riječi: *Jérôme Lejeune, Downov sindrom, trisomija 21, pokret protiv pobačaja*