

Cécile Wandersman, Professor at the Institut Pasteur and a recognized expert in the field of bacterial secretion, heme transport and metabolism, passed away on December 21, 2014 at age 67.



PASSION UNDER INFLUENCE: DISCOVERING BACTERIAL GENETICS WITH CÉCILE WANDERSMAN.

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My encounter with Cécile and scientific research was a stroke of luck at a time of deep personal doubt. Trained in General biology to become a teacher, I was having second thoughts about my professional path, and, after one year of teaching in a high school, I felt that something, some spark, was missing. I then had the opportunity to take a leave of absence to follow a new multidisciplinary course that required a 6-month laboratory internship. I vividly remember snatching Cécile's offer to study *E. chrysanthemi* protease secretion off the information board and running to a pay phone to set up an appointment. This is how I joined Cécile's group in Maxime Schwartz's laboratory at the Institut Pasteur in 1990.

At the time, Cécile, Philippe Delepelaire and Sylvie Létoffé had already started to use *E. coli* as a heterologous host to study the secretion of *E. chrysanthemi* proteases PrtB and PrtC by a dedicated transport system, consisting of only 3 membrane proteins, including an ATP-Binding Cassette transporter. This ABC-dependent secretion system (now called Type 1 secretion system or T1SS) was used by proteins lacking the classical N-terminal signal sequence, such as *E. coli* α -hemolysin and Cécile had the foresight to choose *Erwinia* and *Serratia* metalloprotease secretion as model systems and use them to characterize their enigmatic C-terminal secretion signal and secretion mechanism.

The project Cécile first gave me was to study a gene close to *prtB* and *prtC*, and potentially encoding another *E. chrysanthemi* metalloprotease. I was her first student, and Cécile took my training to heart, while Philippe and Sylvie cocooned me so kindly that, after 6 months, I decided to further postpone going back to teaching and started a PhD thesis under Cécile's supervision - and I have never regretted it. During my time in Cécile's lab, we identified other T1SS proteins, which led to the genetic and structural analysis of their C-terminal signals with the NMR laboratory headed by Muriel Delepierre. We also identified a new secreted heme-binding protein (HasA), thus opening the way to a detailed characterization of what is now considered a widespread bacterial heme acquisition system.

Cécile always tried to keep doing experimental work throughout her whole career. For a long time, her bench and mine were side by side and I was constantly exposed to Cécile's truly eruptive enthusiasm and passion for science, her articulated (and non-negotiable) critics of the latest book or movie and her opinionated political positions. She was fun, joyful, witty and almost painfully imaginative, so much that I often felt exhausted after discussing ideas with her, desperately trying to keep up.

On the campus, Cécile was known to be very out-spoken. Her bluntness and very (very) expressive nods during seminars or meetings were famous, and, to some extent, interacting with her could be intimidating. She could indeed be very critical, and she had little tolerance for poor scientific grasp or ill-conceived experiments. Once, after weeks of failures and around the clock attempts to make a specific genetic construct and test some hypotheses about PrtA secretion, I finally got exciting results. I knew that I still had a few things to double check, but the essential information was there, and I was so happy that I could not wait to tell Cécile. It was Sunday morning, so I simply arranged the Petri dish and hand-written notes on her bench, hoping that she could share my joy when she would come into the lab later in the day. She indeed came and left a note for me to see the next day- she asked for more controls, with 3 exclamation points... She did, however, come to see me at some point with a big smile, but a compliment from Cécile was no small gift.

Nevertheless, many, on the campus and beyond, sought her advice and guidance. When puzzled by a result involving bacterial genetics, you could go knock at her door and she always seemed to have time on her hands to talk – or argue- with you. I particularly admired and appreciated the way she had to mentor her students. She knew when to put her impatience aside and be kind and constructive when your project was at its lowest. She had this marvelous ability to put you back on track and to make sense of the most confusing results - or she just had the guts to advise you to cut your losses and move on.

Far from being directive, Cécile encouraged her collaborators to improve themselves and to explore their own ideas, loving nothing more than to engage them into discussing their data. You could then see the pleasure she took at juggling multiple scientific questions. Moreover, her remarkable scientific intuition often led her to propose decisive experiments, or helped new ideas emerge from these exchanges. She was so immensely happy and proud when she guessed right! On the other hand, what a glowing feeling to be able, during these sort of scientific battles, to convince her of the value of a new idea or of performing this or that experiment.

Working in Cécile's lab also meant being exposed to a very extended network of superb bacterial geneticists from all over the world. Cécile cherished her scientific family, seemingly united by a common love for genetic screens and the pride taken in addressing and solving difficult scientific questions - sometimes with no more than (preferably re-usable) wooden toothpicks.

Retrospectively, I feel extremely fortunate to have met Cécile. I could not have asked for a more passionate mentor, or a better scientific influence. I am immensely indebted to her for providing the spark I was longing for, and for showing me how exhilarating bacterial genetics could be (well, on some days).