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Introduction to Dendritic Cells

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### Discovery

Steinman Laboratory

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## Discovery

Dendritic cells were discovered in 1973 by Ralph Steinman and the late Zanvil A. Cohn at the Rockefeller University. At the time, Steinman and Cohn were studying spleen cells to understand the induction of immune responses in a major lymphoid organ of the mouse. They were aware from research in other laboratories that the development of immunity by mouse spleen required both lymphocytes and "accessory cells," which were of uncertain identity and function. The accessory cells were thought to be typical macrophages, but despite extensive laboratory experience with macrophages, Steinman and Cohn encountered a population of cells with unusual shapes and movements that had not been seen before. Because the cells had unusual tree-like or "dendritic" processes, Steinman named them "dendritic cells."

When Steinman evaluated this population of cells, they had little, if any, resemblance to the well-known macrophages. Dendritic cells lacked an abundant membrane enzyme that was typical of macrophages. In contrast to macrophages, the dendritic cells detached from culture surfaces, had poor viability, and their turnover in spleen was rapid. Also unlike macrophages, dendritic cells had few digestive bodies or lysosomes, lacked the key receptors for antibody-coated particles (Fc receptors), and were poorly phagocytic in vivo and in vitro. Accordingly, the research experience of the Cohn-Steinman laboratory with the cell biology of macrophages enabled the confident identification of dendritic cells as novel cells having distinct properties and, eventually, functions.

By 1979, Steinman had learned to enrich the small population of dendritic cells (normally comprising one percent of the cells in the spleen). Once a sufficient quantity of cells could be obtained, with a high degree of purity, then functional studies on the new cells could begin. These studies revealed their potent stimulatory role in immune function. Comparable dendritic cells were

found in many organs and animal species, including in human blood. Subsets of dendritic cells were identified, each having its own surface markers. Dendritic cells were seen in the T-cell areas of organs of the lymph system, the ideal location for initiating immunity. Laboratories worldwide started to study dendritic cells and demonstrate their potent immune stimulatory functions.

These observations also permitted studies on the origin of dendritic cells from bone marrow, where their development was traced through a pathway shared with macrophages and granulocytes. By 1992, Steinman, with critical input from colleagues in Europe and Japan, developed methods to generate a large number of dendritic cells from their progenitors. At this point, dendritic cells were readily available for cellular and molecular biologists, and their studies have greatly expanded dendritic cell research.

Continuing discoveries of the physiological capacities of dendritic cells are providing many surprises. The following sections describe some functions for which the dendritic cells are currently best known.