# B Cell Lineages and Immunologic Memory

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Immunologic memory was originally defined in terms of the *in situ* anamnestic response that occurs when an individual re-encounters an antigenic stimulus. As the development of *in vitro* and adoptive transfer methods enabled identification of the cells participating in memory responses, however, a subtle redefinition occurred and immunologic memory came largely to mean the presence of such "memory" cells in a stimulated animal, regardless of whether they were detected *in situ* (by production of an anamnestic response), in vitro, or in a secondary host.

The importance of the ambiguity introduced by this redefinition became clear in later studies which showed that the presence of memory B cells and T cells is necessary but not sufficient for an anamnestic response. These findings, reviewed comprehensively in the first volume of Annual Reviews of Immunology (1), demonstrate the existence of an "epitope-specific" regulatory system that often blocks the *in situ* expression of memory cells whose activity is readily demonstrated in adoptive and in vitro assays. The cellular basis for this epitope-specific regulation has yet to be defined; however, the cells involved clearly "remember" previous antigenic stimulation. Thus, the immune system must contain at least one more functional memory cell than is currently recognized.

The recognition of a second B cell lineage introduces another level of complexity to the definition of immunologic memory, particularly with respect to memory B cells. Until the recent discovery of the Ly-1 B cell lineage, all antibody responses were thought to derive from (what we now call) conventional B cells, which rearrange and differentiate continually from Ig negative progenitors in the bone marrow and are relatively short-lived unless they encounter antigen and are triggered to differentiate further to long-lived memory B cells. By and large, these are the self-replenishing, easily transferred memory cells that produce the high affinity IgG1 and IgG2a anti-hapten responses (e.g., anti DNP, anti NP) from which so much of our information about B cell memory development and expression is derived.

Ly-1 B lineage cells have certain properties in common with these memory cells in that they are also long-lived and self replenishing; however, as the evidence summarized below demonstrates, the Ly-1 B cells are phenotypically and functionally distinct from conventional B cells (2-5). Furtherrmore, they have a unique developmental pathway that results in their repertoire being defined early in life and maintained thereafter without the influx of newly rearranged Ig genes (5-7).



F. Melchers et al. (eds.), *Progress in Immunology*

# B Cell Lineage Characteristics

| | Ly-1 B | Conventional B |
|---|---|---|
| Ontogeny | Arise first | Arise later |
| Main location | Serosal Cavities (peritoneal, pleural) | Lymphoid Organs |
| Adult population | Self-replenishing (no new entrants) | Constantly being renewed |
| Adult source for adoptive transfer | Mature Ly-1 B (PerC) | Ig- progenitors (BM, spleen) |
| Developmental regulation | Feedback inhibition by mature Ly-1 B | unknown |
| Development impaired | Xid (CBA/N) | me $^{v}$ (motheaten) $\mu$ transgenic |
| Phenotype: | | |
| IgM | high | low |
| IgD | low | high |
| B220/6B2 | low | high |
| CD5 (Ly-1) | low | negative |
| CD11a (MAC-1) | positive (only in PerC) | negative |
| CD23 (Fce R) | negative | positive |
| Size | large | small |
| Density | low | high |
| Function: | | |
| Serum IgM, IgG3 | +++ | + |
| IgG1 | + | +++ |
| IgG2a, IgG2b | +-++ | ++-+++ |
| IgM autoantibody | +++ | +(?) |
| IgM anti bacterial ab | +++ | +-+++ |
| Anti hapten, anti protein | +(?) | +++ |