The Major Novelty of Vaccine AZEE CRA 01, Newly Discovered and Developed Vaccine

Zelalem Kiros Bitsue MD, PhD
United States of African Health Organization "US-AHO"

Abstract

The ACE-2 is a trans membrane metallo-carboxy-peptidase, plays a significant role in the entry of the SARS-CoV-2 particle to the human lung epithelial cells

The spike glycoprotein (S1) interacts with host cell epithelial angiotensin-converting enzyme 2 (ACE-2) receptors.

The nano-luciferase-based assay shows that the virus's 1 protein has a strong binding affinity with the ACE-2 receptors (2).

Reports illustrate the S-protein antigenic epitope of SARS-CoV-2 binds with the TLR4/ MD-2 complex by strong molecular bonding interactions (4).

The pool of miRNA based studies shows that TMPRSS2 acts as promising regulators for the SARS-CoV-2 entry checkpoint (8).

Recent report stated that the AT1R phosphorylates JAK2 in the lung cells, which activates STAT-3 transduction to the nucleus (12).

In this article, I discuss the Pathogenesis Mechanisms of SARS-COV-2, Normal Activation of Immune system, The Novelty of Vaccine AZEE CRA 01, The Major Novelty of Vaccine AZEE CRA 01, Mechanisms of Action of Vaccine AZEE CRA O1 and The Challenges on development

Key Words: SARS-COV-2, Vaccine AZEE CRA 01, B Cell Activation, CD4 T Cell Activation, CD8 T Cell Activation and cGMP manufacturing

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1. Introduction (The Mutations SARS-COV-2)

Since SARS-COV-2 outbreak December, 2019, several SARS-COV-2 mutations created (New variants). More than 500 million people infected and more than 6 million peoples died and continuing; for the first time since out break more than 3000,000 new cases recorded per day; Variant Omicron 200 to 300 times transmissible than Delta, slightly lower infectious; Variant B.1.640.2 50 times transmissible than omicron, and also not yet data about infectious;More than 46 new mutation and 37 deletion in the new variant B.1.640.2 than Omicron; The Mutations SARS-COV-2 continuing; Deltacron , BA.2, XE. XF, XD variant new variant born... No vaccine yet controlled the SARS-COV-2 virus mutations, replication and spread.

2. Pathogenesis Mechanisms of SARS-COV-2

A recent report demonstrated that spike protein had been O-glycosylated on the amino acid threonine (T678) adjacent to the furin cleavage site. Liquid chromatography-mass spectrometry analysis showed that the spike protein's LacdiNAc structural motifs and polyLacNAc structures (1). The spike glycoprotein (S1) interacts with host cell epithelial angiotensin-converting enzyme 2 (ACE-2) receptors. The nano-luciferase-based assay shows that the virus's 1 protein has a strong binding affinity with the ACE-2 receptors (2). The ACE-2 is a trans membrane metallo-carboxy-peptidase, plays a significant role in the entry of the SARS-CoV-2 particle to the human lung epithelial cells. The ACE-2 degrades its substrate angiotensin II to angiotensin 1-7 and regulates RAS negatively, thereby protects the internal organs (3). Reports illustrate the S-protein antigenic epitope of SARS-CoV-2 binds with the TLR4/ MD-2 complex by strong molecular bonding interactions (4).

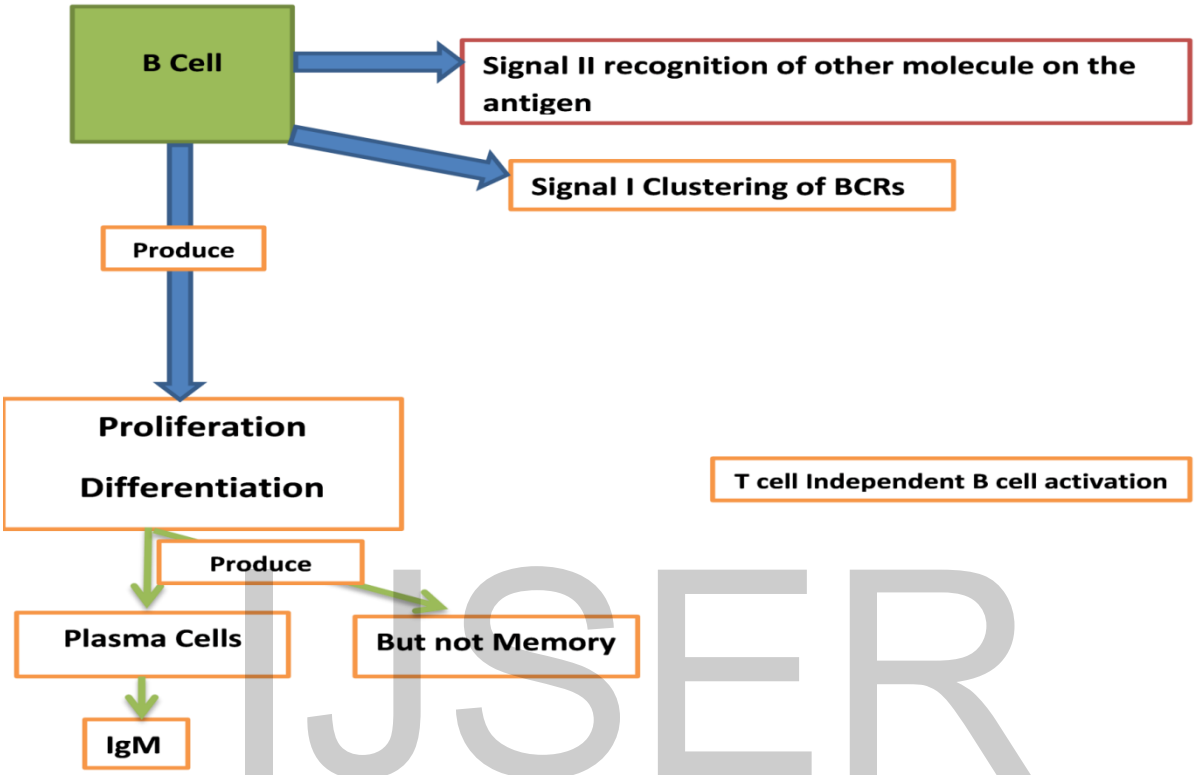
The human trans membrane protease serine 2 (TMPRSS2) processes the viral spike protein and exposes fusion peptide present in the S2 subunit to the host receptor ACE-2 (5). This S protein processing and priming by the TMPRSS2 is an essential step in the SARS-CoV-2 infection (6). SARS-CoV-2 uses cysteine proteases like cathepsin B and L (CatB/L) and promotes virus-plasma membrane fusion (7). The pool of miRNA based studies shows that TMPRSS2 acts as promising regulators for the SARS-CoV-2 entry checkpoint (8). Moreover, SARS-CoV-2 down-regulates the expression of ACE-2 resulted in the up-regulated expression pattern of Ang II.

Ang II is formed by the degradation of Ang I by the enzyme ACE-2 (9). The overexpressed Ang II binds with its plasma membrane receptor AT1R. This membrane-bound ATIR transduces the signals to the inflammatory transcription factors like NF-ƙB, NF-ƙB, mediates several inflammatory cytokines' activation and overexpression (10),(11).

Recent report stated that the AT1R phosphorylates JAK2 in the lung cells, which activates STAT-3 transduction to the nucleus (12). The STAT-3 is a signal transducer and activator of transcription, which initiates the active transcription of inflammatory cytokines. The Ang II/AT1R interaction activates macrophages to produce excessive inflammatory cytokines. Further contribute to "cytokine storm" and development of Acute Respiratory Distress Syndrome (ARDS) (13),(14). The cytokine storm led to multiple organ failure and subsequent mortality (15).

3. Normal Activation of Immune system

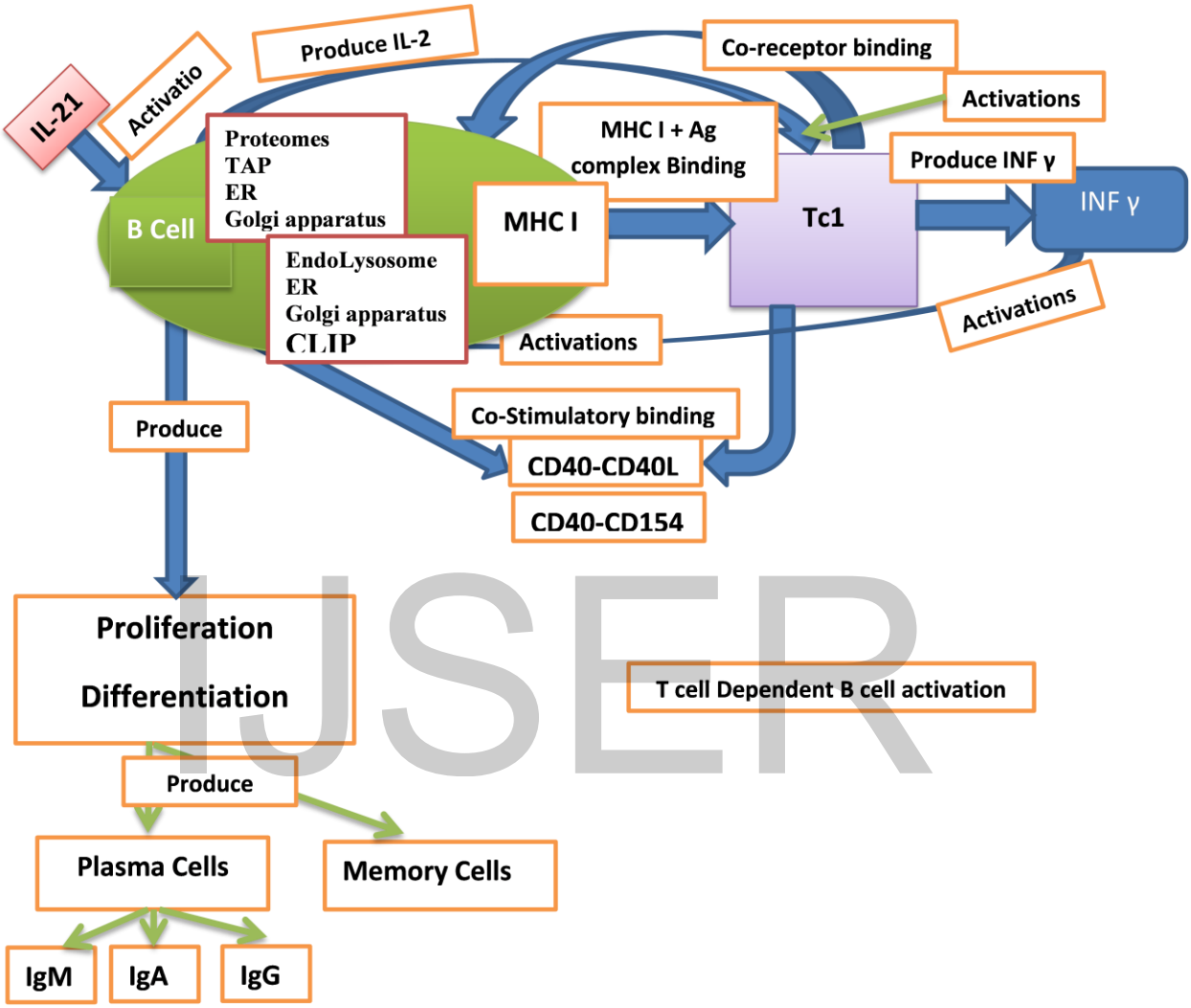
3.1. T Cell Independent B Cell Activation



Complete binding and activations requires

1. Clustering of BCRs
2. Recognition and binding with other molecules on the antigen

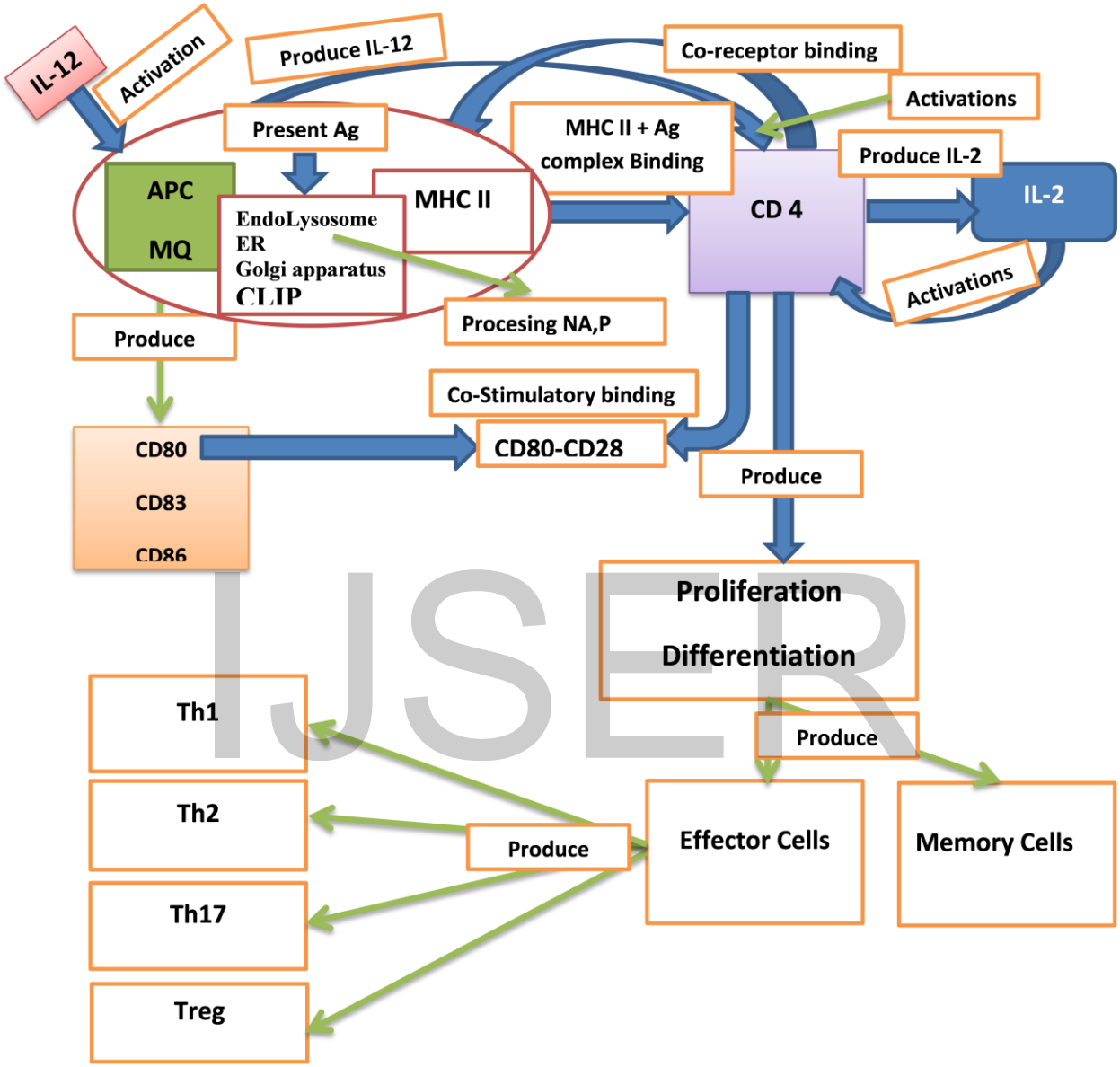
3.2.T Cell dependent B Cell Activation



Complete binding and activations requires

1. Co-receptor binding
2. Antigen - MHC II complex binding
3. Co-Stimulatory binding
4. Produces INFγ and B cell Self activation by INFγ

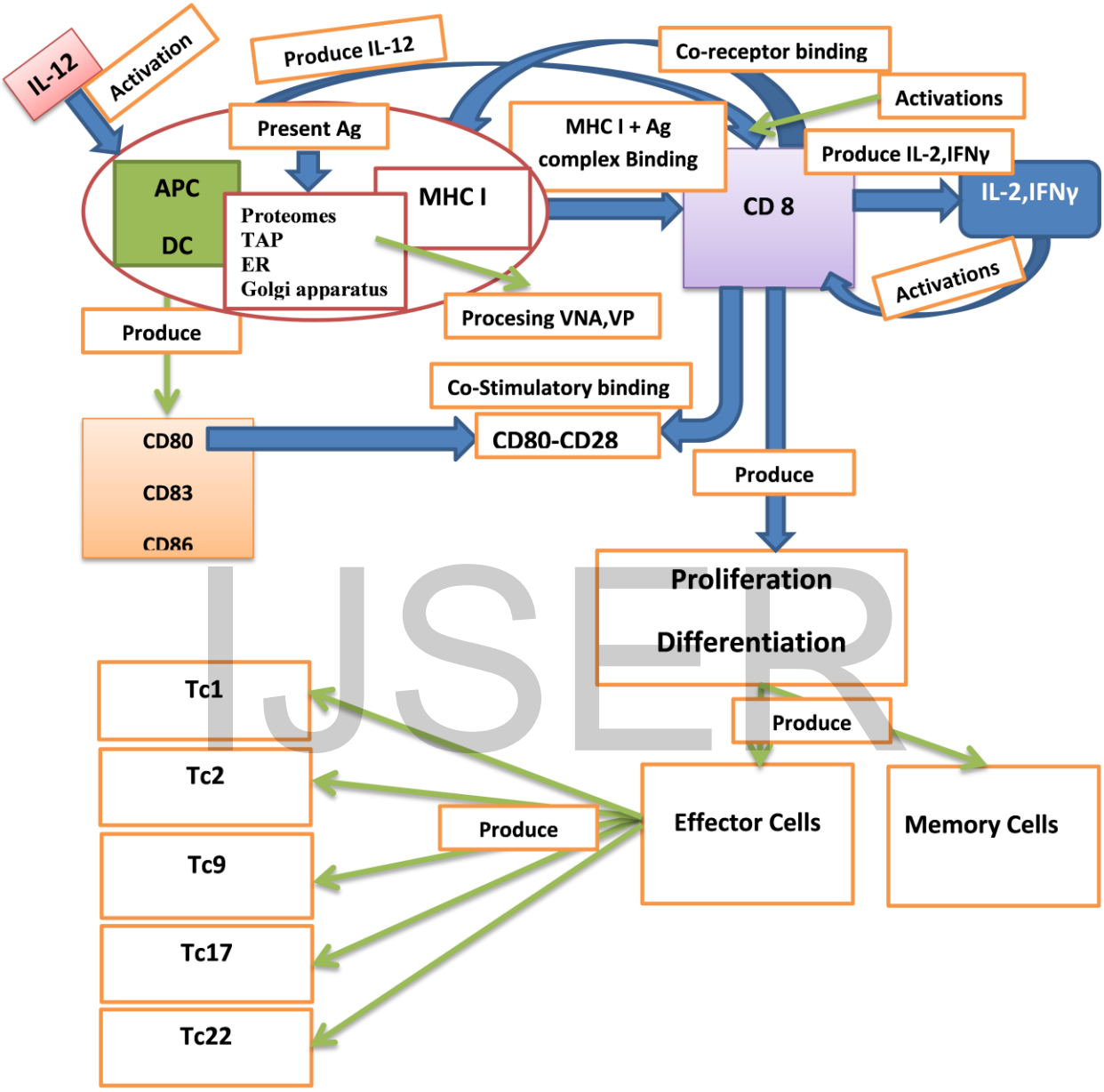
3.3.CD4 T Cell Activation



Complete binding and activations requires

1. Co-receptor binding
2. Antigen - MHC II complex binding
3. Co-Stimulatory binding
4. Produces IL-2 and CD 4 Self activation by IL-2

3.4.CD8 T Cell Activation



Complete binding and activations requires

1. Co-receptor binding
2. Antigen – MHC I complex binding
3. Co-Stimulatory binding
4. Produces IL-2/**IFNγ** and CD 8 Self activation by IL-2/**INFγ**

4. The Novelty of Vaccine AZEE CRA 01

On the novelty of the vaccines, it is natural for questions to arise on their effectiveness. Efficacy refers how a vaccine performs under ideal lab conditions, such as those in a clinical trial. Effectiveness refers to how it performs in the real world. In other words, in a clinical trial, a 90% efficacy means that there are 90% fewer cases of disease in the group receiving the vaccine compared with the placebo group

The new vaccine AZEE expects to have very rare common side effects

- Mild Pain at the injection site
- Mild Headache
- Mild Fever
- Temporary Redness at the injection site

Vaccine AZEE CRA 01 from Adjuvant and Injectable; Crucial for getting a stronger, longer-lasting, broader immune response, Especially among those with weakened immunity, like pediatrics, children, pregnant women and elderly." Crucial for restore functions causes immune cells dysfunction and improve the normal immune function and balance modifications.

Preventive and therapeutic and working with your body's natural defenses to build protection; When you get a Vaccine AZEE CRA 01It: Inhibits viral replication and spread; Humeral and Cellular immune response; Recognizes the invading virus the respiratory system; Produces antibodies (IgM,IgG,IgA);Remembers the disease and how to fight it(entire normal signaling, effector and memory cell created

Vaccine AZEE a safe and clever way to produce an immune response in the body, without causing illness, affecting immune cells function and with respect of biochemical properties of immune cells. Our immune systems are designed to remember, when we create suitable environment for natural immune cell signaling, mechanism and function.

This is what makes vaccines so effective. That's how exactly Vaccine AZEE discovered, designed, and developed. Able to achieved the Goal of Effectiveness, which able to boast 100% of efficacy. Once the immune cell kills to foreign antigen, digested, processed, present, produce the entire activation and naturally functioning, we typically remain protected against a disease for years, decades or even a lifetime.

5. The Novelty of Vaccine AZEE CRA 01

1. SARS COV-2 with all type of Variants Preventions and therapeutic

2. Future Respiratory infectious Pandemic Preventions

3. Produce an immune response in the body, without causing illness, affecting immune cells function, and with respect of biochemical properties of Immune cells.

4. without affecting genes transcriptions and expression

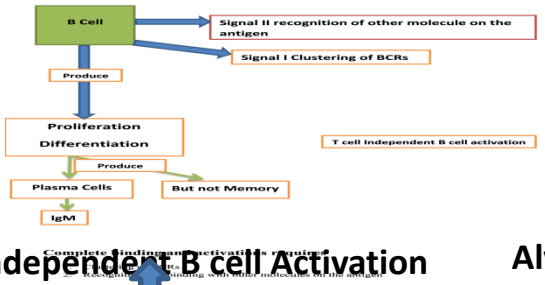
5. Long lasing, Very Safe, Well known components

6. I discovered that B cell synthesis both Intracellular and Extracellular pathogen

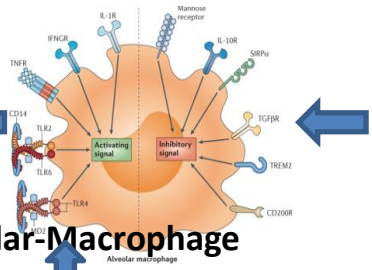
7. Further, B cell has both Proteasome, Lysosome, Endosome components

8. In addition, B Cell Interacts both with Cytotoxic T cell and T helper cells to make T Dependent B Cell Activation

6. Mechanisms of Action of Vaccine AZEE CRA O1

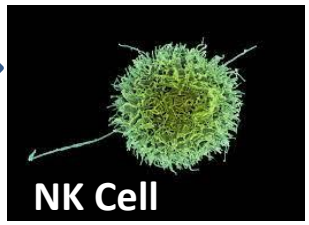


T Independent B cell Activation



Alveolar-Macrophage

Inhalation



NK Cell

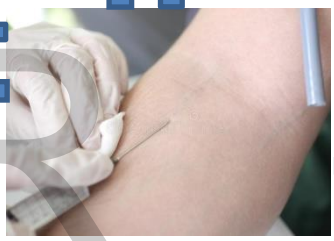
IFNγ

MQ

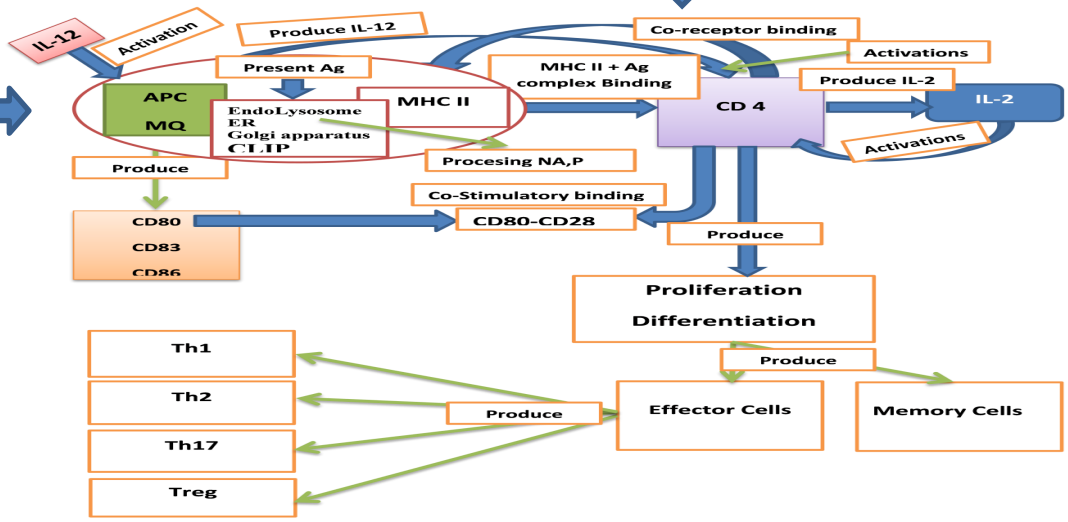
TNFα

IL-12

Vaccine AZEE



IV -injection



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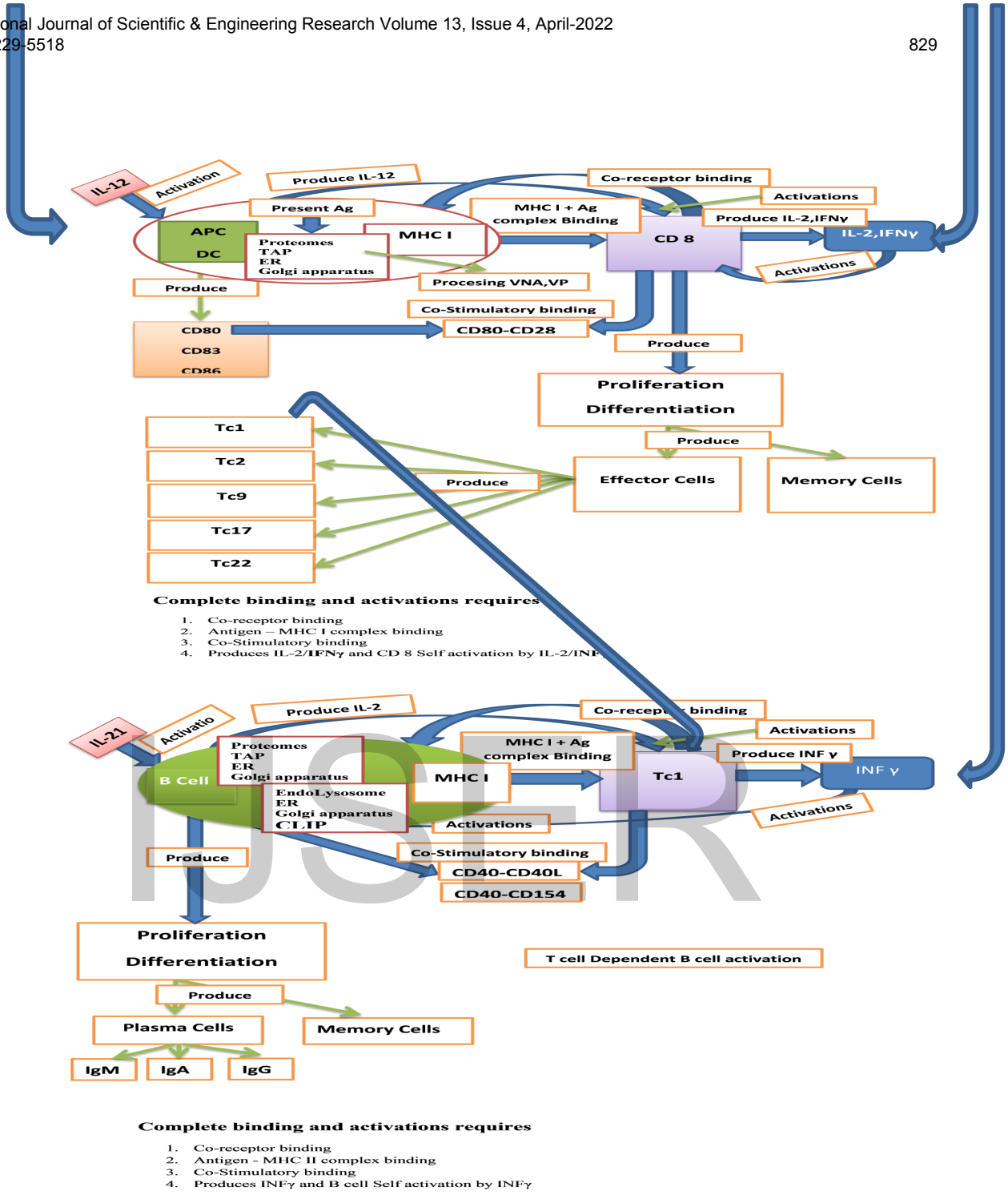

7. Formulation and cGMP Manufacturing of Vaccine AZEE CRA 01

Formulations are ready for manufacturing and to initiate clinical trials and approval

8. Vaccine AZEE CRA 01 Approval

I need sponsor for AZEE CRA 01 (Universal Vaccine) cGMP manufacturing and US-FDA, EMA and SFDA and or Local approval, Further, AZEE CRA 01-14 Vaccines Projects

9. Challenges

March 2020, I develop Protocol Vaccine AZEE CRA01,

June 2020, I submitted protocol to US-FDA Emergency use approval,

October 2020, US-FDA recommended having collaborators to work as demonstrator the safety and efficacy and cGMP manufacture Vaccine AZEE CRA 01

November 2020, since then based on the US-FDA recommendation to initiate clinical trial; I have been looking collaborators,

May 2021, I made collaborators, start developing…

But still sponsors highly needed (manufacturing a vaccine is costs)

Africa not adapted such research projects and I have not have access to all necessary resources to initiate vaccine development

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