Amanda E. I. Proudfoot 1949–2019

Amanda Proudfoot, internationally recognized for her seminal contributions to the field of chemokine biology, passed away on 19 December 2019 in France. Her research focused on the development of anti-inflammatory and anti-infective therapeutic agents, and many of the advances in chemokine biology can be traced back to the discoveries she made. Amanda's research broke new ground and led to the elaboration of several important aspects of the immune system. Amanda was a generous and enthusiastic collaborator and a loyal and warm friend.

Born in Johannesburg, South Africa, Amanda received her BSc, with Honors, from the University of Witwatersrand, Johannesburg. She then relocated to Europe to complete a PhD in Biochemistry at the University of Geneva. Her career thrived in Geneva, first at Glaxo Wellcome, then as Head of Protein Biochemistry at the Serono Pharmaceutical Research Institute. In 2007 she was principal scientist at the Merck Serono Geneva Research Centre, and until recently served as a consultant for several biopharmaceutical companies. Amanda led two therapeutics through preclinical development into clinical trials.

In the early days of chemokine research, her group identified and characterized novel chemokines, including CXCL8 and CXCL4, and in collaborative studies cloned the chemokine receptors CCR1, CCR2 and CCR4. Her discoveries led the field of chemokine research, and her goal was to interfere with the chemokine network to ameliorate diseases. Cognizant that several viral pathogens successfully target the chemokine system, Amanda's strategy was "if pathogens can successfully inhibit the chemokine network, why can't we?"

Amanda identified a potent CC chemokine antagonist, Met-RANTES, formed by retaining the initiating methionine in the prokaryotic expression system. Met-RANTES proved extremely useful in elucidating the power of inhibiting the chemokine system in numerous disease models. Met-RANTES competes with wild-type RANTES and CCL3 for binding to cell receptors and inhibits T cell chemotaxis, eosinophil function and infection with HIV-1. Extension of the amino terminus of RANTES, to generate the variant AOP-RANTES, resulted in a potent anti-HIV infectivity agent. The use of AOP-RANTES provided the first demonstration that inhibition of infection of primary macrophages through inhibition of CCR5 was feasible.

Credit: Ruth Bisig

Amanda then turned her attention to a second essential chemokine characteristic: their low-affinity binding to cell surface glycosaminoglycans (GAGs). Using chemokine variants in which GAG binding was abrogated, her group was able to demonstrate that this interaction was essential for chemokine-mediated cell recruitment in vivo. Abrogation of this interaction invokes anti-inflammatory activity, again providing a novel therapeutic pathway.

Knowing that ticks must evade host immune-cell recruitment for successful infection Amanda's group screened a cDNA library constructed from the salivary glands of the common dog tick to identify proteins that bind and inhibit chemokines. She identified a protein they designated Evasin-1. Evasin-1 is a selective inhibitor of CCL3, CCL4 and CCL18. She later identified tick Evasin-3, which binds CXCL1 and CXCL8, and Evasin-4, which binds CCL5 and CCL11, all exhibiting potent anti-inflammatory activity.

Amanda established many successful collaborations and partnerships over the years. Beyond generously sharing materials, Amanda was an enthusiastic collaborator, bringing the right people together, someone whose energy and enthusiasm were infectious, motivating those around her. I met Amanda in 1998 at a conference in Jerusalem, and being among the few female scientists there, we gravitated toward each other. Amanda had an infectious laugh, and her joie de vivre was evident. From those days forward, we built a friendship that, although we were separated by thousands of miles, was enduring. My collaboration with Amanda led to the discoveries that CCL5 activated JAK tyrosine kinases, best known to function in cytokine signaling, and the need for glycosaminoglycan binding for CCL5-mediated T cell apoptosis. Her intellect and insightfulness pioneered new concepts, creating new fields of research. Her status as the 'Queen of Chemokines' was undeniable, yet Amanda was unassuming and self-effacing, reticent to take center stage. Amanda brought people into her circle of science, with warmth and friendship, whether they were trainees, young investigators or colleagues. During her time in industry, Amanda instituted student programs and supervised many MSc and PhD students. Amanda took personal responsibility for trainees in her group, as a mentor and advocate. She was a role model and inspiration for women in science. Amanda was an active member of the International Cytokine Society and then the International Cytokine & Interferon Society, and was awarded an Honorary Lifetime Membership Award, acknowledging her service to the societies.

Amanda was someone who loved life, as demonstrated by her passion for horse riding from an early age and her love of photography especially when on safari in southern Africa and during her extensive world travels. Most recently, she discovered a joy in painting, capturing memorable scenes of her travels. New adventures, new ideas and new goals. Amanda was spontaneous; she flew to Toronto to be at my first art show. Amanda was devoted to her family: husband, Bernard; her stepchildren, Florence and Philippe; and her brother, Charles. She was the glue for her family — their anchor. Her many lifelong friends and colleagues will remember her sharp intellect and inquisitive mind, her joyful exuberance, her loyalty and her generosity; she had an impact on so many, and these will be our lasting memories of Amanda. ❐

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