François Kourilsky

1934–2014

Bernard Malissen

François Kourilsky, who passed away on 31 May 2014, made important contributions to both basic and translational immunology and, with his fellow immunologist Michel Fougereau, founded the Centre d'Immunologie de Marseille-Luminy (CIML).

After studying medicine in Paris, François moved to the New York University School of Medicine in 1962 as a postdoctoral fellow in the laboratory of Baruj Benacerraf. There he established that IgG1 (then known as γ 1) guinea pig antibodies were responsible for anaphylaxis sensitization, whereas the fixation of complement and the lysis of cells were exclusively the properties of γ 2 (IgG2) antibodies. These results revealed for the first time that different biological properties could be assigned to distinct immunoglobulin isotypes. They led to the later demonstration that antibody heavy chains, and particularly their Fc fragments, contained sequences responsible for their biological properties. Upon his return to France at the Research Institute on Leukemias at Saint Louis Hospital in Paris, François, along with the hematologist Jean-Paul Lévy, focused on immune responses directed against leukemias caused by mouse retroviruses. The mouse major histocompatibility complex (H-2) had recently been linked to inherited susceptibility to some of those leukemias. In humans, an equivalent complex called HLA was just in the process of being dissected by Jean Dausset, also working at the Saint Louis Hospital. This led François and Dausset to analyze whether particular HLA alleles could account for susceptibility to certain cancers. In 1968, they published the first study comparing the distribution of the few known HLA alleles in patients suffering from acute leukemia and in unaffected controls, which did not demonstrate such connections in humans. Using antibody-induced redistribution of membrane antigens, François further established, with Catherine Neauport-Sautes, that the gene products from the D and the K ends of the H-2 region are expressed on independent molecules, an important finding at a time when molecular biological techniques had not become widespread among immunologists.

In the mid-1970s, together with Michel Fougereau, François established the first institute in France devoted exclusively to immunology and funded by the Institut National de la Santé et de la Recherche Médicale (INSERM) and the Centre National de la Recherche Scientifique (CNRS). The Centre d'Immunologie de Marseille-Luminy opened in 1976 in Luminy, in southeast France. Although Luminy had the benefit of being (and indeed still is) one of the few pieces of pristine land on the Mediterranean coast, at that time, scientifically speaking, the campus was in the middle of nowhere. Considering the centralized nature of French institutions, very few people were betting on the success of a scientific operation developing so far away from Paris. The organization of the CIML, as established by its two founding fathers, was quite unusual in the French research landscape, which was dominated by large laboratories with many scientists working under the umbrella of a 'director for life'. Not only was the CIML headed by a rotating directorship, but it was

composed of small, independent research teams revolving around core facilities operated by a dedicated technical staff. The new center grew rapidly, and its expansion included several groups headed by European and US scientists. Importantly, teams were nonpermanent and subjected to regular evaluation by a scientific advisory board composed primarily of foreign members, among whom luminaries such as Benacerraf, Cesar Milstein, Klaus Rajewsky and Max Cooper provided much insightful help. For the first ten years of the CIML's life, its scientific advisory board had to convene in an almost clandestine manner to avoid upsetting the sensitivities of French funding bodies and their then quite traditional, nationally based evaluation panels.

From its inception, the CIML caught the 'immunology wave', a tremendously exciting time for adaptive immunology that started with the discovery of MHC restriction and the generation of immunoglobulin diversity via somatic site-specific recombination. What followed, coinciding with the early years of the CIML's existence, was a sustained period of discovery encompassing the dissection of the HLA complex, the first sequencing of an HLA class I gene (with the help of Philippe Kourilsky, François's brother, working at the Pasteur Institute in Paris), the cloning of the genes for the adhesion molecule N-CAM and the T cell regulatory molecule CTLA-4, and the elucidation of the molecular basis of cell-mediated cytotoxicity.

In 1978, during a sabbatical in Oxford, François became acquainted with the novel technology of hybridomas, and on his return to the CIML he teamed up with Michel Pierres, another former Benacerraf postdoctoral fellow, to apply it on a massive scale for the identification and dissection of the molecules encoded by the H-2 complex, including the elusive I-J-encoded products. François rapidly became aware that these technological advances had industrial application for cell analysis as well as for dosing hormones, tumor markers and cytokines. In 1982 this led him, with Michel Delaage, to develop Immunotech Inc., one of the first French biotech companies and today a subsidiary of Beckman Coulter.

The unique organization of the CIML also fostered an exciting atmosphere in which science, rather than rank and power, had priority. In what little free time he had during his directorship, François would sit at the bench next to me, a PhD student, contributing in a decisive manner to the screening of monoclonal antibodies against T cell surface molecules! François' organizational skills led him to accept increasingly heavy administrative responsibilities, culminating in his service from 1988 to 1994 as head of the CNRS, the largest governmental research organization in France and one of the largest basic science agencies in Europe.

François's outstanding contributions, entrepreneurship, mentorship and collaborative spirit will be sorely missed. His scientific and organizational insights permitted the development within the CIML of a thriving community of immunologists now disseminated into both clinical and basic immunology departments. Training with François was intense. We learned from him the need to exercise some control over the working environment, how to build a research career with the confidence and strength to go one's own way, and not least, how to convey enthusiasm for immunology to the next generation.

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