Jean Dausset 1916–2009

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Jean Dausset, who received the Nobel Prize of Medicine in 1980 for his discovery of the human major histocompatibility complex (human leukocyte antigen (HLA)), died in Palma de Majorca, Spain, on 6 June 2009, at the age of 92.

Jean Dausset was born on 19 October 1916 in Toulouse, France. He studied medicine in Paris. In 1949, after a sabbatical year at Harvard Medical School, he returned to the Transfusion Center of Saint Antoine Hospital (Paris) and studied patients with an abnormally low number of leukocytes (leukopenic patients). Using their serum, he discovered the existence of antibodies able to bind the leukocytes of another person. This was the principal experiment that directed his whole life from 1952 onward.

Soon after, Dausset showed that these leukocyte antibodies were due to the many transfusions the patients had received. They were not the autoantibodies responsible for leukopenia. Thus, there are groups of leukocytes, as there are groups of erythrocytes. However, unlike the blood groups A, B and O, the antibodies to leukocytes do not exist in the natural state; immunization by transfusion or pregnancy is necessary for their generation.

At this point, Dausset imagined a simple strategy: using the blood of a single donor to transfuse a patient, who then could immunize himself only against the leukocytes of a sole donor. This was done. After a few weeks, Dausset noted the appearance of antibodies able to bind the leukocytes of half the panel of voluntary donors. Thus, 50% of the population tested had the first leukocyte group, which was called 'MAC', an acronym made of the initials of the first three donors of the panel whose leukocytes were not bound by the serum. This discovery was published in 1958 in *Acta Haematologica* in which Dausset already emphasized the possible importance of these groups in transplantation.

Two other teams adopted their technique of leukoagglutination. One, directed by Jon J. van Rood in The Netherlands, showed the existence of a clear division of the population into two allelic groups (4a and 4b); the other, directed by Rose Payne in California, showed that three distinct antigen groups (LA1, LA2 and LA3) were probably products of the same gene. In 1965, an intense international collaboration began: the 'HLA workshops'.

Jean Dausset was the first to realize that this discovery concerned a complex genetic system similar to the H2 system of the mouse. To prove this, he tested 50 serum samples from 50 people using leukoagglutination and a leukocyte lysis test. The results proved the existence of at least eight groups that belong to a single system Dausset called 'Hu-1' according to the nomenclature suggested by George Snell for systems similar to the H2 system (where 'Hu' indicates 'man' and '1' indicates it is the first system).

It had then to be proven that, like the H2 system, the Hu-1 system determines the fate of grafts. In 1964, with the American immunologist-surgeon Felix Rapaport, Dausset performed a series of skin grafts

on volunteers. He showed that there was a correlation between the compatibility determined by the Hu-1 system and the survival of the skin grafts. This proved that the leukocyte groups were actually tissue groups, called HLA; this opened the way to organ transplantation. To find compatible donors, Jean Dausset created the first organization for the exchange of organs, France-Transplant.

Beginning in 1968, Dausset had the intuition that these tissue groups could account for certain susceptibilities to diseases. He was the first to find an equivalent in humans to the correlation between the H2 system and mouse leukemia. Many other allelic associations were found. It became possible to detect, in a family or in the general population, people likely to develop a certain disease if they had the corresponding allele. This led Jean Dausset to introduce, in 1972, the concept of 'predictive medicine'.

The detailed description of the HLA system discovered by Dausset had tremendous consequences at the philosophical level, in fundamental biology and in therapy. First, the considerable polymorphism of the HLA system allowed the demonstration that each person is unique. Second, in fundamental biology, the HLA system made it possible to understand one of the essential mechanisms of immunity: the recognition of self and non-self, thanks to the presentation of foreign peptides by HLA molecules. Third, on the therapeutic level, the most obvious consequence was its immediate application to tissue transplantation. Finally, the discovery of the HLA system permitted the association of many traits with particular HLA alleles.

Jean Dausset had the presentiment of the importance of this predictive medicine. This is what pushed him, in 1984, to create the Center for the Study of Human Polymorphisms, with the aim of detecting, in the genome, the genes of predisposition that were up to that point only suspected, even those not included in the HLA system. For this purpose, it was first necessary to establish physical and genetic maps of the human genome. Dausset then made available to the scientific community the families he had recruited to study the genetics of the HLA system. Ray White, who had described the first markers of DNA (restriction fragment length polymorphisms), joined the project, adding to it large families from Utah. One hundred laboratories in the world contributed to this project. It was the first international biological material of reference and is still in existence today. This made it possible for the Center for the Study of Human Polymorphism to generate markers of the human genome, which thereafter allowed cloning and identification of disease-associated genes, a major advance in medical genetics.

Moreover, in 1991, Jean Dausset became interested in a new aspect of HLA and, together with me, studied the molecule HLA-G, which, contrary to other HLA molecules, is involved in tolerance and in particular maternal-fetal tolerance.

Dausset was member of the Academy of Sciences, a foreign member of the American Academy of Sciences, an honorary member of the American Academy of Arts and Sciences and a founding member of the Organization of the Human Genome. He received many prestigious prizes, such as the Landsteiner Award and those of the Koch Foundation and Wolf Foundation. He was also the advisor of very many research institutions.

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