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Dimensions of immunologic memory

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praemonitus, praemunitus.

(Idiom, circa (pre?) 16th century)

The more constraints one imposes, the more one frees one's self of the chains that shackle the spirit.

(Igor Stravinsky)

Most will know the idiom stated above as "forewarned is forearmed." This succinctly summarizes the entire phenomenon of immunologic memory, the capacity of a host to "remember" a previous antigenic/infectious encounter in a manner that facilitates enhanced survival upon rechallenge. The idiom seems appropriate, not only because it contains the root from which we derive our word "Immunity" but also because it may well just be one of the few statements to which immunologists can universally agree. Outside this, opinions abound in regard to which cells in the immune system contain this "memory," how long it lasts, what is required for its persistence/maintenance, and how it might be enhanced or curtailed. For this issue of Immunological Reviews, we have gathered 17 contributions from a range of experts that altogether cast an array of fresh perspectives onto a cardinal immunological concept so uniquely situated between past and future.

With the aim of enlivening the discussion of the subject, and guided by the spirit of Stravinsky's quote above, we deliberately introduced certain limitations to the process of selecting contributors and topics to this issue devoted to immune memory. First, we invited only scientists in the field who work outside of the United States. While geographical boundaries certainly do not restrain the exchange of scientific ideas as they once did, the dynamics of scientific practice as a social discipline continue to be shaped by local and regional interactions that will inevitably favor certain perspectives over others. The view from outside the dominant US biomedical research complex may reveal some otherwise underappreciated points of view. Second, and as alluded to above, we specifically encouraged our contributors to give voice to their scientific passions and opinions rather than simply providing a literature review. Immunological Reviews already has a format that focuses on a synthesis of the literature with the individual investigator's contributions and governing ideas about the topic of focus, so our wish to emphasize author opinion over

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This article introduces a series of reviews covering the topic of Immunologic Memory appearing in Volume 283 of *Immunological Reviews*.

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literature overview fit very well with this format. Informed opinions are not only the most influential, they are also the most fun to read. Third, we have to admit that our own preoccupation with a particular topic (T- cell memory) as well as the familiarity, or lack thereof, with the relevant work of our colleagues inadvertently introduced yet another bias. While we, therefore, cannot claim impartiality in putting together this volume, we expected the overall direction of this issue to emerge in a somewhat unpredictable and "self-organizing" fashion. Which it did, and several ideas acquired a particular prominence.

This is perhaps best illustrated by the prominence of "memory inflation," the numerical expansion of virus- specific memory T cells in certain experimental and naturally occurring scenarios as emphasized by several contributors.[–] At the same time, the very concept of "immunological memory" has undergone a substantial "inflation" (as it were) of its own, being now invoked for cell types other than T and B cells (innate lymphocytes, monocyte/macrophages) and species other than vertebrates (invertebrates, plants, archaea, and bacteria).[–] Another topic extensively discussed throughout this issue is the role of persisting antigen in shaping immunological memory in the context of chronic viral infections, cancer and the preservation of protective immunity.[–,–] This perspective in turn is complemented by reviews that outline the particular role of antigen receptors and other facets such as cytokines and fat metabolism in control of memory generation and maintenance.[–] Perhaps not surprisingly, the diverse dimensions of immunological memory are expounded by more reviews for $CD8^+$ T cells[–,–,] than those devoted to additional T- cell subsets[,,,] or B cells.[,,–] We assume this to be more the result of the collective research attention (what one might call "herd immunology") than the importance of any one cell type in immunological memory and host protection.

Yet another organizing principle for the presentation of the articles in this volume is the preferred temporospatial context explored for immunological memories. An emphasis on anatomic niches such as primary and secondary lymphoid organs,[,] non-lymphoid tissues including tumors[–] is accompanied by temporal considerations that range from details of T- and B-cell memory generation and maintenance[–,,,,] to evolution at large.[,] Altogether, we agree with the conclusion proposed in the introductory review; that immunologic memory is best conceived of as a multi-dimensional concept with physical correlates in far more components of the adaptive and innate immune system than previously appreciated.

We thank *Immunological Reviews* for providing us the opportunity to organize this issue and for all of their assistance in bringing to fruition its publication. Most of all we thank authors for their contributions to this diverse, wide- ranging, and occasionally provocative collection of expert perspectives. We hope they will stimulate future and animated discussions about the nature, importance, limitations, and practical relevance of immunological memory as well as its diagnostic, prophylactic, and therapeutic exploitation.

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