



Immunity, Genetics and Medicine

Alain Fischer



Electronic version

URL: <https://journals.openedition.org/lettre-cdf/2148>

DOI: 10.4000/lettre-cdf.2148

ISSN: 2109-9219

This article is a translation of:

Immunité, génétique et médecine - URL : <https://journals.openedition.org/lettre-cdf/1929> [fr]

Publisher

Collège de France

Printed version

Number of pages: 13

ISSN: 1628-2329

Electronic reference

Alain Fischer, "Immunity, Genetics and Medicine", *La lettre du Collège de France* [Online], 9 | 2015, Online since 25 September 2015, connection on 17 August 2022. URL: <http://journals.openedition.org/lettre-cdf/2148> ; DOI: <https://doi.org/10.4000/lettre-cdf.2148>

This text was automatically generated on 17 August 2022.

All rights reserved

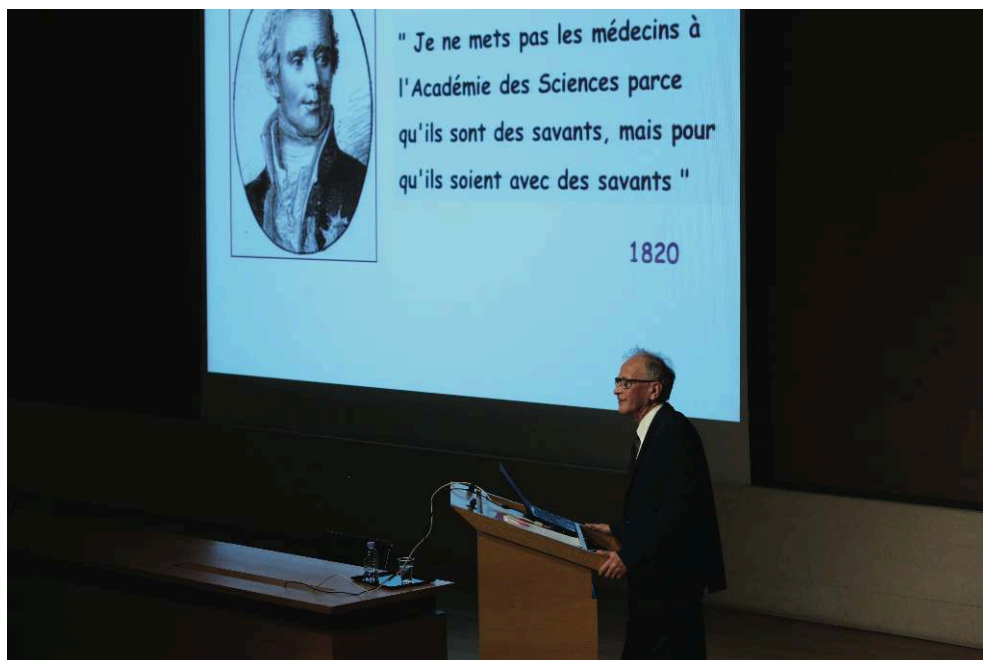
Immunity, Genetics and Medicine

Alain Fischer

EDITOR'S NOTE

Excerpts from the Inaugural Lecture 15 May 2014

Source: *La lettre*, no. 39, March 2015



- 1 The study and understanding of infectious, autoimmune, and inflammatory diseases, as well as allergies falls largely under immunology.
- 2 The challenge is huge as their determinism varies, combining hereditary and environmental components that are difficult to reconstruct. Genetics has contributed to the recent progress of immunology, particularly to that of human immunology. It

has long been observed that vulnerability to infectious agents varies from one individual to the other. During the 1950s, Anthony Allison was the first to demonstrate that a genetic trait could be selected in the human species because it confers a capacity of resistance to an infectious agent. Epidemiology has furthermore demonstrated the weight of heredity in the occurrence of infectious diseases: twenty-five years ago, Thomas Teasdale showed that the risk of premature death caused by infection during adulthood is 5.8 times higher if a biological parent has themselves died prematurely of an infection, whereas we do not observe this risk in the case of an adoptive parent's premature death from infection. What is this risk, and how can it be assessed?

- 3 This is where my medical field comes into play: that of rare and hereditary immune system diseases called *primary immune deficiencies* (Pid). A whole series of rare or even exceptional diseases (for example 1 case/1 million births) exists, during which the immune system is altered, variably causing vulnerability to infection, autoimmune or inflammatory diseases, allergies and sometimes cancers. It has been estimated that one in 5,000 individuals are born with this type of condition, of which approximately 250 have been described to date. These conditions are caused – or so it seems – by a single event: the mutation of a gene responsible for the loss or, more rarely, the gain of a function of the corresponding protein. The study of these Pids – like that of many other rare genetic diseases – offers an exceptional observatory of human biology and its anomalies. The value of this approach is threefold: identifying piece by piece the key elements of the immune system necessary to its development, its effector functions and its regulation; in so doing contributing to the understanding of the mechanisms involved in controlling an infection or preventing excessive inflammation, or autoimmune responses; and allowing for a precise diagnosis of these diseases and sometimes the elaboration of a therapy. This approach has proven to be and still is fruitful.
- 4 One example relates to self-tolerance, the failure of which causes autoimmune diseases. The T and B lymphocytes reacting against our own antigens are normally non-pathogenic. How are they effectively controlled? The answer to this question stems partly from the study of rare hereditary diseases that are responsible for susceptibility to autoimmunity. Our main contribution, with Frédéric Rieux-Laucat, has consisted in identifying the hereditary anomalies of the gene coding a protein called FAS in patients suffering from an autoimmune lymphoproliferative syndrome. FAS is a membrane receptor which is notably present on the surface of T and B lymphocytes. Its bond by a ligand, the FAS ligand, present on the surface of activated T lymphocytes, causes the death of chronically activated lymphocytes – which is exactly the situation encountered for specific lymphocytes of self-antigens. This molecular communication system, which can act intra- or intercellularly, thus controls the potential escape of autoreactive T and B lymphocytes. It has also been shown that “acquired” somatic mutations of the same gene could encourage the emergence of autoreactive lymphocytes and consequently of certain autoimmune diseases, since such lymphocytes acquire a selective survival advantage. This observation underpins a hypothesis likely to explain common autoimmune diseases: the accumulation of somatic mutations of genes controlling cell death or division within autoreactive T and/or B lymphocytes may facilitate their escape and therefore the induction of autoimmunity, following a model similar to oncogenesis.

• A video of the Lecture can be found at www.college-de-france.fr, on the professor's page.

AUTHOR

ALAIN FISCHER

Experimental Medicine