Blood cells Part four – Lymphocytes and lymphoid-derived cells

**AUTHOR** Ken Campbell, MSc Clinical Oncology, is clinical information officer, Leukaemia Research Fund (written in a private capacity).

This article, the fourth in this series on blood cells, describes lymphocytes and lymphoid-derived cells. Along with granulocytes and monocytes, lymphocytes are part of the immune system.

**Immune response**
Granulocytes and monocytes form the innate immune system that acts against invading organisms but has no memory. Lymphocytes and lymphoid-derived cells are the key players of the adaptive immune system. This learns from encounters with invading organisms enabling it to take action quickly on re-encountering a previous challenge.

The adaptive immune system has a slower response to a novel challenge than the innate immune system. It must be primed by an initial encounter and can then generate memory cells that trigger a rapid response to the priming antigen. This immunological memory has been shown to persist for more than 50 years (Crotty et al, 2003).

Lymphocytes have surface receptors that can recognise a staggering number of antigenic structures. This is achieved by having components that combine to produce antigen recognition sites. There are several different versions of each component, giving a modular approach that has been estimated to be able to generate some $10^{11}$ structures.

At the genetic level during acquisition of receptors, the lymphocyte must break and rejoin the DNA sequences that code for the antigen recognition sites. This recombination process is unique to lymphoid cells. It is potentially hazardous and most lymphoid malignancies involve translocation of coding. If rejoining is defective and the immune system genes combine with a gene driving cell replication, this may be enough to make the cell malignant.

The majority of lymphocytes are B cells, which are responsible for production of antibodies, or T-cells,
that regulate the immune response and cell-mediated defences against infection and tumour cells. T cells that are capable of killing target cells directly are termed cytotoxic T cells.

A minority of lymphocytes are neither B nor T cells. These were known as null cells but are now called NK cells. They directly kill target cells that express low levels of a surface marker called HLA-11. Such low levels of expression are seen on virally infected cells and on cancer cells. NK cells can attack a target cell on first encounter, so may be thought of as a lymphoid component of the innate immune system.

**B cells**

B cells can recognise and respond to a massive number of antigenic stimuli. They do this by bearing internally produced antigen recognising molecules – B cell receptors – on their surface. Each B cell carries only one specificity of receptor, although there may be many B cell clones sharing the same specificity.

B cells acquire their antigenic specificity before leaving the marrow. On entering the circulation, a B cell seeks out its corresponding antigen – if it does not encounter a matching antigen, it will undergo apoptosis (programmed cell death).

If a B cell encounters a matching antigen, the result depends on whether the antigen is self or non-self (Figs 1-4). If the antigen is recognised as self, the B cell will either self-destruct or be inhibited by regulatory T cells. If the B cell encounters a corresponding non-self antigen, an identical clone is generated. All members of this clone will bind to the same antigen. Most of the clone will become antibody-producing plasma cells; a small number will become long-lived memory cells.

During their typical lifespan of 4-5 days, plasma cells release about 2,000 antibody molecules per second (Hoffbrand et al, 1992). Although B cells do not change their antigenic specificity, they can change the class of antibody they produce in a process called class switching or isotype switching. There are five different immunoglobulin (Ig) types, called IgG, IgM, IgD, IgE and IgA. Different Ig classes have different functions and are secreted at different sites within the body (Parkin and Cohen, 2001).

Antibodies rarely destroy invaders directly. In almost all cases, it acts by binding to the target and triggering attacks on this target by effector cells including neutrophils or other granulocytes, macrophages, T cells and NK cells.

While responding to an antigen, a single B cell can generate an enormous number of antigen-specific progeny. Once the infectious agent is cleared from the body, the antibodies are no longer required and can be cleared from the circulation. This is achieved very simply by ensuring that antibody-producing plasma cells only remain alive if they continue to encounter their matching antigen. Once the antigen has been cleared, the clone of B cells specific to that antigen will be eliminated. The exceptions to this mechanism are memory cells, which remain in the body for many years (Hoffbrand and Pettit 2000).

**T cells**

T cells have a number of roles. They derive their name from the selection/maturaton process they undergo in the thymus (Parkin and Cohen, 2001). They normally constitute about 70 per cent of lymphocytes in the circulation. During an antibody response, numbers of B cells rise rapidly so this may change.

T cells carry antigen recognition complexes on their surface called T cell receptors. There are marked similarities between the structure of B cell receptors and T cell receptors (Marchalonis et al, 1997). Like B cells, each T cell has a single antigen specificity.

A number of functionally distinct subsets of T cells can be defined (Griffin, et al, 2003b).

Helper T cells are normally the major population in circulating blood, while suppressor/cytotoxic T cells predominate in the marrow. Helper and suppressor T cells control the function of B cells and other T cell types by the release of specialised cytokines called lymphokines. Lymphokines are locally acting cell messengers. The dendritic cell may play a role in determining which cytokine is released by the T helper cell, which in turn determines which type of immune response is induced (Banchereau, 2002).

**NK cells**

NK cells are important for clearance of virus-infected cells and tumour cells. Both may evade detection and destruction by failing to show tissue type markers on their surfaces. The NK cell responds to cells seeking to hide identity in this way by attacking and lysing them. T killer cells can only kill in collaboration with other cells and their cell killing capacity is limited by MHC (tissue type) reactions. NK cells can attack and destroy without MHC restriction and can also carry out antibody-dependent cellular cytotoxicity (ADCC), in which any cell coated with antibody is prone to attack and destruction.

**Normal values**

Although B and T cells are usually described separately, they are functionally linked. In most clinical contexts, there is no need to consider subsets of lymphocytes since total number is sufficiently informative. Lymphocytes are:

- Increased – viral infections, toxoplasmosis, whooping cough, brucellosis, and chronic lymphocytic leukaemia;
- Decreased – steroid therapy, marrow infiltration or failure, systemic lupus erythematosus, Legionnaire’s disease, uraemia, Aids and post chemo- or radiotherapy.

In certain situations, such as in cases of HIV infection or lymphoid malignancy, it may be necessary to use special techniques to determine numbers of different subsets of lymphocytes.

**REFERENCES**


Dubuque, IA: W.C. Brown.


This article has been double-blind peer-reviewed.

For related articles on this subject and links to relevant websites see www.nursingtimes.net
### Table 1 Subsets of T cells

<table>
<thead>
<tr>
<th>Subset</th>
<th>Markers</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helper T cell</td>
<td>CD3(+)</td>
<td>Cell mediated immunity</td>
</tr>
<tr>
<td>Th1</td>
<td>CD4(+)</td>
<td></td>
</tr>
<tr>
<td>Th2</td>
<td></td>
<td>Allergic type response</td>
</tr>
<tr>
<td>Treg</td>
<td>CD4+CD25+</td>
<td>May help to inhibit autoimmune responses</td>
</tr>
<tr>
<td>Suppressor/Cytotoxic T cell</td>
<td>CD3(+) CD8(+)</td>
<td>Lyse target cells – regulation of B cell response</td>
</tr>
<tr>
<td>Memory T cell</td>
<td>CD3(+)</td>
<td>Retain immunological memory, enhance future response to rechallenge</td>
</tr>
<tr>
<td>NK cell</td>
<td>CD16(+) CD56(+)</td>
<td>Lymphoid component of innate immune system, lyse cells lacking MHC class I markers</td>
</tr>
</tbody>
</table>

[fig] B lymphocyte
(John please redraw the top image – I have included the lower one as an indication of colours – the central purple one is the lymphocyte)

[fig 2] [John please remove the cartoon faces and make this more serious it can go along or down or in a triangle depending on space – ta terry ]