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Review

Neutrophils and macrophages work in concert as inducers and effectors of adaptive immunity against extracellular and intracellular microbial pathogens

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ABSTRACT

Emerging data suggest new facets of the concerted participation of neutrophils and macrophages in antimicrobial immunity. The classical view is that DCs and macrophages are the inducers of adaptive antimicrobial immunity, but there is evidence for neutrophil participation in this task as cytokine and chemokine producers and APCs. On the other hand, the concept that the T_H1 response is only associated with control of infections by intracellular pathogens through activation of macrophages by IFN-γ, and the T_H17/IL-17 axis is only involved in protection against extracellular pathogens through mobilization and activation of neutrophils is simplistic: There is evidence suggesting that T_H1 and T_H17 responses, separately or in parallel, may use macrophages and neutrophils against infections by extracellular and intracellular microbial pathogens. Opsonization by pathogen-specific Igs enhances the antimicrobial capabilities of neutrophils and macrophages in infections by extracellular and intracellular microbes. The functional partnership between macrophages and neutrophils as inducers and effectors of adaptive antimicrobial immunity conforms to their affiliation with the myeloid phagocyte system and reveals a strategy based on the concurrent use of the two professional phagocytes in the adaptive defense mechanisms. Starting from a common myeloid precursor in the bone marrow, macrophages and neutrophils split during differentiation but come together at the infectious foci for a cooperative strategy that uses modulator and effector activities to attack invading microbial pathogens. *J. Leukoc. Biol.* 87: 805–813; 2010.

Introduction

When microbial pathogens pass epithelial defenses and invade normally sterile body territories, they encounter innate defense mechanisms that are activated directly by pattern recognition receptors with broad specificities for conserved and invariant molecules of microbial origin [1]. Innate immunity is crucial for controlling a primary infection but is frequently insufficient to overcome the virulence mechanisms of pathogens, and adaptive immunity is put to work. In the adaptive immune response, the antimicrobial defense mechanisms are activated indirectly by T cells and antibodies in an antigen-specific manner. Adaptive immunity responds to pathogen invasion through antigen-specific clonal expansion of a selected number of lymphocytes whose antigen receptors bind microbial antigens in the context of MHC. Naive T cells differentiate into $CD4^+$ T_H cells, which recruit and activate effector phagocytic cells that cooperate in pathogen clearance, and provide help for differentiation of antigen-specific B cells into antibody-producing plasma cells and memory B cells. Some naive T cells also differentiate into memory cells that trigger future defense against repeated attacks by the same pathogen.

The present review highlights data favoring the interpretation that the host defenses use neutrophils and macrophages as inducers and effectors of the adaptive antimicrobial immune responses to infection by extracellular and intracellular pathogens.

NEUTROPHILS CLUSTER WITH MONOCYTES/MACROPHAGES AT INFECTIOUS FOCI DURING ADAPTIVE IMMUNITY

The small number of phagocytes in resting tissues is essentially composed by resident macrophages and DCs, but following microbial invasion, neutrophils and monocytes are recruited quickly to infectious foci. Recruited monocytes give rise locally to a subset of DCs [2] and to inflammatory macrophages [3].

Recruitment of neutrophils and monocytes/macrophages has been analyzed mainly in the initial phases of the antimicrobial innate immune response when infectious inflammation is triggered early after pathogen invasion. When innate immune defenses fail to clear the infection, phagocytes continue to be recruited during the adaptive antimicrobial responses. In

Abbreviations: BCG=bacillus Calmette-Guérin, DC=dendritic cell

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adaptive immunity associated to previous immunization (in secondary infections or in vaccinated hosts), fresh phagocyte recruitment is triggered quickly and intensely upon detection of invading pathogens.

Neutrophil and monocyte/macrophage accumulation is consistently present at infectious foci in adaptive responses to extracellular (see, for example, refs. [4–6]) and to intracellular pathogens. Occurrence of persistent neutrophilia in infections by intracellular pathogens was a novel and surprising finding and was reported initially in mouse experimental mycobacterioses [7]. Following i.p. inoculation of pathogenic mycobacteria in mice, the initial innate neutrophil response is continued by persistent neutrophil accumulation, which is a facet of adaptive immunity [8], being antigen-specific and mediated by $CD4^+$ and $CD8^+$ T cells [8, 9]. In accordance with the acquired character of this neutrophilia, it is enhanced in mice immunized with *Mycobacterium bovis* BCG before *Mycobacterium avium* challenge [8]. Also, in *Mycobacterium tuberculosis*-infected guinea pigs, previous *M. bovis* BCG immunization results in increased secretion of the neutrophil chemoattractant CXCL8 by alveolar macrophages [10]. The persistent peritoneal neutrophil recruitment observed in mice infected with mycobacteria is accompanied by monocyte/macrophage accumulation [8, 9]. More realistic conditions mimicking natural situations in terms of inoculum dose and infection routes also revealed persistent neutrophil influxes associated with accumulation of monocytes/macrophages in *M. tuberculosis*-infected mice [11]. Recruitment of neutrophils and monocytes/macrophages during adaptive immune responses has also been described in experimental infections by natural routes with the intracellular pathogens *Salmonella* [12] and *Toxoplasma gondii* [13]. The peritoneal influx of neutrophils and monocytes/macrophages following inoculation of *Listeria monocytogenes* in immunized mice is increased as compared with that in nonimmunized controls [14]. Also, in prolonged mouse aerogenic infection by a low dose of *M. tuberculosis* T_H cells, macrophages and neutrophils are clustered persistently in the lungs [11]. Pleurisy as a result of *M. tuberculosis* is a good model for evaluating leukocyte dynamics during protective adaptive immune responses to intracellular pathogens in humans, as it can be self-cured through a T_H response [15]. Pleural exudates of patients with tuberculous pleurisy contain T_H cells, macrophages, and neutrophils [16], showing that the leukocyte dynamic described in animal models of adaptive immune responses also occurs in humans.

These data indicate that neutrophils and monocytes/macrophages are recruited to and cluster at infectious sites during adaptive responses against extracellular and intracellular pathogens. This clustering promotes the concerted participation of neutrophils and macrophages at the inducer and effector phases of adaptive antimicrobial immune responses, as discussed below.

NEUTROPHILS COOPERATE WITH DCS AND MACROPHAGES IN THE INDUCTION OF ADAPTIVE IMMUNE RESPONSES

The classical view is that antigen presentation and induction of T_H cells are tasks performed by DCs and macrophages [17]. However, accumulating data show that neutrophils cooperate with macrophages and DCs in the induction of protective antimicrobial adaptive immunity.

Activated neutrophils play a key role in initiating adaptive immunity by producing important proinflammatory cytokines and chemokines that attract monocytes and immature DCs [18, 19]. Human neutrophils induce IL-12 production by DCs and therefore, may trigger T_H1 polarization indirectly [20]. Moreover, IL-12 is also secreted by human neutrophils in response to infection [21, 22]. Neutropenia induced in mice at an early stage of infection with *Legionella pneumophila* inhibited the development of the T_H1 response [23]. Moreover, neutrophils play a role during T_H17 cell differentiation through the production of IL-6, IL-1β, and IL-23 [21, 24, 25].

Neutrophils shuttle intracellular pathogens to lymph nodes [26, 27] and deliver microbial antigens, including from intracellular pathogens, to macrophages and DCs, thus helping in the cross-presentation of microbial antigens to T_H cells [28–30]. Human neutrophils can be induced to express MHC class II molecules in vitro [31, 32] and in vivo [33, 34] and to present microbial antigens directly to T cells [28, 32]. Moreover, neutrophils induce T_H1 cell proliferation and IFN-γ secretion [35].

Another relevant contribution of mouse and human neutrophils for the development of adaptive immune responses involves the secretion of cytokines and chemokines that mobilize T_H1 and T_H17 cells from lymphoid organs to infectious foci. Among those chemokines are inducible protein 10 (CXCL10), monokine induced by IFN-γ (CXCL9), and IFN-γ-inducible T_H cell α chemoattractant (CXCL11), which attract T_H1 cells [21, 36, 37]. These cells predominantly express the chemokine receptors CXCR3 (which binds CXCL9, -10, and -11) and CCR5 (which binds CCL3) [36, 38]. On the other hand, human neutrophils also attract T_H17 cells by secreting CCL20 [37]. Significantly, secretion of CCL2 by human neutrophils may attract T_H1 and T_H17 cells [37], promoting their common presence at infectious foci.

Besides cytokines and chemokines, neutrophils also use proteins released through degranulation to induce the recruitment and maturation of DCs [39–41]. Moreover, neutrophil granule proteins, such as LL-37 [42] and defensins [39, 43], also induce recruitment of T_H cells to infectious foci. Lactoferrin induces recruitment of naive T cells [40] and stimulates the secretion of IL-12 by macrophages [44].

In conclusion, the above reviewed data show that several tasks related to the induction of adaptive immune responses classically attributed to macrophages and DCs are also performed by mouse and human neutrophils, namely: antigen presentation to naive T cells; induction of T_H 1 cell differentiation, proliferation, and mobilization to infectious foci and induction of IFN-γ secretion by these cells; and induction of T_H17 cells and mobilization of these cells to infectious foci.

NEUTROPHILS COOPERATE WITH MACROPHAGES AS EFFECTORS OF ANTIMICROBIAL ADAPTIVE IMMUNITY

Adaptive immunity uses innate effector mechanisms mediated by macrophages and neutrophils

The occurrence of a protective role of neutrophils in adaptive immunity has been supported by results from depletion exper-

iments with mice infected with the extracellular pathogens *Bordetella pertussis* [45, 46], *Helicobacter pylori* [6], and *Streptococcus pneumoniae* [47] or with intracellular pathogens such as *Francisella tularensis* [48], among others.

Moreover, adequate depletion experiments demonstrated the dual participation of macrophages and neutrophils in adaptive immune responses to infection by extracellular or intracellular pathogens. Mice immunized previously by infection with *S. pneumoniae* use macrophages and neutrophils to clear a secondary infection [47]. This protective participation of the two professional phagocytes was confirmed by selective neutrophil or macrophage depletion. Selective depletion of macrophages or neutrophils also inhibited adaptive protection in mice infected with *F. tularensis* [48].

An indication that neutrophils and macrophages are necessary for an efficient host defense against infection is the fact that they are not able to replace each other as crucial elements of antimicrobial immunity, as shown by the serious pathology associated with some human and murine phagocyte deficiencies [49].

Besides elimination by phagocytosis, professional phagocytes participate as effectors in host adaptive antimicrobial defense through direct macrophage/neutrophil cooperation for the control of intramacrophage pathogens, as observed in mouse models of infection [7, 50, 51] and with human phagocytes in vitro [52]. This cooperation enhances the limited antimicrobial capabilities of macrophages [53], including through the transfer to macrophages of potent neutrophil antimicrobial molecules [7, 52]. Moreover, neutrophil granule molecules enhance macrophage phagocytic activity [54].

Classical view of the roles of antimicrobial phagocytic effector mechanisms dependent on T_H cells

In mammals, antigen-carrying cells migrate to lymphoid organs, where they interact and present antigen to conventional, naive $\alpha\beta$T cells, leading to the differentiation into T_H cells (reviewed in refs. [55, 56]). Besides the classical T_H1 and T_H2 cells [57], T_H17 cells constitute a third subset described recently with relevant functions in adaptive immunity in mice and humans [58–60]. Whereas T_H2 cellular response is classically associated to eosinophils, basophils, and mast cells and their activities against helminths (reviewed in ref. [61]), T_H1 and T_H17 are the relevant subsets for directing the activation of phagocyte antimicrobial effector mechanisms.

The IL-12/IFN-γ axis is crucial for host defenses by activating adaptive immunity to kill pathogens and infected cells through induction of T_H1 cells. IL-12 is the main cytokine produced in response to infection by macrophages, DCs, and neutrophils to induce production of IFN-γ by T_H1 cells [22]; IFN-γ feeds back to infected macrophages to enhance their antimicrobial capacities [62–64]. This module of adaptive immunity is classically associated with the control of infections by intracellular pathogens in mammals [64, 65].

T_H17 cells of mice and humans are not identical in terms of cytokine production [66], but in both cases, they secrete the IL-17 family of proteins [59, 60, 66]. This family includes several related cytokines with some specialization in terms of participation in antimicrobial defense and in the induction of pathology [67, 68].

Differentiation of mouse T_H17 cells requires TGF-β and IL-6, whereas human, naive T cells develop into T_H17 cells in the presence of IL-1β, IL-23, and possibly TGF-β (reviewed in ref. [69]). These cytokines are produced by several nonimmune and immune cells including macrophages, DCs, and T cells [70] and also by neutrophils [21, 24].

Interestingly, IL-17 is also produced by activated mouse neutrophils [71, 72], providing these phagocytes with a mechanism to increase and sustain their own presence at infectious/inflammatory sites during adaptive immune responses.

IL-17 has protective effects in controlling the infectious process during adaptive immunity [73]. Classically, T_H17 cells and IL-17 have been involved in protection against extracellular pathogens [73, 74].

IL-22 [75] and IL-17, secreted by activated T_H17 cells, mobilize neutrophils. With IL-17, this effect results from indirect expansion of neutrophil numbers through regulation of G-CSF and by recruitment through induction of CXCL1, CXCL2, and CXCL8 by several mouse and human cell types, including epithelial and endothelial cells and macrophages [70, 76, 77]. Human neutrophils can also be recruited directly through the secretion of CXCL8 by activated T_H17 cells; furthermore, these cells can activate neutrophils and reduce their apoptosis by an IL-17-independent mechanism involving secretion of GM-CSF, TNF-α, and IFN-γ [37].

New scenarios in the contributions of T_H1 and T_H17 responses to antimicrobial defenses

The above concepts evolved before the recognition of the surprising plasticity of T_H cell development, and several recent results reviewed below suggest that the association of the T_H1 response to macrophages and of the T_H17 response to neutrophils is not strict.

(i) As mentioned above, neutrophils and macrophages are recruited to and cluster at infectious sites during adaptive immune responses to infection in mammals. Characterization of the cells involved in these responses revealed that antigen-specific phagocyte accumulation in adaptive immunity is dependent on T_H cells in infections by extracellular [78, 79] or intracellular [80] pathogens.

Through the secretion of IFN-γ, TNF-α, and ELR^+ CXC chemokines, the T_H1 response attracts and activates mouse and human neutrophils (**Table 1**), enhancing their phagocytic and microbicidal activities, and IFN-γ increases neutrophil survival [79, 90, 91]. IL-1β, IL-6, and IL-23 are produced by mac-

Table 1 Publications Showing that Macrophages and Neutrophils Are Activated by T_H1/IFN-γ and by T_H17/IL-17 Responses

	Activation by T_H1/IFN-γ response	Activation by T_H17/IL-17 response
Macrophages	[62–64]	[47, 58, 81–85]
Neutrophils	[64, 86–89]	[47, 77, 78]

rophages activated by IFN-γ and are involved in the development and expansion of T_H17 cells [92, 93]. The canonical T_H17 cytokine IL-17, which as mentioned above, is typically described as mobilizing and activating neutrophils, also has these activities toward mouse and human monocytes/macrophages (Table 1), which express IL-17R [94].

(ii) T_H1 and T_H17 responses were considered mutually antagonistic previously, but recent data show that they may occur in parallel in humans [95, 96], including in infection [94, 97, 98]. The presence of a common subunit (p40) in IL-12 and IL-23, cytokines associated with the development of T_H1 and T_H17 cells, respectively, and of a shared subunit in their receptors (IL-12Rβ1) [99] may promote parallel T_H1/T_H17 responses.

(iii) Coexistence in the same in vivo microenvironment of T_H1, T_H17, and cells with the ability to secrete IFN-γ and IL-17 concomitantly (T_H17/T_H1 cells [100]) is discussed elsewhere [69, 101]. T_H17/T_H1 cells have been described in vitro after stimulation of human and mouse $CD4^+$ cells with PMA/ionomycin [102] and in inflammatory disorders in mice [103] and humans [100], but they also may occur in infection of human cells in vitro [104, 105]. Moreover, the transition from IL-17-producing T_H17 cells to IFN-γ-producing T_H1 cells in response to IL-12 signaling has also been reported [106–108].

(iv) Some results suggest that the concept considering the T_H1/IFN-γ response only associated with the control of infections by intracellular pathogens and the T_H17/IL-17 axis only involved in protection against extracellular pathogens through mobilization and activation of neutrophils is simplistic. On the one hand, protective T_H17/IL-17 responses have been described in experimental infections by intracellular pathogens such as *L. monocytogenes* [109], *M. tuberculosis* [110–114], *Salmonella* [115, 116], *Mycoplasma pneumoniae* [117], *Cryptococcus neoformans* [118], and *Leishmania donovani* [119]. On the other hand, protective T_H1/IFN-γ responses have been reported in infections by extracellular pathogens in mouse models, including by *Candida albicans* [120], *S. pneumoniae* [121], *Klebsiella pneumoniae* [74], and *B. pertussis* [94, 122], as well as in human infection by *H. pylori* [123]. IL-17 produced by T_H17 cells may induce a protective T_H1 response against intracellular pathogens [113, 119, 124–126].

Taken together, the data reviewed above suggest that the classical dichotomy relative to the contribution of T_H1 and T_H17 responses in the mouse and human antimicrobial mechanisms summarized in the previous section is not absolute. Most relevant is the recognition that T_H1 and T_H17 responses mobilize and activate neutrophils and macrophages and that besides T_H1 and T_H17 cells, T_H17/T_H1 cells may also participate in antimicrobial immune defense. This reveals a strategy of the immune system based on the concurrent use of the two professional phagocytes in the adaptive defense mechanisms against extracellular and intracellular microbial pathogens. The possibility of an antimicrobial immune strategy using—simultaneously or successively—more than one pathway increases the chances of mobilization of macrophages and neutrophils for a cooperative participation, leading to enhanced efficiency of the host defense against infection.

Opsonization by pathogen-specific Igs enhances macrophage and neutrophil antimicrobial capabilities

One mechanism of antibody-mediated antimicrobial activity is opsonization, which improves recognition, ingestion, and killing of microbial pathogens by phagocytes via Ig receptors (FcRs), thus contributing to a more efficient adaptive immune response. FcRs are expressed on human neutrophils and monocytes/macrophages [127], although expression of some FcRs in neutrophils requires previous stimulation by cytokines, including IFN-γ [128, 129]. The antimicrobial capabilities of neutrophils [130] and macrophages [131] are activated by the uptake of pathogens opsonized via FcRs.

Extracellular pathogens, living and multiplying essentially outside of cells, are readily susceptible to phagocytosis by neutrophils and macrophages, provided the antiphagocytic pathogenicity mechanisms of evasion are overcome by the host immune defenses [132]. A crucial mechanism of adaptive host defense against these microbes is opsonization by pathogen-specific antibodies, which allow the host to bypass those evasion mechanisms through the improved use of neutrophils and macrophages [132]. A paradigmatic example of infection by an extracellular pathogen, where protection through adaptive immunity is achieved by cooperative activities of neutrophils and macrophages, is pneumonia as a result of *S. pneumoniae*. In this infection, neutrophils and monocytes/macrophages are recruited to the infected lung [133], and both phagocytes ingest the pathogen [134], which is susceptible to killing by neutrophils [135] and macrophages [136]. The antimicrobial activities of neutrophils [47] and macrophages [137] against this pathogen are enhanced by opsonization by pathogen-specific Igs. Mice immunized by a previous infection with *S. pneumoniae* use macrophages and neutrophils to clear a secondary infection [47].

Conversely, intracellular pathogens promote their entry into macrophages and then evade their antimicrobial activities [138]. For safe entry into macrophages, intracellular pathogens use receptors such as complement receptors and mannose receptor [139, 140] or active penetration [141], thus preventing phagocyte activation and the associated triggering of antimicrobial mechanisms. However, the life cycle of intracellular pathogens includes phases of extracellular location. This occurs when the pathogens transit from one host cell to the next; additionally, some of them may have phases of extracellular residence and multiplication in the host [142], as in human tuberculosis [143]. Antibodies are produced during infections by intracellular pathogens in mice and humans [144, 145], and these microbes can be exposed easily to pathogen-specific Igs when they are outside their host cell. Entry of opsonized intracellular pathogens into macrophages via FcRs switches the intramacrophage niche to a nonpermissive one [131]. Moreover, the occurrence of phases of extracellular residence in the life cycle of intracellular pathogens makes these microbes targets for FcR-mediated phagocytosis by recruited neutrophils, exposing them to enhanced antimicrobial effector mechanisms [130]. Several publications, with data about mice, rabbits, and humans, report on the enhancement of antimicrobial capabilities of macrophages and neutrophils toward intra-

cellular pathogens by antibody-mediated opsonization; examples include *M. bovis* BCG [146], *L. monocytogenes* [147, 148], *F. tularensis* [48, 149], *L. pneumophila* [150], *C. neoformans* [151, 152], and *Histoplasma capsulatum* [153, 154].

In conclusion, the studies reviewed above about the role of antibodies in infections by intracellular parasites resulted in the redefinition of the classical concept that antibody-mediated and cell-mediated immunity are restricted to defense against extracellular and intracellular microbes, respectively. Moreover, those data indicate that neutrophils and macrophages are affected positively by pathogen opsonization with enhancing of protective immune responses to extracellular and intracellular pathogens.

NEUTROPHILS AND MACROPHAGES IN INFECTION-ASSOCIATED TISSUE DAMAGE

A protective role of phagocytes associated to antimicrobial immune responses is dependent on a correct regulation, which directs neutrophils and macrophages to a balanced intervention without promoting significant tissue injury. Infection triggers an inflammatory process, and some degree of collateral tissue damage accompanies adequate infectious inflammation [155]. However, uncontrolled immunity leads to excessive inflammation with ensuing immunopathology. Neutrophils are relevant in infection-induced pathogenic inflammation, as they are mobilized in high numbers and are extraordinarily rich in inflammatory mediators and in proteases and oxidants, which if released in excess, can damage many types of cells with the potential to produce tissue injury [156]. Macrophages also contain tissue-damaging molecules, including several proteases, although to a lesser degree, as compared with neutrophils [157], so they are less important as inducers of inflammation-associated pathology.

T_H1, T_H17, and T_H17/T_H1 cells can participate in pathological inflammatory responses [158–160], but IL-17 cytokines have been described frequently as particularly relevant in neutrophil-dependent inflammatory pathology associated with infection by bacterial [161–163], fungal [120], or protozoan [164] pathogens. Persistent human *H. pylori* gastritis [165, 166] and lung necrotic lesions in active human tuberculosis [167] and in mouse progressive mycobacterial infections [168] are examples where intense neutrophilia is inefficient for clearance of the pathogen and rather a factor contributing to important inflammatory immunopathology.

CONCLUDING REMARKS

The outcome of the presence of a microbe within a host is dependent on the nature of the host–microbe interaction [169]: When such an interaction progresses with advantage to the microbe, an infectious disease ensues, but when the host is capable of mounting an immune response that provides a balanced protection, infection is prevented or controlled. To achieve protection against microbial infections, adaptive immunity uses antigen-specific activation of innate effector mechanisms mediated by macrophages and neutrophils. For this activation, the infected host uses T_H1, T_H17, and T_H17/T_H1 cells induced through activities of not only macrophages and DCs but also neutrophils. Additionally, the scenario that has been emerging is that neutrophils and macrophages are recruited and operate together against extracellular and intracellular microbial pathogens during adaptive responses following mobilization and activation by T_H1, T_H17, and T_H17/T_H1 cells and the help of pathogen-specific Igs (**Fig. 1**). This functional partnership between macrophages and neutrophils as inducers and effectors of adaptive antimicrobial immunity conforms to their affiliation with the myeloid phagocyte system [170] and reveals a strategy based on the concurrent use of the two professional phagocytes in the adaptive defense mechanisms as in innate immunity [170].

Starting from a common myeloid precursor in the bone marrow [171], macrophages and neutrophils split during differentiation [172] to acquire specialized features and come together at the infectious foci for a cooperative strategy to attack invading microbial pathogens.

Data discussed here document the progressively emerging richness of our knowledge of the neutrophil capabilities, which encompass modalities of participation in antimicrobial immune responses, unpredictable not so long ago. It is expected that new neutrophil capabilities will emerge in the future, as research about this fascinating phagocyte progresses, taking advantage of a more open-minded approach to the study of immune mechanisms in antimicrobial defense, revealing new facets of the functional closeness between macrophages and neutrophils and of their joint participation in immune responses.

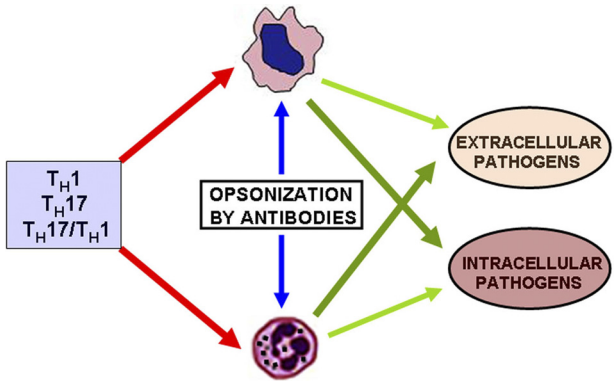

Figure 1. The classical view is that T_H1 and T_H17 responses are relevant against intracellular and extracellular pathogens, respectively, and that neutrophils are the phagocytic effectors against extracellular pathogens, and macrophages are used against intracellular pathogens. However, recent data reviewed here suggest the interpretation that T_H1, T_H17, and T_H17/T_H1 responses operate against the two types of microbial pathogens concurrently using macrophages and neutrophils. Additionally, opsonization by pathogen-specific Igs enhances the phagocytic and antimicrobial capacities of the two professional phagocytes against extracellular and intracellular pathogens.

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