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Delineation of T cell effector classes and activation states in HIV using cellular assays

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The successful control of viral infections such as HIV typically involves synergistic activities of various components of the immune system. In addition to specific antibodies, $CD8^+$ T cells are critical for controlling the infection via cytokine secretion and killing. Like $CD4^+$ cells, $CD8^+$ cells can secrete cytokines upon antigen encounter and recruit cells of the innate immune system to participate in the host defense. $CD8^+$ cells frequently secrete IFN-γ that shuts down viral replication in the infected cell and upregulates MHC expression in these cells. In addition, IFN-γ is a potent activator of macrophages and NK cells. IFN-γ measurements have become the gold standard for monitoring $CD8^+$ cells by ELISPOT. While IFN-γ assays clearly detect Tc1 cells, they will miss other $CD8^+$ effector arms that do not express IFN-γ. Presently, it is unclear what proportion of the antigen-specific $CD8^+$ cell repertoire these "alternative" $CD8^+$ cells constitute, and which other products or cytokines released are the most informative. During this talk, I will cover our studies utilizing granzyme B, perforin, TRAIL and IFN-γ ELISPOT assays for monitoring HIV-specific T cells in infected individuals. I will highlight our experience in documenting the existence of "helpless/frustrated/lethargic" $CD8^+$ T cells in humans, that is cells that have been primed in the absence of $CD4^+$ T cell help, and the crucial role that such cells might play in HIV infection.

Biography

Dr. M. Tary-Lehmann is an Adjunct Associate Professor of Case Western Reserve University (CASE) Department of Pathology, Co-Founding Scientist and Chief Scientific Officer for Cellular Technology Limited (CTL). She has published more than 65 papers in peer-reviewed journals. She provides guidance and oversight for technical operations in the GLP laboratory, ensuring the ongoing scientific excellence of CTL. Over the past decade, she has worked with clients and regulatory agencies to develop and validate reference samples and controls for use in regulated immune monitoring assays.