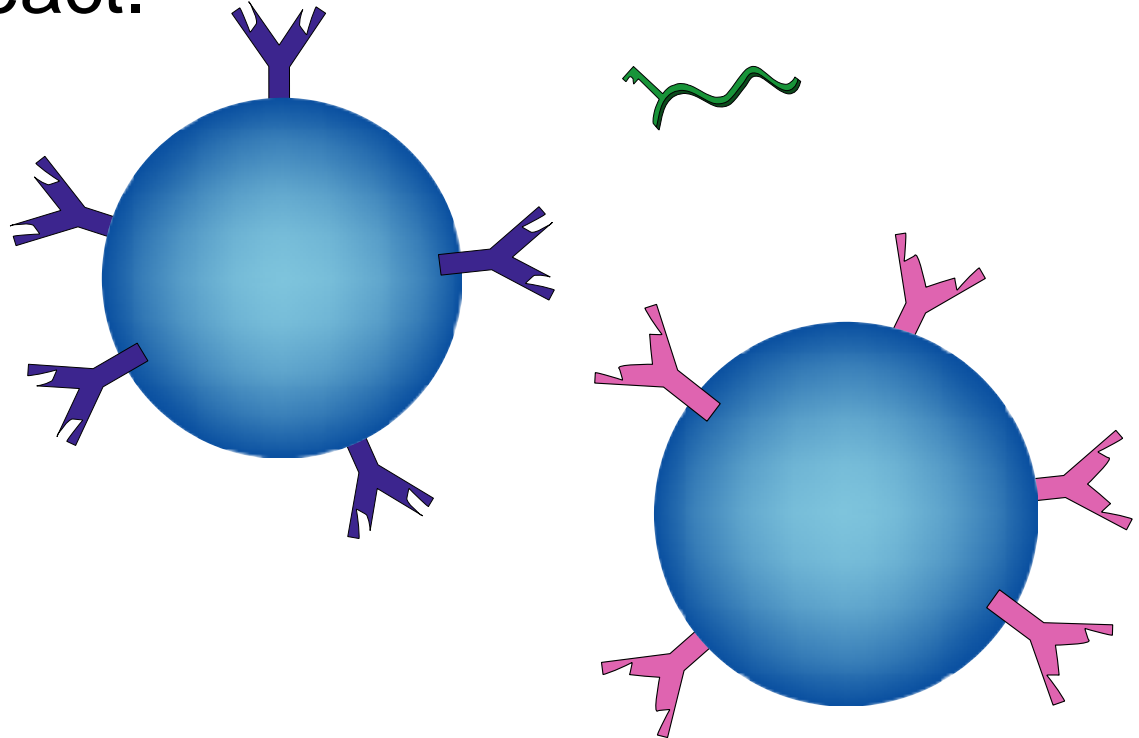
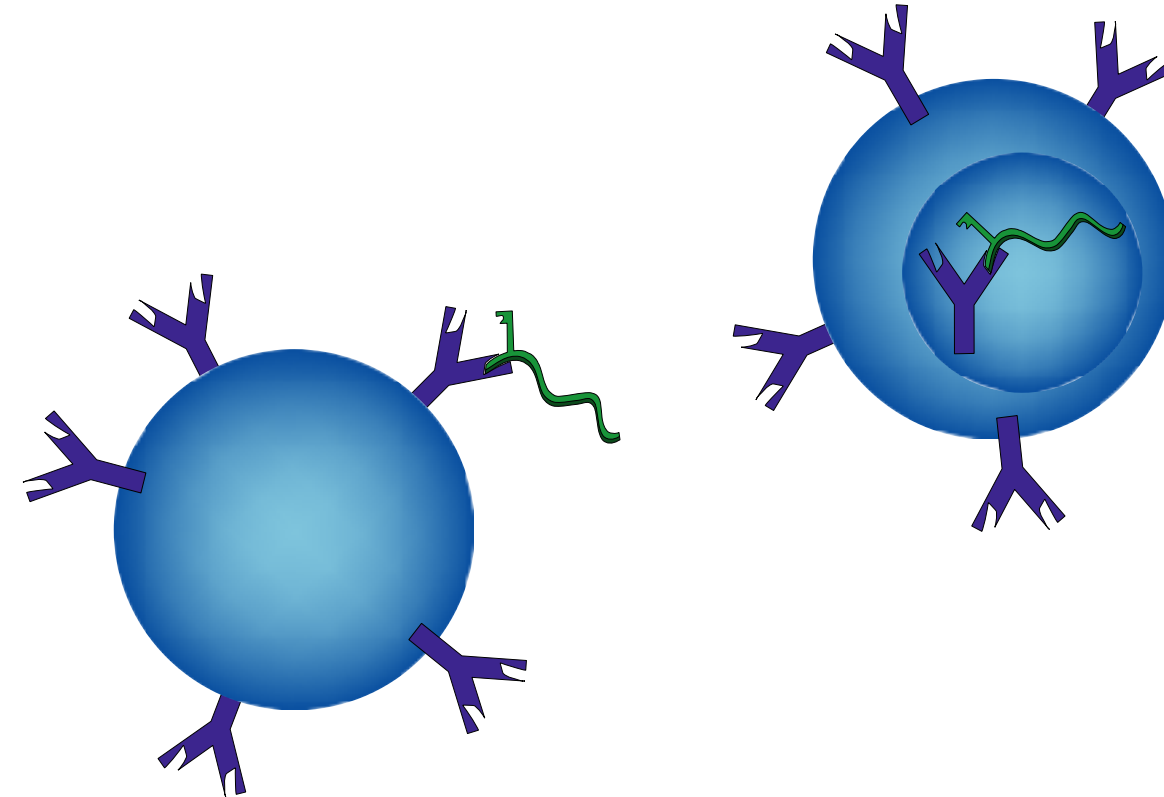


# Anti-gp120 Antibody Elimination: B Cell Clonal Toxin to Delete the Antibody Response

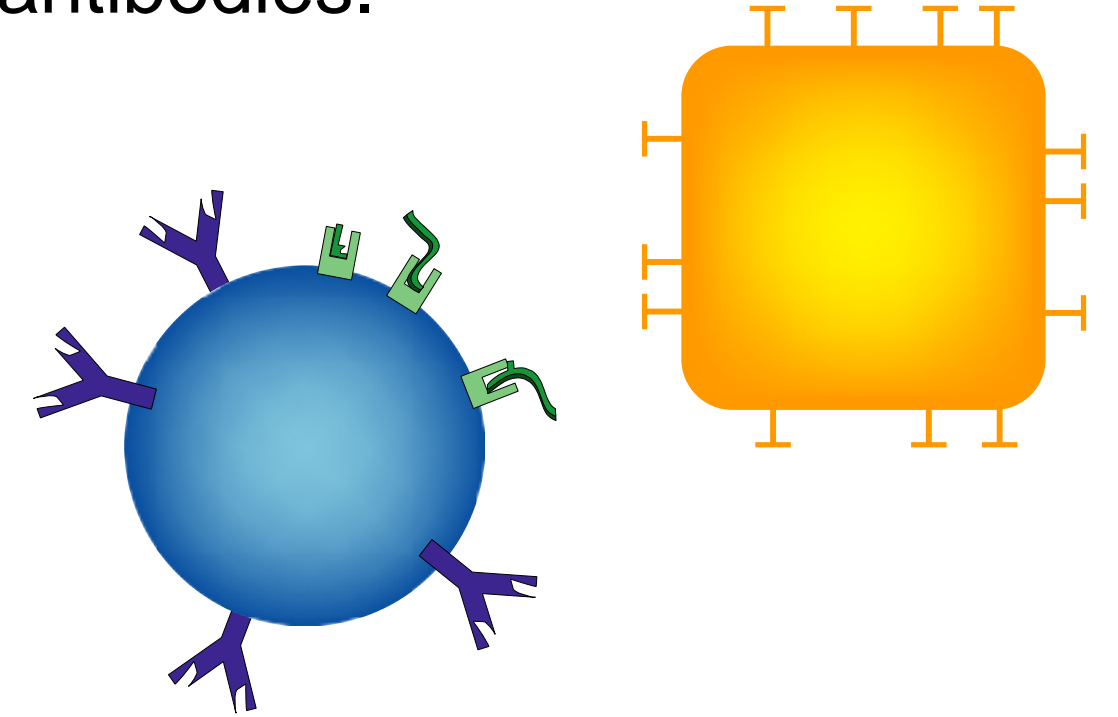
*Background:* B cells display IgD antibody receptors on their surface. These receptors bind antigens to which this cell can react.



After binding an antigen, the B cell internalizes the antigen and the receptor in a lysosome, where it is digested.



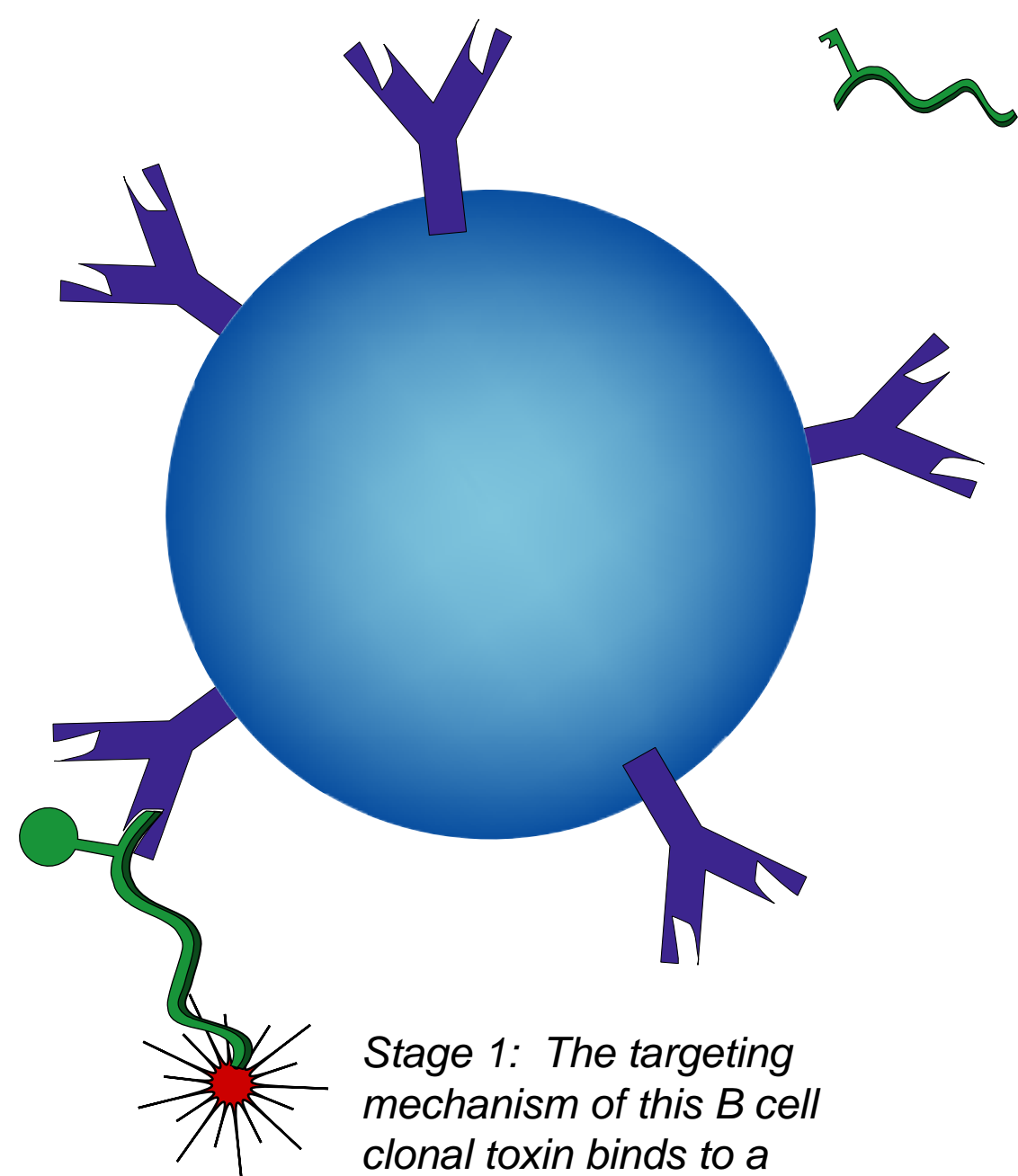
The fragments of antigen are then displayed in the context of MHC-2 for T<sub>4</sub> cell approval before the B cell begins making antibodies.



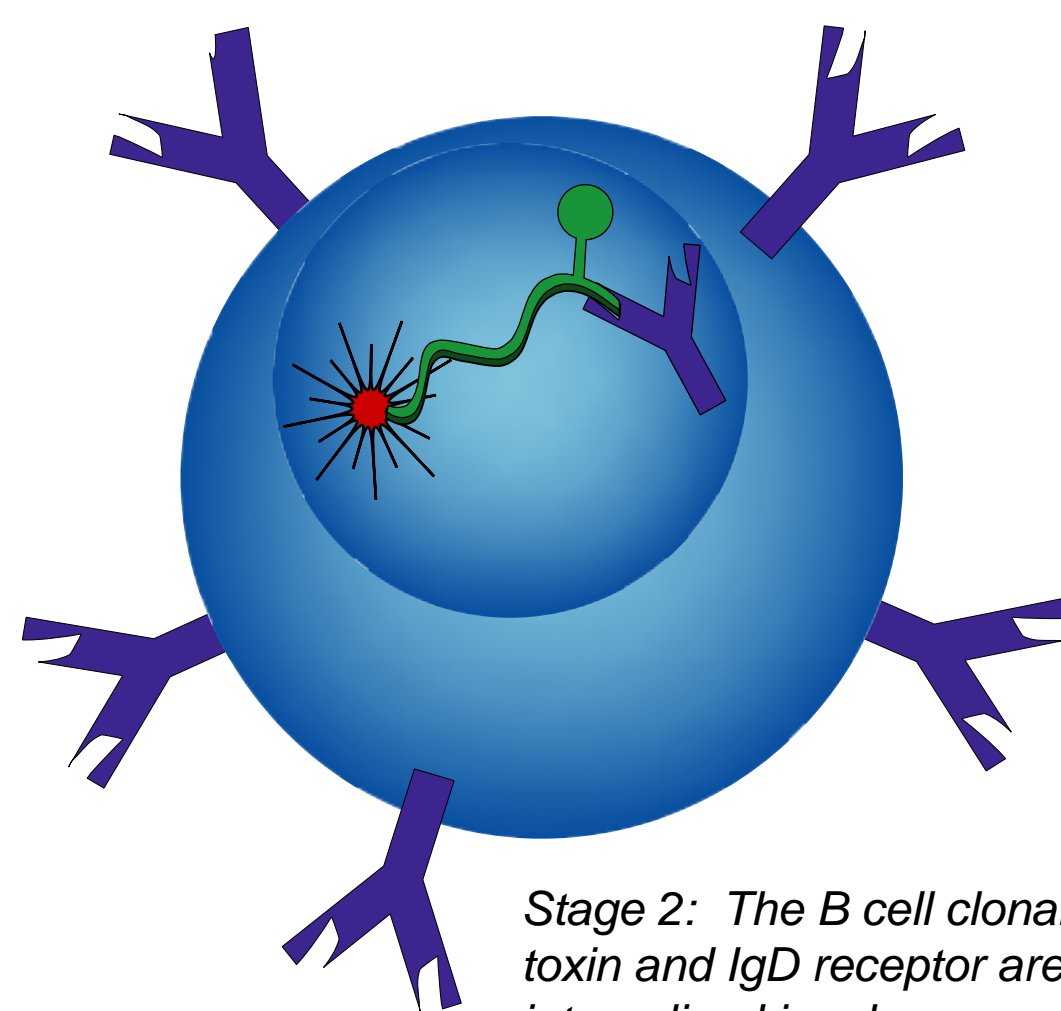
Disease progression in AIDS is closely correlated to the interaction of the concentration of gp120 in the bloodstream and anti-gp120 antibody titer. It is apparent that *both* gp120 and antibodies against it are necessary for disease progression. Removing either gp120 or the antibodies against it should stop disease progression and allow for immune system reconstitution.

Antiretrovirals, by suppressing viral load, suppress gp120 concentrations in the blood and reduce bystander cell death, until drug resistance is developed.

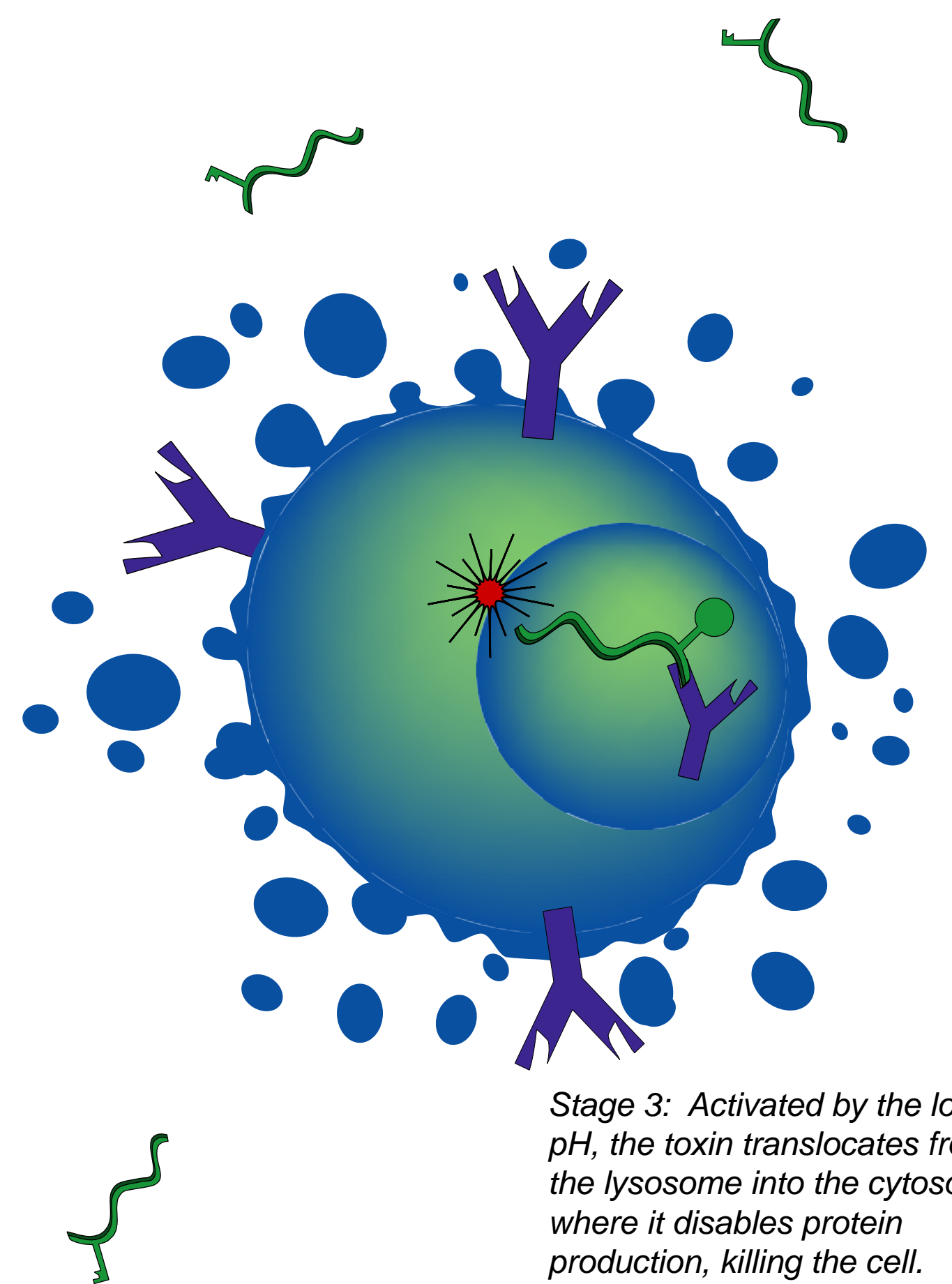
The other option for medical intervention is to eliminate anti-gp120 antibodies, which is accomplished easily by the selective destruction of the B cells which produce them. A B cell clonal toxin, modeled after HASA (Hot Antigen Suicide Agent) compounds, is used to selectively eliminate gp120-reactive B cells.



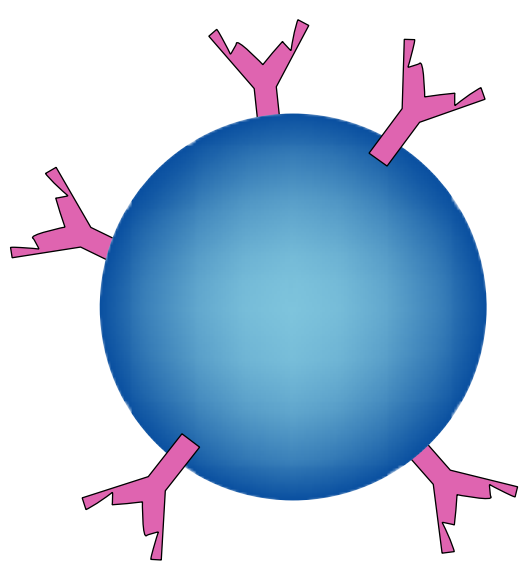
Stage 1: The targeting mechanism of this B cell clonal toxin binds to a gp120-reactive B cell.



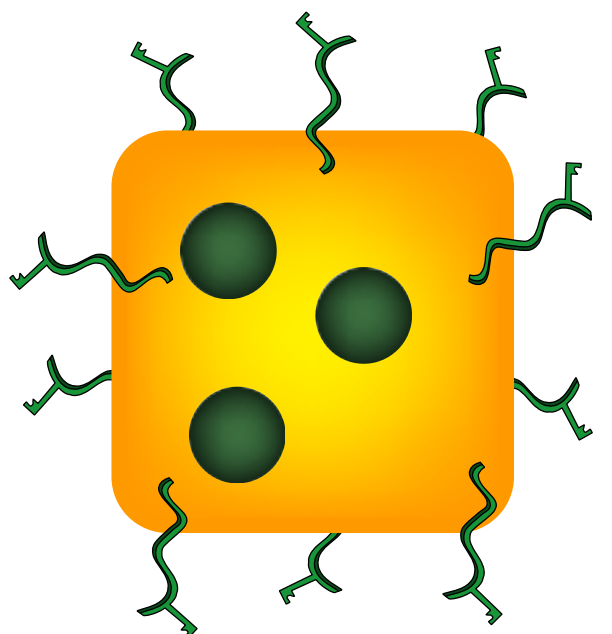
Stage 2: The B cell clonal toxin and IgD receptor are internalized in a lysosomal compartment for processing.



Stage 3: Activated by the low pH, the toxin translocates from the lysosome into the cytosol, where it disables protein production, killing the cell.



B cells which do not react to gp120 will be unaffected by this treatment.



HIV, and T<sub>4</sub> cells which are infected with HIV, will be unaffected by this treatment. Because this treatment does not affect the virus, there is no selective pressure towards resistance.

Because the CD4 binding site has been removed, the drug will not bind other T<sub>4</sub> cells. Small amounts of exogenous IL-2 will reverse energy caused by binding of free gp120.

## Immune System Reconstitution Possible

The same mechanism that causes bystander cell death appears to cause T cell progenitor (thymocyte) loss in AIDS. All thymocytes display CD4 early in maturation, which makes all of the future T<sub>8</sub> and T<sub>4</sub> cells vulnerable to bystander cell death by crosslinking.

