A Mathematical Model on Germinal Center Kinetics and Termination

Can Keşmir and Rob J. De Boer

We devise a mathematical model to study germinal center (GC) kinetics. Earlier models for GC kinetics are extended by explicitly modeling 1) the cell division history of centroblasts, 2) the Ag uptake by centrocytes, and 3) T cell dynamics. Allowing for T cell kinetics and T-B cell interactions, we study the role of GC T cells in GC kinetics, GC termination, and B cell selection. We find that GC T cells play a major role in GC formation, but that the maintenance of established GC reactions requires very few T cells only. The results therefore suggest that the termination of a GC reaction is largely caused by lack of Ag on the follicular dendritic cells and is hardly influenced by Th cells. Ag consumption by centrocytes is the major factor determining the decay rate of the antigenic stimulus during a GC reaction. Investigating the effect of the Ag dose on GC kinetics, we find that both the total size of the GC and its duration are hardly influenced by the initial amount of Ag. In the model this is due to a buffering effect by competition for limited T cell help and/or competition between proliferating centroblasts. The Journal of Immunology, 1999, 163: 2463–2469.

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finity maturation during the humoral immune response to T cell-dependent Ag occurs in germinal centers (GCs) (1, 2). GCs are specialized environments in the B cell follicle that allow for somatic mutations and extensive proliferation of B lymphocytes (3, 4). Due to high rates of B cell division, somatic mutation, and selection, GCs are highly dynamic environments. Ag is stored in the form of immune complexes on follicular dendritic cells (FDCs). Ag is the main selective agent during a GC reaction because (mutated) B cells have to bind Ag to avoid apoptosis (5). This allows for the selection of high affinity B cells. Following Ag-based selection, GC B cells have to perform cognate interactions with GC T cells to increase their survival chance (6, 7). As the GC T cells are specific for the Ag driving the GC reactions (8, 9), this cognate interaction may represent a check on the correct Ag specificity of the (mutated) B cells.

To initiate a GC reaction, B cells present Ag to the activated T cells surrounding the follicle (10). The initial dependence of a GC reaction on T cell help continues well after GCs are established. Interference with the cognate interaction between GC T and B cells disturbs the GC reaction (11–15). The administration of Abs against CD40 ligand (CD40L, which is expressed on activated T cells) disrupts an established GC reaction (12–14). GC T cells play a significant role in the selection of GC B cells (7, 16, 17). For example, it was shown that the somatic mutation patterns of hapten specific B cells depend on carrier proteins that was used (18). The in vivo expression of CD40L is transient at the site of the cognate interaction (16); i.e., CD40L+ B cells induce down-modulation of CD40L on activated T cells. This suggests that CD40L+ T cells trigger a particular cognate B cell and then are not able to stimulate other B cells.

We extend previous mathematical models of GC reactions with GC T cells and with the Ag uptake by centrocytes. This enables us to study the factors controlling the termination of GC reactions, an aspect that was excluded from earlier models (19–23). Termination is an important issue and is a difficult question to address experimentally (24). Our model accounts for the kinetics of a primary and secondary (or carrier primed) GC reaction and accommodates most available data on GC reactions. Focusing on GC kinetics, rather than on affinity maturation, we show that 1) the main effect of T cells on GC kinetics is confined to the early phase of the GC reaction, 2) the duration of the reaction is largely determined by Ag availability and hardly by the availability of T cell help, and 3) both the Ag dose and the half-life of immune complexes have a negligible effect on the GC kinetics.

The Model

The model describes the dynamics of a single GC as illustrated in Fig. 1 and translated into a mathematical model in the Appendix. The first stage in a humoral follicular immune response is a rapid expansion in the number of B blasts from 3–5 seeder cells to more than 10^4 cells within 3 days (25, 26). Once the B blasts have filled the FDC network, they start to differentiate. A certain fraction (i.e., the centroblasts) stays in the cell cycle, down-regulates their surface Ig, and creates the dark zone of the GC. The remaining cells (i.e., the centrocytes) move to the opposite pole of the FDC network, re-express their surface Ig, and create the light zone. Centrocytes do not proliferate and die rapidly unless they are “rescued” (see below). For simplification, the model does not differentiate between B blasts and centroblast cells: the simulations start with centroblasts only.

It remains unclear how centroblast proliferation is regulated. Centroblasts do not express surface Ig, and there are very few T cells in the dark zone. Thus neither T cells nor Ag seem a limiting factor for centroblast proliferation in the dark zone. After a certain number of cell divisions centroblasts revert to the centrocyte phenotype (25). GC reactions start oligoclonally (27), and only when the total cell numbers reach a population size of about 10^8 cells (i.e., after ~10 cell division) do the light and dark zones become
are forming conjugates with GC T cells regain centroblast phenotype (30).

The recycling of centrocytes to the dark zone is an assumption essential for our model. Because at the end of the proliferation cascade each centroblast terminally differentiates into a centrocyte, the dark zone in our model is not able to maintain itself in the absence of this source of centrocytes.

Recent data suggest that the memory B cell population is generated throughout the GC reaction (31). Early in the response B cells leave the GC and migrate into other lymphoid tissues; e.g., plasma B cells migrate into the bone marrow (32). Therefore, in our model we allow for an emigration of rescued centrocytes throughout the GC reaction.

Modeling the kinetics of the GC T cells is difficult because little is known about their dynamics. In the first 5 days after immunization, the increase in the number of follicular T cells is due to immigration from the T cell zones. This dependence was shown in experiments where follicular T cells during the first 5 days took up very little 5-bromo-2'-deoxyuridine (BrdUrd) (9, 33). Around day 12 the follicular T cell proliferation reaches its maximum. Despite high proliferation, GC T cells display a gradual increase only (33). This can be due to a high rate of cell death as many apoptotic T cells are found in GCs (9). In our model it is assumed that the proliferation of GC T cells is driven by the Ag presentation by centrocytes. The interaction between centrocytes and GC T cell can be either cognate or be based upon local cytokine secretion (see Appendix). Additionally, GC T cell proliferation may be down-regulated by nonspecific competition for local resources like cytokines and space.

In the human tonsil GC structures form a clear spatial separation of zones of proliferation, hypermutation, and selection (34). Clonal expansion and hypermutation take place in the dark zone and selection occurs in the FDC-rich light zone. This spatial zonation is not essential for our model, however. The model remains valid whenever 1) GC T cells do not regulate centroblast proliferation, and 2) centroblasts do not compete with centrocytes for T cell help. Indeed, in GCs occurring in splenic tissue after immunization with a T cell-dependent Ag, there is no apparent spatial organization (34).

**Results**

The behavior of our model resembles the characteristics of a GC reaction. The simulations are started with only three centroblasts (27). The GC reaction starts around day 5 after immunization (see Fig. 2A), which is in agreement with in vivo data (26). The peak of the GC reaction is reached at around day 12, when the total number of GC B cells reaches a population size of about 7000 cells. This “GC-size” is also within the range of data reported earlier by histological analysis (26).

The parameter values used in the model were tuned within reasonable limits to obtain a realistic model behavior (see Table I). A crucial parameter in the model is the probability $p_r$, with which a rescued centrocyte recycles back to the dark zone. When $p_r = 0$, the influx to the centroblast compartment is zero, and the GC reaction can not be maintained. Once positive, the size, onset time, and duration of a GC reaction is further influenced by the precise value of $p_r$. For example, varying the recycling probability between 0.2 to 0.6 changes the GC size 3-fold. In the latter case the GC reaction starts 2 days earlier and lasts for slightly less than 3 wk. Another effect is visible on the GC production (i.e., on the population size of the memory/plasma cells, $M$). An increase in $p_r$ from 0.2 to 0.6 results in an increase of the GC output by 2-fold.

Several parameter values are not well established experimentally and need further discussion. In the simulations we set the
length of the proliferation cascade to \( n = 10 \) cell divisions. Thus, the centroblast differentiation to the centrocyte phenotype occurs after 10 cell divisions. To obtain our results \( n \) should be large enough, i.e., \( n > 4 \), but need not be 10. For small values like \( n = 2 \), the GC reaction starts very early and burns out rapidly. Note that for \( n > 4 \), and with an average cell division time of \(-6\) h, the centroblasts stay in the dark zone for more than 24 h. The rate of Ag consumption per centrocyte, \( u \), and the saturation constant for FDC-centrocyte complex formation, \( s_A \), are also unknown. Assuming that there are more than 100 FDC per GC, and that a single FDC can bind 3–7 B cells (35), we set the initial Ag concentration \( A(0) = 500 \). The parameters \( u \) and \( s_A \) are then tuned such that the model fits the kinetics of an in vivo GC reaction. In the majority of simulations the competition between proliferating centroblasts is disabled by setting \( s_T = \infty \). Only when studying the effect of the Ag dose on GC kinetics we alter this parameter.

The role of T cells

It has been known for some years that T cells influence the kinetics of a GC reaction. Animals preprimed with a certain carrier develop a GC reaction within \( 36 \) h when immunized with haptons conjugated to the same carrier (25). The follicle response in these animals develops with the same speed and size as is typical for the secondary ant hapten response (25). The major effect of prepriming with a carrier is an increase in the number of carrier-specific T cells. This we simulate in Fig. 2B by a 10-fold increase in the influx of T cells into the follicular area. Indeed this results in a faster and larger GC reaction.

The main set of experiments that suggests a regulatory role of T cells in GC reactions involves the blockage of cognate interactions. When animals are treated with anti-CD40L Ab at day 6 after immunization, all established GC reactions diminish (13). However, soluble CD40-Ig fusion protein (CD40-Ig) injected in the same time window fails to have an effect either on GC formation, or on memory induction (14). Injection of anti-CD40L Ab results in the total blockage of T-B cell cognate interactions, for example, by deleting Ag-specific T cells (13). In the model we simulate anti-CD40L Ab treatment by reducing the formation of T-B complexes.

In Fig. 3A, the dotted line represents the GC-kinetics for a 6-fold increase of the T-B complex saturation constant \( s_T \). The GC reaction terminates soon after the treatment, which is in agreement with the experimental data. Cognate interactions can also be blocked with CD40-Ig protein (14). Because this is probably less efficient than blocking with anti-CD40L Ab, this can be incorporated by increasing \( s_T \) 3-fold (instead of 6-fold). In Fig. 3A, the dashed line shows that this partial blocking with CD40-Ig protein marginally affects the GC reaction. The effect of partial blocking depends on its timing, however (see Fig. 3B). When this treatment is given during the first 2–3 days after immunization, it markedly affects the induction of B cell memory (Fig. 3B). Later treatments have much smaller effects. Thus, the effect of treatments resulting in a partial blockage of the cognate interactions are apparent only when the treatment is given early.

These results suggest that T cells play a major role in the formation of GC reactions, and that their role decreases once the GC

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### Table 1. Initial conditions and parameter values

<table>
<thead>
<tr>
<th>Parameter or Initial Condition</th>
<th>Value</th>
<th>Ref.</th>
</tr>
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<tbody>
<tr>
<td>Number of seeder cells per GC ((B_0(0)))</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Initial number of immune complexes on FDCs ((A(0)))</td>
<td>500</td>
<td>35</td>
</tr>
<tr>
<td>Maximum proliferation rate of centroblasts ((\mu))</td>
<td>4 day(^{-1})</td>
<td>25</td>
</tr>
<tr>
<td>Maximum rate at which centroblasts differentiate to centrocytes ((d))</td>
<td>2 day(^{-1})</td>
<td>25</td>
</tr>
<tr>
<td>Length of the centroblast proliferation cascade ((n))</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Maximum apoptosis rate for centrocytes ((\delta_c))</td>
<td>3 day(^{-1})</td>
<td>41</td>
</tr>
<tr>
<td>Death rate of centroblasts ((\delta_b))</td>
<td>0.8 day(^{-1})</td>
<td>42</td>
</tr>
<tr>
<td>Maximum proliferation rate of GC T cells ((\rho))</td>
<td>2 day(^{-1})</td>
<td>33</td>
</tr>
<tr>
<td>Death rate of GC T cells ((\delta_T))</td>
<td>0.8 day(^{-1})</td>
<td>33</td>
</tr>
<tr>
<td>Average lifetime of immune complexes on FDCs ((1/c))</td>
<td>50 days</td>
<td></td>
</tr>
<tr>
<td>Saturation constant for centrocytes binding FDC ((s_A))</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>Saturation constant for centrocyte-T cell interaction ((s_T))</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Consumption of antigen per centrocyte-FDC complex ((n))</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Influx of T cells to a GC ((\sigma))</td>
<td>5 day(^{-1})</td>
<td>33</td>
</tr>
<tr>
<td>Probability of recycling ((p))</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Constant for density dependent centroblast proliferation ((K_b))</td>
<td>(10^4, 10^3, \infty)</td>
<td></td>
</tr>
<tr>
<td>Constant for density dependent T cell proliferation ((K_T))</td>
<td>100, (\infty)</td>
<td></td>
</tr>
</tbody>
</table>
reaction is established. This behavior can be explained by the following argument. The GC T cell dynamics affect the number of centrocytes that get rescued, and with that the influx of B cells into the dark zone. Initially, there is a limited number of centroblasts in the dark zone that are expanding by vigorous proliferation. As long as centroblast numbers are low, an increase by the recycling of centrocytes has a strong affect. Once the GC reaction is established, however, the impact of the T cell-dependent recycling becomes small compared to the vigorous proliferation of the large centroblast population. This effect becomes even stronger if the centroblasts compete for nonspecific factors: supplying more centroblasts by the recycling of centrocytes will only intensify the competition. Note that this argument applies to the effects on the GC size only: if affinity selection were the issue, the recycling of rescued centrocytes would remain important throughout the GC reaction (19).

**Dynamics of immune complexes on FDCs**

Centrocytes need the Ag available on FDCs both for being rescued and for presenting Ag to the GC T cells. We study how the GC kinetics is influenced by the dose of Ag and by the half-life of immune complexes on FDCs. Remember that the initial number of immune complexes on FDCs was assumed to be proportional to the initial dose of antigen.

The immune complexes on FDCs decay by “natural” decay, (i.e., each immune complex has an expected half-life) and due to the internalization by centrocytes. In our model the latter is numerically most important. This is shown in Fig. 4A, where we compare a system with no Ag consumption by centrocytes (i.e., the solid line) with one where Ag is taken up from FDCs by centrocytes (i.e., the dashed line). The GC reaction lasts much longer in the former case. In the presence of Ag consumption by centrocytes the half-life of the immune complexes on FDCs barely affects the duration of a GC reaction. In Fig. 4B the dashed, solid, and dotted lines correspond to simulations where the average life-span of immune complexes is 500 days (z = 0.002); the solid line is for an average life-span of 50 days (z = 0.02) and the dotted line is for an average life-span of 20 days (z = 0.05).

The Ag dose is another parameter that might affect the GC kinetics. Experimental in vivo data suggest that the GC kinetics is fairly independent of the initial number of immune complexes bound to the FDCs (36). Fig. 5 depicts simulations with two different antigen doses: 500 and 5000 (see the solid and the dashed lines, respectively). The higher the Ag availability on FDCs, the more centrocytes receive rescue signals from the FDC. The GC duration is hardly affected by the Ag dose, however, because large number of centrocytes consume the Ag faster (see Fig. 5, C and D). If T cell help remains limiting (Fig. 5A), only a small fraction of the Ag-presenting centrocytes get rescued to recycle. This results in a GC that is only slightly larger than the GCs during a low dose response. If, on the other hand, T cell help is not limiting (which can be realized by setting $K_T = \infty$), almost all of Ag-presenting centrocytes are rescued and recycle to the dark zone. Even allowing for competition between proliferating centroblasts (e.g., $K_B = 10^3$, see Fig. 5B dotted lines), this results in several-fold increase in GC size. Obviously, it is possible to limit the GC size, by making centroblast competition stronger (e.g., $K_B = 10^5$, see Fig. 5B dashed line). Having similar numbers of centrocytes, however, the Ag competition remains normal and hence for higher Ag dose we observe GC kinetics and sizes when the Ag dose is high can be explained by 1) larger number of Ag-presenting centrocytes and therefore faster consumption of Ag, and 2) the competition for cognate interaction with a limited population of T cells.

**Duration**

In our model the termination of a GC reaction is determined by the availability of Ag. When Ag vanishes, the first survival signal of
centrocytes decreases. Consequently too few centrocytes get rescued, which reduces the influx to the dark zone such that the GC reaction eventually terminates.

To study the effect of the GC T cells on the duration of a GC reaction, we relax the T cell-based selection by increasing the maximum number of T cells per GC 10-fold; e.g., by setting $K_T = 1000$. When T cells are nonlimiting, all centrocytes that interact with FDCs also receive the second survival signal. This causes an increase in the GC size (to $\sim 7$-fold), because more rescued centrocytes recycle back to the centroblast compartment. As was demonstrated above, a larger GC rapidly consumes the available Ag and therefore lasts for a shorter time (results not shown). This result is interesting because it opposes the view that GC T cells can be crucial in determining GC termination (24).

Discussion

We have developed a new model for GC reactions allowing for GC T cells and their regulatory effects. To address the issue of GC termination, we explicitly modeled the cell division history of centroblasts and the Ag uptake by centrocytes. The model has many characteristics of a GC reaction and allows us to study the regulation of GC duration, the dynamics of GC B cells in different Ag doses, and the effect of GC T cells during the different phases. Focusing on the kinetics of a GC reaction, the results suggest that the duration of a GC reaction depends largely on Ag availability, but hardly on parameters such as the Ag dose and the half-life of immune complexes (see Figs. 4B and 5). The size of a GC reaction and the availability of T cell help affect GC duration in such a way that the kinetics remain similar for a wide array of Ag parameters. T cells play a major role at the onset of the GC reaction (Fig. 2B); later very few T cells suffice to maintain a GC reaction. This is because during the later stages of the GC reaction, there are sufficient centroblasts to keep the GC going.

The reason why the termination of a GC reaction depends largely on the availability of Ag, and hardly on T cell help, has to do with the order of the survival signals and the proliferation of the GC T cells. The order of the survival signals does not allow the centrocytes to interact with T cells before they have bound, and taken up, Ag on the FDCs. Thus, when the Ag availability is low, the first survival signal is limiting, and most centrocytes die rapidly by apoptosis even before they can interact with T cells. When, on the other hand, Ag availability is high, GC T cells are also not limiting because they proliferate in response to the Ag presented by centrocytes.

Vora et al. (36) demonstrated that the GC kinetics, and affinity maturation, stay intact if the number of immune complexes bound to FDCs is increased on average 10-fold. Based on these observations, the authors suggest that the selection of B cells does not depend on the amount of Ag available. In contrast to this suggestion, we have demonstrated that in a model that is based on Ag-driven selection, the kinetics of GC reactions remain quite similar for a wide range of Ag doses (see Fig. 5). In our model, it is mainly the size of the GC reaction that is influenced by the initial Ag load. However, due to competition for a limited number of T cells, even the size of the GC reaction changes less than proportional with the Ag dose.

The results of our model suggest a correlation between the half-life of the immune complexes on FDCs with the GC size but not with the GC kinetics (Fig. 4B). In an earlier study, however, it was suggested that GCs induced by viral proteins terminate later than hapten-induced GCs, because viral proteins create immune complexes that persist longer on FDCs (37). This view is not generally accepted, however. A recent study suggests that hapten-induced GCs can also persist over long times. At the later phases they just become too small to be detected by histological methods (31).

Our results suggest that once GCs are formed, only a few T cells are required to keep a GC reaction going. GC T cells play a crucial role in GC formation only, which is in agreement with some in vivo observations. For example, Bachmann et al. (37) reported persistent GC reactions at a time when very few Ag-specific T cells are left in the follicles. Moreover, in persistent GCs, e.g., in the human tonsil, the frequency of proliferating T cells is very low (2).

The obvious continuation of this project is to study the effects of the (evolving) B cell repertoire on the GC kinetics. Our current results suggest that the major differences are to be expected when high affinity centrocytes pick up more Ag from the FDCs than low affinity centrocytes can. One possibility is that the kinetics and size of any GC is likely to be influenced by the “BeR repertoire” it contains. As yet, there seem to be no data supporting this speculation. GCs seeded by low, or by high affinity, cells show no detectable differences in size or kinetics (38, 39).

Appendix: Model Equations

The interactions described in the Model section and in Fig. 1 can also be described by the following system of differential equations:

\[
\frac{dC}{dt} = dpB_n + \mu C.
\]

\[
\frac{dC*}{dt} = \mu C_A - \mu C^*.
\]

\[
\frac{dM}{dt} = (1 - p_n)\mu C_A.
\]

\[
\frac{dT}{dt} = \sigma + p\alpha C_T - \delta T.
\]

where the complexes of centrocytes with FDCs and of rescued centrocytes with T cells are described by

\[
C_A = \frac{CA}{s_A + A}
\]

and

\[
C_T = \frac{CT}{s_T + C^*}
\]

respectively. The $\alpha_n$ and $\alpha_T$ terms are density dependent “expansion terms” defining nonspecific resource competition within the centroblast, and within the GC T cell compartment, i.e.,

\[
\alpha_n = \frac{K_n}{K_n + \sum_{i=0}^{n} B_i}
\]

\[
\alpha_T
\]
and

$$\alpha \tau = \frac{K_T}{K_T + T}. \quad (11)$$

Thus centroblasts move through the proliferation cascade at rate $\rho$, maximally yielding one new cell per round of cell division, i.e., in the absence of competition when $\Sigma B_i < K_B$, the expansion term $\alpha \tau = 1$. Similarly, the GC T cells reduce their proliferation rate at high T cell numbers, i.e., their proliferation is halved when $T = K_T$. In our simulations we may switch off the competition by setting $K_B$ and/or $K_T$ to infinity.

Equations 1 and 2 describe the dynamics in the proliferative compartment, i.e., the dark zone. The variable $B_i$ represents the number of centroblasts that has been through $i$ cell divisions. Equation 1 defines the dynamics for centroblasts that have not divided yet. The first term in both equations gives the influx. The $B_i$ population is increased by $B_{i-1}$ cells (see the $pB_{i-1} (1 + \alpha \theta)$ term). The $B_0$ equation is populated by a fraction of the rescued centrocytes (see the $p\rho C^*\theta$ term). A centroblast $B_i$ completes cell division at a rate $\rho_i$ depending on the nonspecific competition, $\alpha \theta$, this may succeed in two cells at the $B_{i+1}$ stage. After $n$ cell divisions, i.e., when the proliferation cascade is complete, a centroblast differentiates to a centrocyte. Centroblasts die at rate of $\delta \tau$ per day.

We denote unselected centrocytes by $C^*$, Ag-presenting centrocytes by $C_A^*$, complexes of centrocytes with FDCs by $C_A^*$, and complexes of Ag-presenting centrocytes with T cells by $C_T^*$. Equations 3 and 4 describe the centrocyte dynamics. The unselected centrocytes are populated by centroblasts that have made $n$ divisions, i.e., by the $dpB_n \theta$ term. The centroblasts gain centrocyte phenotype at rate $d$. Both unselected centrocytes and Ag-presenting centrocytes disappear with rate $\mu$ due to the formation of complexes with FDCs or T cells or due to apoptosis. We assume the following reaction for the formation of the centrocyte-FDC complex:

$$C_F + A \rightleftharpoons C_{AF}.$$ 

Here $C_F$ denotes the free centrocytes and $C_A$ denotes the centrocytes in complex with FDC. Equation 8 is derived by applying the classical Michaelis-Menten approximation to the above scheme, i.e., by assuming that 1) $C_F$ can be regarded as in equilibrium, and 2) by the conservation $C = C_F + C_A$. The parameter $s_2$ is the Michaelian saturation constant. While in complex with FDC each centrocyte may succeed in two cells at the $B_{i+1}$ stage. B cells that manage to form complexes with Ag-presenting centrocytes proliferate at a maximum rate $p$. At high GC T cell numbers the proliferation rate may decrease. GC T cells die at a rate of $\delta \tau$ per day.

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**References**

25. Liu, Y. J., J. Zhang, P. J. Lane, E. Y. Chan, and I. C. MacLennan. 1991. Sites of...


29. Casamayor-Palleja, M., M. Khan, and I. C. MacLennan. 1995. A subset of CD4+ memory T cells contains preformed CD40 ligand that is rapidly but transiently expressed on their surface after activation through the T cell receptor complex.


