Cancer as an immune dysfunctional disorder: pro-tumor TH1-like and γδ T cells immune response and anti-tumor THαβ immune response based on the complete updated framework of host immunological pathways

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Abstract
The framework of host protective immunological pathways is provided in this article. Clonal anergy is mediated by IgD B cells and γδ T cells. γδ1 T cells are for clonal anergy for food in intestine, γδ2 T cells are for clonal anergy for self-antigens, and γδ3 T cells are for clonal anergy for food metabolites in liver. Host immune responses can be categorized into eradicable immune reactions and tolerable immune reactions. Eradicable immune responses are triggered by follicular helper T cells and include TH1, TH2a, TH2b, TH22, and THαβ. Tolerable immune responses are triggered by regulatory T cells and include TH1-like, TH9, TH17, and TH3. TH1/TH1-like immune reactions are host protective immunities against intracellular micro-organisms (bacteria, fungi, and protozoa). TH2a/TH2b/TH9 immune reactions are host protective immunities against parasites. TH2a is the immunity against endoparasites (helminths). TH2b is the immunity against ectoparasites (insects). TH22/TH17 immune reactions are host protective immunities against extracellular micro-organisms (bacteria, fungi, and protozoa). THαβ/TH3 immune reactions are host protective immunities against infectious particles (viruses and prions). Based on this framework of host immunological pathways, we can find out that pro-tumor immune response is mainly TH1-like immune response and anti-tumor immune response is mainly THαβ immune response. γδ T cells and IgD B cells also play vital roles in clonal anergy for tumor cells. If know that cancer is associated with an immune dysfunctional disorder, we can develop therapeutic strategies to diagnose or treat solid tumors.

Introduction

Host immunological pathways are complicated. Host immune reactions can only recognize pathogens from different locations of our body. Thus, host immunological pathways can react against infectious particles, intracellular micro-organisms, extracellular micro-organisms, parasites (endoparasites and ectoparasites). Thus, host
immune responses can react with different type of pathogens in different body locations. Host immune reactions can be categorized into eradicable immune reactions and tolerable reactions[1]. The eradicable immunological pathways can be triggered by initiatory host immune cells. The tolerable immunological pathways are triggered by regulatory host immune cells. There are four types of pathogens and four types of hypersensitivities. Thus, both eradicable immunological pathways and tolerable immunological pathways can be divided into four groups. This article tries to explain this framework in detail and provides an update since my previous work in the journal.

Cancer is associated with host immune dysfunction. Chronic inflammation is proved to be related to solid tumor pathogenesis. Cancer microenvironment is associated to the disease mechanism of cancer development, invasion, and metastasis. Immune cells in cancer microenvironment are also very important. Pro-tumor immune cells can promote cancer growth. On the contrary, anti-tumor immune cells can prevent cancer growth. Thus, cancer can be thought as an immune dysfunctional disease. Here, this article will discuss the pro-tumor TH1-like immunity and the anti-tumor THαβ immunity[2-4].

Overview of host immunological pathways
Host immunological pathways can be grouped into IgG dominant eradicable immune responses and IgA dominant tolerable immune responses[1,5,6]. Follicular helper T cells help the development of eradicable immune reactions by promoting antibody class switch from IgM to IgG. In the eradicable immune responses, there are four branches in react to four types of pathogens. TH1 immunity is the host immunity against intracellular micro-organisms (intracellular bacteria, protozoa, and fungi)[2]. TH1 immunity includes M1 macrophages, IFN-γ producing CD4 T cells, iNKT1 cells, CD8 T cells (Tc1,EM4), and IgG3 B cells [7,8]. TH1 immunity is related to type 4 delayed type hypersensitivity. TH2 immunity is the host immunity against parasites. There are two subtypes of TH2 immunity[9]. TH2a immunity is the host immunity against endoparasites (helminths). TH2b immunity is the host immunity against ectoparasites (insects). TH2a immunity includes inflammatory eosinophils(iEOS), interleukin-4/interleukin-5 producing CD4 T cells, mast cells-tryptase (Mct), iNKT2 cells, and IgG4 B cells[10-13]. TH2b immunity includes basophils, interleukin-13/interleukin-4 producing CD4 T cells, mast cells-tryptase/chymase (MCtc), iNKT2 cells, and IgE B cells[14-16]. TH2 immunity is related type 1 allergic hypersensitivity. TH22 immunity is the host immunity against extracellular micro-organisms (extracellular bacteria, protozoa, and fungi). TH22 immunity includes neutrophils
(N1), interleukin-22 producing CD4 T cells, iNKT17 cells, and IgG2 B cells[17,18]. TH22 immunity is related to type 3 immune complex mediated hypersensitivity. THαβ immunity is the host immunity against infectious particles (viruses and prions)[3,4,19]. THαβ immunity includes NK cells (NK1), interleukin-10 producing CD4 T cells, iNKT10 cells, CD8 T cells(Tc2,EM1), and IgG1 B cells[20]. THαβ immunity is related to type 2 antibody dependent cytotoxic hypersensitivity.

Tolerable immune responses are IgA dominant immune responses and they can also be categorized into four groups coping with different pathogens. Regulatory T cells help the development of tolerable immune reactions via antibody class switch to IgA[5]. TH1-like immunity is the host tolerable immunity against intracellular micro-organisms (intracellular bacteria, protozoa, and fungi). TH1-like immunity includes M2 macrophages, TGFβ/IFN γ producing CD4 T cells, iNKT1 cells, CD8 T cells (EM3), and IgA1 B cells[21]. TH1-like immunity is related to type 4 delayed type hypersensitivity. TH9 immunity is the host tolerable immunity against parasites (insects and helminths). TH9 immunity includes regulatory eosinophils (rEOS), basophils, interleukin-9 producing CD4 T cells, iNKT2 cells, mast cells (MMC9), and IgA2 B cells[22,23]. TH9 immunity is related to type 1 allergic hypersensitivity. TH17 immunity is the host tolerable immunity against extracellular micro-organisms (extracellular bacteria, protozoa, and fungi). TH17 immunity includes neutrophils (N2), interleukin-17 producing CD4 T cells, iNKT17 cells, and IgA2 B cells. TH17 immunity is related to type 3 immune complex mediated hypersensitivity[24,25]. TH3 immunity is the host immunity against infectious particles (viruses and prions). TH3 immunity includes NK cells (NK2), interleukin-10/TGFβ producing CD4 T cells, iNKT10 cells, CD8 T cells (EM2), and IgA1 B cells[26,27]. TH3 immunity is related to type 2 antibody dependent cytotoxic hypersensitivity.

Mechanism of clonal anergy
First of all, host immune cells must distinguish foreign antigens from self-antigens. If immune cells encounter self-antigens, they will generate no immune response. Because each T cell or B cell can only recognize one specific antigen, this is called a clonal mechanism. If a clonal T cell or B cell recognize a self-antigen, then it will generate no immune response called clonal anergy. The clonal anergy mechanism should be mediated by gamma delta T cells or IgD B cells. Gamma delta T cells develop in the thymus earlier than the development of alpha beta T cells. Thus, if a T cell clone recognizes a self-antigen such as protein antigen, it will become gamma delta T cells first. Thus, the later on development of alpha beta T cells won’t recognize self-antigen and they will only recognize foreign antigens. When gamma delta T cells recognize self-
antigens, it will cause clonal anergy[28-31]. The similar mechanism can apply for B lymphocytes. Mature B cell co-express IgD and IgM antibody in its surface. When a self-antigen recognized by IgD antibody on B cell surface, it will cause clonal anergy with no immune response. When a foreign antigen recognized by IgM antibody on B cell surface, it will cause immune response against foreign pathogens. Subsequently, IgM bearing B cell can undergo antibody isotype class switch to IgG, IgE, or IgA antibody. This is the clonal anergy for T lymphocytes and B lymphocytes. Several previous studies have pointed out IgD infusion can alleviate autoimmune arthritis in animal model[32,33]. And, gamma delta T cells can protect hosts from graft versus host disease after organ transplantation[34,35]. These all suggest that gamma delta T cells and IgD B cells have key role in immune tolerance. It is worth noting that γδ T cells have two subtypes. It is due to the types of delta chain of γδ T cells. γδ1 T cells are usually found in intestines, so they are responsible for inducing clonal anergy to common food related antigens. Thus, common food proteins won’t trigger immune reaction. This is the mechanism of oral tolerance. γδ2 T cells are circulating in the peripheral blood. They are responsible for clonal anergy for self-antigens. γδ3 T cells are usually found in liver, so they are responsible for inducing clonal anergy to common food related antigens which are metabolized in liver. Liver is also responsible for producing proteins for our body and is an immune tolerance organ. Thus, γδ3 T cells is important in maintaining liver tolerance. Another TCR γδ chain positive NKT cells are also important for lipid antigens for clonal anergy. γδ NKT cells are also found in intestine, liver, and blood.

Triggering of eradicable host immune reactions
The eradicable immunological pathways are triggered by follicular helper T cells (Tfh). Follicular help T cells are characterized by CXCR5 chemokine receptor expression and by secreting of interleukin-21[6,36,37]. BCL6 and STAT5B are key transcription factors in mediating Tfh immune reaction. The main function of Tfh is to initiate antibody production from B cells in germinal center and cause antibody class switch from IgM to IgG antibody. This is mediated by interleukin-21. Other immune cells in the Tfh immunological pathway include DCfh, iNKTfh, and ILCfh.

Eradicable immunological pathway
TH1 immunological pathway is the host immunity against intracellular microorganisms (intracellular bacteria, fungi, and protozoa). Key immune cells of TH1 immune reaction include type 2 myeloid dendritic cells (mDC2), type 1 innate lymphoid cells (ILC1), type 1 macrophages (M1), IFN-γ secreting CD4 T cells, CD8 T cells (Tc1), type 1 iNKT cells (iNKT1), and IgG3 B cells. The driven cytokine for TH1
immune response is interleukin-12. The key transcription factors of TH1 immunity are STAT4 and STAT1α. The key effector cytokine, IFN-γ, can activate M1 macrophages via iNOS activation to use free radicals to cause lipid membrane peroxidation to kill digested micro-organisms. TH1 immunological pathway is related to type 4 delayed type hypersensitivity[2].

TH2 immunological pathway is the host immunity against parasites. However, there are two subtypes of TH2 immunity: TH2a and TH2b. TH2a is the immunity against helminths (endoparasites), and TH2b is the immunity against parasitic insects (ectoparasites). In TH2a immune response, the antigen presenting cells are Langerhans cells and the innate lymphoid cells are type 2 interleukin-25 inducing inflammatory innate lymphoid cells (iILCs2). The key cytokines in TH2a immunity are interleukin-3 and interleukin-5. The key transcription factors for TH2a immunity are STAT6 and STAT1α. The major effector cells of TH2a immunity include inflammatory eosinophils (EOS), mast cells-tryptase (MCt), IL-4/IL-5 CD4 T cells, iNKT2 cells, and IgG4 B cells. In TH2b immune response, the antigen presenting cells are Langerhans cells and the innate lymphoid cells are type 2 interleukin-33 inducing natural innate lymphoid cells (nILCs2). The key cytokines in TH2b immunity are interleukin-4 and interleukin-13. The key transcription factors for TH2b immunity are STAT6 and STAT3α. The major effector cells of TH2b immunity include basophils, mast cells-tryptase/chymase (MCt), IL-4/IL-13 CD4 T cells, iNKT2 cells, and IgE B cells. TH2 immunological pathway is related to type 1 allergic hypersensitivity. TH2a immunity is related to IgG4 dominant allergy and TH2b immunity is related to IgE dominant allergy[2].

TH22 immunological pathway is the immunity against extracellular micro-organisms (extracellular bacteria, fungi, and protozoa). The antigen presenting cells of TH22 immunity are type 1 myeloid dendritic cells (mDC1) and the innate lymphoid cells of TH22 immunity are type 3 NCR+ innated lymphoid cells (NCR+ ILC3). The effector immune cells of TH22 immune reaction are neutrophils (N1), IL-22 secreting CD4 T cells, and IgG2 B cells. The driven cytokines for TH22 immunity are interleukin-1, interleukin-6, and TNF-α. The effector cytokine for TH22 immunity is interleukin-22. The key transcription factors for TH22 immunity are STAT3α and STAT4α. Neutrophils activation with phagocytosis and NETosis can destroy the extracellular micro-organisms. Free radical generation during neutrophil phagocytosis can cause membrane lipid peroxidation of extracellular micro-organisms to kill these pathogens. TH22 immunological pathway is related to type 3 immune complex mediated hypersensitivity[17].
THαβ immunological pathway is the immunity against infectious particles (viruses and prions). The antigen presenting cells for THαβ immunity are plasmacytoid dendritic cells and the innate lymphoid cells for THαβ immunity are interleukin-10 producing innate lymphoid cells (ILC10). The effect immune cells for THαβ immunity are NK cells (NK1), interleukin-10 producing CD4 T cells, CD8 T cells (Tc2), and IgG1 B cells. The driven cytokines for THαβ immunity are type 1 interferons and interleukin-10. Interleukin-10 is the major effector cytokine in THαβ immunity. The key transcription factors for THαβ immune reaction are STAT1α, STAT1β, and STAT3β. NK cell with IgG1 mediated antibody dependent cellular cytotoxicity is the effector function of THαβ immunity to cause virus or prion infected cell apoptosis. During apoptosis, DNA fragmentation will destroy viral DNA or RNA and protein digestion via caspases will destroy prion pathogen proteins. Type 2 antibody dependent cellular cytotoxic hypersensitivity is related to THαβ immunological pathway [3,38].

Triggering of tolerable host immune reactions
Regulatory CD4+CD25+ T cells are the key cells to initiate tolerable immune responses. These FOXP3+ Treg cells can produce TGFβ to activate STAT5α and STAT5β to trigger tolerable immunity. TGFβ can cause B cell antibody isotype class switch to IgA. Other immune cells related to Treg cells are DCreg, Breg, and ILCreg. If the pathogen infections are so severe or diverse, it is difficult for host to eradicate all the pathogens in the body because eradication may cause severe organ damage or failure. Thus, host tolerable immunological pathways are initiated to cope with these situations [39].

Tolerable immunological pathways
TH1-like immunological pathway is the host tolerable immune response against intracellular micro-organisms (intracellular bacteria, fungi, and protozoa). The effector cells of TH1-like immunity are macrophages (M1), IFNγ/TGFβ secreting CD4 T cells, CD8 T cells, iNKT1 cells, and IgA1 B cells. The antigen presenting cells for TH1-like immunity are type 2 myeloid dendritic cells and the innate lymphoid cells for TH1-like immunity are type1 innate lymphoid cells (NCR- ILCs1). The driven cytokines for TH1-like immunity are interleukin-12 and TGFβ. TH1-like immunological pathway is related to type 4 delayed type hypersensitivity [21].

TH9 immunological pathway is the host tolerable immune response against parasites (ectoparasites and endoparasites). The effector cells of TH9 immunity are regulatory eosinophils (rEOS), basophils, mast cells (MMC9), IL-9 secreting CD4 T cells, iNKT2 cells, and IgA2 B cells. The antigen presenting cells for TH9 immunity are Langerhans cells
and the innate lymphoid cells for TH9 immunity are TSLP inducing type 2 innate lymphoid cells. The driven cytokines for TH9 immunity are interleukin-4 and TGFβ. TH9 immunological pathway is related to type 1 allergic hypersensitivity[22].

TH17 immunological pathway is the host tolerable immune response against extracellular micro-organisms (extracellular bacteria, fungi, and protozoa). The effector cells of TH17 immunity are neutrophils (N2), interleukin-17 secreting CD4 T cells, iNKT17 cells, and IgA2 B cells. The antigen presenting cells for TH17 immunity are type 1 myeloid dendritic cells and the innate lymphoid cells for TH17 immunity are type 3 innate lymphoid cells (NCR-ILCs3). The driven cytokines for TH17 immunity are interleukin-6 and TGFβ. TH17 immunological pathway is related to type 3 immune complex mediated hypersensitivity[40].

TH3 immunological pathway is the immunity against infectious particles (viruses and prions). The antigen presenting cells for TH3 immunity are plasmacytoid dendritic cells and the innate lymphoid cells for TH3 immunity are interleukin-10 producing innate lymphoid cells (ILC10). The effect immune cells for TH3 immunity are NK cells (NK2), interleukin-10/TGFβ producing CD4 T cells, CD8 T cells, and IgA1 B cells. The driven cytokines for THαβ immunity are TGFβ and interleukin-10. Interleukin-10 and TGFβ are the major effector cytokine in THαβ immunity. The key transcription factors for THαβ immune reaction are STAT1α, STAT1β, STAT3β, and STAT5α/β. Type 2 antibody dependent cellular cytotoxic hypersensitivity is related to THαβ immunological pathway[26].

Pro-tumor immunological pathway

Cancer microenvironment can promote the growth of solid tumors. Chronic inflammation is thought to be related to carcinogenesis. Thus, cancer can be thought as an immune dysfunctional disorder. Among the host immunological pathways, TH1-like is the immune response mostly related to pro-tumor immune response. First of all, regulatory CD4 T cells (Treg) are related to the cancer immune tolerance. Regulatory CD4+CD25+ T cells can produce TGFβ which is an immune-suppressive cytokine. Via the up-regulation of TGFβ, cancer cells can avoid the attack from other immune cells. Thus, other adaptive immune cells such as CD8 T cells or effector CD4 T cells can be suppressed. In addition, DCreg antigen presenting cells and ILCreg innate lymphoid cells also play important roles in mediating the tolerable immune reaction. They can help host to develop TH1-like immunity pathway from original TH1 immunological pathway[41].
In addition, cancer pathogenesis is related to macrophages, especially tumor associated macrophages. Macrophages in tumor microenvironment can produce cytokines and growth factor or angiogenesis factor to promote cancer growth and angiogenesis which is required for solid tumor development. Besides, macrophages can fuse with cancer cells to let cancer to have invasion as well as metastasis ability. Macrophages can digest environmental materials via phagocytosis. This is related to cancer invasion ability. After cancer fused with macrophages, cancer can migrate to macrophages destination sites such as liver (Kupffer cells), lung (alveolar macrophages), bone (osteoclasts), brain (microglia), lymph nodes (monocytes), and peritoneal/pleural/pericardial space (mesothelial cells)[42]. That is the mechanism of cancer metastasis. IFNγ, a potent macrophage activator, also can promote cancer migration for metastasis[43]. Macrophage M2 is especially important to promote cancer pathophysiology. M2 macrophage can also produce TGFβ to suppress adaptive effector anti-tumor lymphocytes. Monocytes/macrophages in cancer microenvironment can also promote angiogenesis in the tumor structure. TH1-like immunity is the host tolerable immunity against intracellular micro-organisms (intracellular bacteria, protozoa, and fungi). TH1-like immunity includes M2 macrophages, TGFβ/IFNγ producing CD4 T cells, iNKT1 cells, CD8 T cells, and IgA1 B cells. In addition, regulatory CD8 T cells (CD27-CD28-) are also component cells in TH1-like immunological pathway. These kinds of CD8 T cells cannot potently kill solid tumor cells via TCR engaged cell apoptosis. And, these CD8 T cells only mildly control solid cancers. These kinds of CD8 T cells are also contributing to pro-tumor immunity. Thus, TH1-like immune reaction is the pro-tumor host immunological pathway. Cancer can be thought as an immune dysfunctional disorder by up-regulation of TH1-like immune response. TH1-like immunity is important in cancer pathogenesis[44-46].

Besides, γδ T cells and IgD B cells may also play vital roles in the pro-tumor immune responses. γδ T cells and IgD B cells play roles in clonal anergy. Thus, they will recognize self-antigens from cancer cells and will not trigger host immune reactions, especially eradicable immune reactions[47]. Among then, the role of γδ T cells in tumor microenvironment is studied most. Some studies suggested that γδ T cells have anti-tumor activities. However, majority of these studies use IFNγ to decide the immune activity of γδ T cells. However, TGFβ/IFNγ producing CD4 T cells are main component in pro-tumor immune reactions. Thus, it is not suitable for using gamma interferon to stand for anti-tumor activities of TGFβ/IFNγ producing CD4 T cells. Actually, several other papers suggested that γδ T cells have pro-tumor activities. This is more reasonable. It is because that γδ T cells can cause clonal anergy to prevent
host immunological pathway against solid tumors. Cancer cells can use γδ T cells to escape from host immune response. Besides, IgD B cells may also play a vital role in pro-tumor activities. IgD is a molecule to induce B cell clonal anergy [32,33,48]. A study which measured the serum concentrations of immunoglobulins and found out that IgD is elevated in oral, breast, and cervix cancer patients [47]. Indirect evidence also showed that IgD- B cells can have anti-tumor immune reaction and this suggested that IgD molecule has pro-tumor effect. Tumor cells can use both γδ T cells and IgD B cell to escape from host immune surveillance.

Anti-tumor immunological pathway

On the contrary, host can generate anti-tumor immunity against the cancer development. The key anti-tumor immune reaction is THαβ immunological pathway. THαβ immunological pathway includes NK cells (NK1), CD27+CD28+ CD8 T cells, interleukin-10 producing CD4 T cells, iNKT10 cells, and IgG1 B cells. THαβ immunity is the protective host immunity against viruses and prions. The mechanism of oncolytic viruses to destroy cancer cells is to initiate host anti-viral immune responses. Cancer is a genetic disorder with upregulation of oncogenes and downregulation of tumor suppressor genes. Chromosome instability or aneuploidy is the hallmark of cancers. THαβ immune reaction can destroy virus infected cells via apoptosis with DNA fragmentation. Thus, we can also use THαβ immunity to destroy cancer cells via apoptosis with oncogene fragmentation. In fact, many THαβ immune mediators have anti-cancer ability. NK cells (NK1) and CD8 T cells (CD28+CD27+) are the main effectors cells in THαβ immunity to mediate antibody dependent cellular cytotoxicity. These subtypes of NK cells and CD8 T cells are components of anti-viral eradicable immune response. They have potent activity to kill cells with oncogene over-expression or mutations. Besides, the antibody subtype IgG1 is the antibody class against viruses. Thus, we can also use IgG1 antibody to kill solid tumor cells with oncogene mutation or over-expression. In fact, many monoclonal antibodies for anti-tumor immunity available currently are all IgG1 antibodies. IgG1 antibody can use its Fc portion to bind to CD16 of NK cells to mediate ADCC. Thus, IgG1 also plays a vital role in anti-cancer immune reaction [3,49,50].

The key THαβ cytokine, interleukin-10, has a potent ability to inhibit cancer cells in vitro and to suppress cancers in vivo. Interleukin-10 can activate host anti-viral ability. It can promote antibody dependent cellular cytotoxicity. Interleukin-10 can also activate CD8 T cells and NK cells. Interleukin-10 can also cause B cell antibody isotype switch to IgG1, an anti-virus antibody. In addition, interleukin-10 can suppress macrophages as well as induce macrophage apoptosis. M2 tumor
associated macrophages are related to cancer pathogenesis. Thus, interleukin-10 can inhibit cancer growth and metastasis via inhibiting M2 macrophages. Another THαβ cytokine, interleukin-27, is also important in anti-tumor immunity. Previous in vivo experiments showed that interleukin-27 has a potent anti-tumor activity. Interleukin-27 is a driven cytokine for THαβ immunity. It can promote CD4 T cells to produce interleukin-10. Thus, interleukin-27 can suppress tumors via itself or via interleukin-10. Type 1 interferons (interferon α/β) are also driven cytokines for induction of THαβ anti-viral host immune reaction. Type 1 interferons can suppress gene transcription and expression. Because cancer is a genetic disorder, suppressing gene expression can reduce the effect of oncogenes. Besides, type 1 interferons can promote antibody dependent cellular cytotoxicity (ADCC) to destroy virus infected cells. Thus, type 1 interferons can also cause cancer cell apoptosis with its oncogene fragmentation. Type 1 interferons can also promote CD4 T cells to produce interleukin-10. Type 3 interferons can also have anti-viral activity like type 1 interferons. In fact, type 1 interferons are current cancer treatment medications such as hairy cell leukemia and renal cell carcinoma[51,52].

Conclusion:
This framework provides a detailed mechanism for host immunological responses against different pathogens. In addition, the relationship between four types of hypersensitivities and these immunological pathways are given. This framework can help to diagnose and treat infectious diseases as well as to manage autoimmune disorders. In addition, knowing the pro-tumor TH1-like host immune reaction and anti-tumor THαβ host immune reaction can help us to better diagnose and treat solid tumors.

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Figure 3.
Figure 4.
Table 1. Summary of host immunological pathways

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<th>Driven cytokines, ILCs, DC</th>
<th>Transcription factors</th>
<th>Effector cells</th>
<th>CD4 T cells</th>
<th>B cells</th>
<th>NKT cells</th>
<th>Pathogen/pathogenesis</th>
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<td>IL-10/TGF-β CD4 T cells</td>
<td>IgA1 B cells</td>
<td>iNKT10</td>
<td>Infectious particles (Viruses/Prions)</td>
<td>Type 2 ADCC</td>
</tr>
</tbody>
</table>

**Note:** The table provides an overview of different immune pathways and their associated transcription factors, effector cells, and characteristics of different immune responses. The table includes regulatory T cells (Treg), tolerable immunities, and hypersensitivities.
References:


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