Legends of Allergy and Immunology – Dean D. Metcalfe

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Abstract

As many other physicians and researchers, we have had the great pleasure to be fellows in the laboratory of Dean Metcalfe, the Laboratory of Allergic Diseases, National Institute of Allergic and Infectious Diseases (NIAID), NIH, Bethesda, USA (Figure [1](#fig-cap-0001)). The open atmosphere, research driven by curiosity, hypotheses originating from clinical observations, and mutual trust and respect are the cornerstones of Dean's mentorship. Dean and his laboratory have made major contributions on mast cell biology, from basic studies on the regulation of mast cell development and functions, to clinical studies on mast cells in diseases, such as systemic mastocytosis. After more than 50 years of exploring human mast cells, Dean's impact on what we know today about these cells, their biology and how they affect diseases is outstanding and unique.

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As many other physicians and researchers, we have had the great pleasure to be fellows in the laboratory of Dean Metcalfe, the Laboratory of Allergic Diseases, National Institute of Allergic and Infectious Diseases (NIAID), NIH, Bethesda, USA (Figure 1). The open atmosphere, research driven by curiosity, hypotheses originating from clinical observations, and mutual trust and respect are the cornerstones of Dean's mentorship. Dean and his laboratory have made major contributions on mast cell biology, from basic studies on the regulation of mast cell development and functions, to clinical studies on mast cells in diseases, such as systemic mastocytosis. After more than 50 years of exploring human mast cells, Dean's impact on what we know today about these cells, their biology and how they affect diseases is outstanding and unique.

It has been almost half a century since Dean started as a Clinical Associate in Allergy and Immunology at the NIAID in 1974, a place he has been loyal to ever since, except for the years 1977-1979 when he was a fellow in Rheumatology and Immunology at Robert B. Brigham Hospital and Harvard Medical School, Boston, MA, in the laboratory of the legendary K. Frank Austen. This time was important for shaping his

future career and interest in the ingenious mast cell. Back at the NIH, he reunited with Michael Kaliner at the Allergic Diseases Section and continued his work on mast cells, while initiating the clinical protocols on mastocytosis. In 1985, Dean was awarded his own section within NIAID named after his beloved cell – "Mast Cell Biology Section", a section that he led until his retirement at the end of 2022. In 1994, he became the Head of the Allergic Diseases Section, which in 1995, became the Laboratory of Allergic Diseases, and where he remained Chief until 2017.

One of Dean's many characteristics is his open mind to novel ideas and to explore new fields. The 1990s started a new era in mast cell biology with the identification of stem cell factor (SCF) and its receptor KIT as being critical for growth and development of the mast cell lineage. Dean's lab was instrumental for early discoveries on human mast cell development from CD34-positive progenitor cells[1], and the effect of SCF on these cells. Besides these seminal discoveries in basic mast cell biology, Dean and his laboratory also have had a major impact on our understanding on the role of mast cells in health and disease including mast cell disorders, particularly mastocytosis. In 1991, Dean published a classification of mastocytosis that served as major model for later classifications through today[2]. He also was one of the key contributors for establishing and later continuously advising the European Competence Network on Mastocytosis (ECNM) until this date. Among his many fundamental discoveries in mastocytosis is the identification of the *KIT D816V* mutation in mastocytosis which became a diagnostic criterion and therapeutic target for mastocytosis (Figure 2)[3]. These aberrant mast cells were also demonstrated in a subset of patients with idiopathic anaphylaxis[4]. More recent work from his laboratory includes the description of exosomal transfer of mutated KIT to other cells [5], and the identification of a new mast

cell-derived condition, i.e., vibratory urticaria [6].

Dean is a true legend in the field of allergy and mast cell biology, a prolific writer, and an outstanding mentor to many well-established scientists and clinicians. Most importantly, his dedication and research has contributed to improving the lives of patients suffering from mastocytosis and other mast cell-driven diseases.

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Box 1. Major discoveries/contributions of Dean Metcalfe.

- 1991 Consensus and classification of mastocytosis.
- 1991 & 1992. Demonstration of human mast cell origin from CD34+ progenitors and SCF to be a major growth factor for mast cells.
- 1995 Identification of *KIT D816V* mutation in systemic mastocytosis.
- 2007 Identification of aberrant mast cells in idiopathic anaphylaxis.
- 2016 Description of a new mast cell-driven condition relating to mechanoreceptors - hereditary vibratory urticaria.
- 2018 & 2021 Detection of exosomes that can transfer mutated KIT to other cells and change their phenotype and function.

Figure legend

Figure 1. Dean Metcalfe

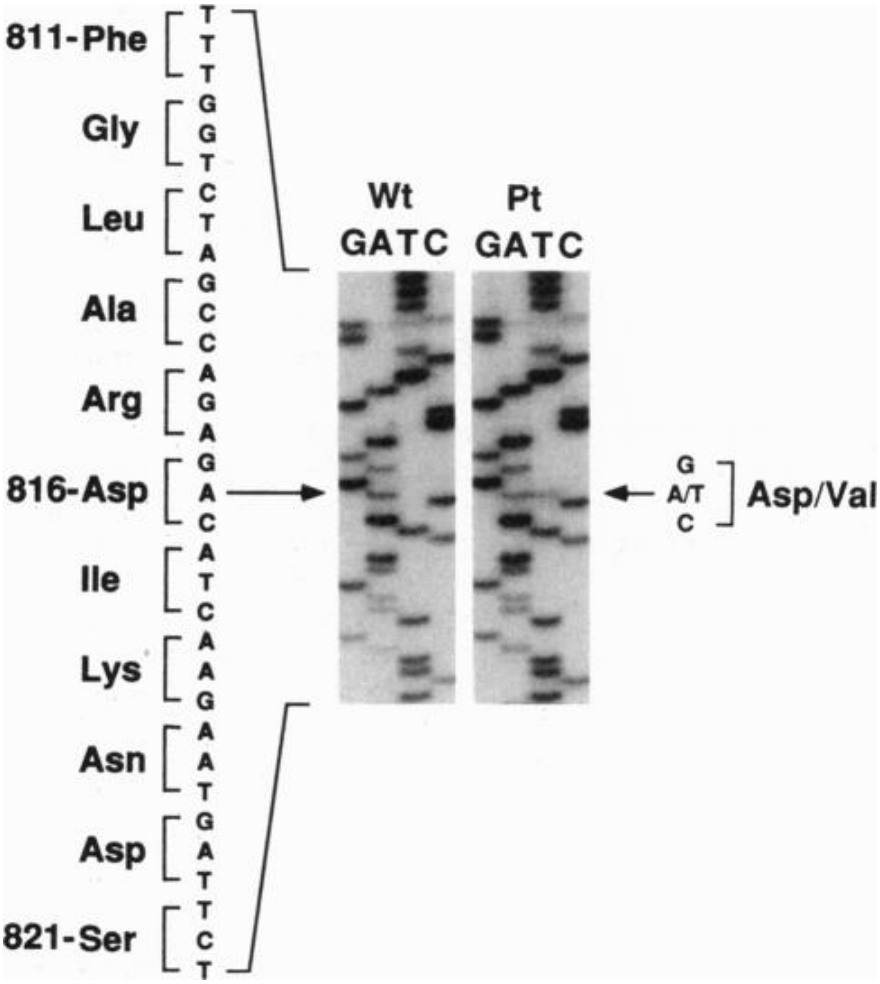

Figure 2. The first description of a base change at codon 816 in the gene*KIT* identified by direct sequencing of PCR products in a patient with systemic mastocytosis[3]. This *KIT* D816V mutation is now a criterion in the diagnosis of systemic mastocytosis.

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