



A tribute to Nilabh Shastri and a special issue on Antigen Processing and Presentation in Paris (APP10, Paris 2019)

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**A tribute to Nilabh Shastri
and a special issue on Antigen Processing and Presentation in Paris
(APP10, Paris 2019)**

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The 10th Antigen Processing and Presentation Workshop was a glorious meeting, when we were all still young and unconscious. Unconscious of the Covid-19 crisis looming, we wandered happily without masks in an exciting flurry of unpublished news and informal exchanges on our preferred topic in a garden in the middle of Paris across the street from Institut Cochin. We heard short presentations from good-humored very famous scientists generously giving their time to presentations from younger scientists. We were inspired by a great scientific EMBO women in science lecture. We discussed posters in depth, and played a game on Immunology in Paris. We had very hot discussions on the relative roles of spliced peptides and other neoepitopes in the induction of T cell responses, and more (1). We were proud to really feature 50% invited women speakers. We were also unconscious of Nilabh Shastri's life coming to an end so soon after, whereas he had given a mysterious title to his Keynote and had promised a future contribution to this special issue 'Immune surveillance of immune surveillance' (Figure 1). After this loss struck our APP community, the special issue linked to the Workshop turned into a Tribute to Nilabh. His trainees at the Johns Hopkins University School of Medicine give us a testimony on their privileged experience 'chasing the rainbow' with his guidance, Jon Yewdell a recollection of testimonies from 'Hoodlums', UC Berkeley students and post-docs, UC Berkeley Faculty and APP colleagues, and Robin Fahraeus, Sebastien Apcher and colleagues focus on Nilabh's pioneering discovery of non-canonical mRNA translation initiation and all its consequences in antigen presentation. We all are deeply sad from this loss of a true groundbreaking genius in our field, who also displayed all his life exceptional elegance, kindness and mentorship.

In this special issue, Julie Magarian Blander reviews the role of the Transporter Associated with antigen processing (TAP) in antigen presentation and cross-presentation, and she details non-canonical cross-presentation which relies on endoplasmic reticulum-Golgi-intermediate Compartment (ERGIC)-derived Class I Molecular Histocompatibility Molecules (MHC-I), without Toll-like receptor control, thus maintaining CD8⁺ T cell priming even when TAP is blocked by viral escape mechanisms. Bénédicte Manoury reviews the role of endoplasmic reticulum stress in the MHC class I antigen presentation pathway of dendritic cells (DC), highlighting the role of the unfolded protein response in this pathway. Louise Boyle presents primary data where she compared MHC-I when it lacks a glycan, like in recombinant molecules derived from bacteria used for in-vitro functional assays, to physiologically glycosylated MHC-I. She found that when MHC-I lacks a glycan, it has a stronger affinity for the peptide editor TAP-binding protein related (TAPBR), thus peptides are more easily dissociated by TAPBR, impacting peptide exchange. MHC-I exerts a strong

immune surveillance on tumors, which escape by multiple mutations at all possible molecular and compartment levels, the consequences of these mutations are reviewed by Marlieke Jongsma, Jacques Neefjes and Robbert M. Spaapen. Finally, as DC remain the 'professional antigen presenting cells' as coined by Ralph Steinman, Justine Mintern and Jose Villadangos discuss how the triggering of different receptors for the constant fragment of immunoglobulins (FcR), especially neonatal FcR vs Fc γ R, regulates the immune functions of the different DC populations, and Elodie Segura proposes a model in which conventional DC and monocyte-derived DC play complementary roles for the induction of T cell responses, by presenting antigens either in lymphoid organs or in inflamed tissues, respectively. The traditional and generous sharing of many more unpublished data of Antigen Processing and Presentation Workshop was vivid and exciting, as testified by the abstracts published in Molecular Immunology (1) and by articles published since.

Nilabh was at the origin of the creation of these Workshops with Betsy Mellins and Eli Sercarz in 1995, a successful series of workshops across the world with a small crowd of aficionados (Table 1). The future Antigen Processing and Presentation Workshop is yet to come, but this rendez-vous is recurrent: now from France to Australia and (unlike a boomerang) in a different location somewhere in the world in the future.

Figure 1. Nilabh Shastri at APP10: 'Immune surveillance of immune surveillance'



Table 1. List of APP workshops

1	1995	Berkeley, Oxnard (USA)	Nilabh Shastri, Elizabeth D Mellins, Eli Sercarz
2	1999	Bar Harbor (USA)	John D. Lich, Janice S. Blum
3	2002	Vaux de Cernay (France)	Sebastian Amigorena, Alexander V Chervonsky, Alexander Rudensky, Peter Van Endert
4	2004	Bar Harbor (USA)	Alexander Rudensky, Alexander V Chervonsky
5	2007	Dunk Island (Australia)	Jose Villadangos, James McCluskey, William Heath
6	2010	Cargese (France)	Philippe Pierre, Kenneth Rock
7	2012	Amsterdam (The Netherlands)	Jacques Neefjes, Emil Unanue (EMBO)
8	2015	Philadelphia (USA)	Lawrence Eisenlohr, Lisa Denzin, Paul Roche, Tim Elliott
9	2017	Salamanca (Spain)	Margarita Del Val, Luis C Antón, Jack Bennink, Vincenzo Cerundolo (EMBO)
10	2019	Paris (France)	Anne Hosmalin, Bénédicte Manoury, Peter Cresswell, Sebastian Amigorena (EMBO)

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References

1. EMBO Workshop. Antigen Processing and Presentation 10 (APP 10), 30 May-02 June 2019, Paris, France. 2022. Mol. Immunol.: 1-37.

The Special Issue is dedicated to the 10th Antigen Processing and Presentation Workshop, set up at Institut Cochin, Paris 2019

It is also a vibrant Tribute to Nilabh Shastri, founder of the APP Workshops, untimely passed away in 2021 and deeply missed by colleagues and friends.

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This is inaccordance with my co-author, Dr Bénédicte Manoury.