

I am Ruella D'souza. Today We will be beginning Unit 5, complement system and in this module we shall be studying the classical activation pathway.

The outline of this module introduction followed by the components of the complement system.

The activation of complement; the steps in the classical pathway, MAC that is membrane attack complex and regulation

at the conclusion of this presentation, the student will be able to understand the complement system.

And comprehend the steps, mechanism, and regulation of the classical pathway.

The complement system is the major effector branch of the humoral immune system in vertebrates.

It comprises of seven functional categories.

The first one -complement component

Initiation, enzymatic mediators.

Membrane binding.

Inflammatory mediators.

Membrane attack proteins

Complement receptor proteins and regulatory proteins.

The components of the complement system

Include soluble proteins and glycoproteins.

This circle as inactive proenzyme's.

That undergo proteolytic cleavage in

order to remove the inhibitory fragment.

These proteins are synthesized

mainly by the liver hepatocytes.

These are designated by numbers,

letters, or common names.

For example,

they may be called factor D or any

one of the factors from C1 to C9.

The fragments made upon activation

are two and have different sizes.

The smaller fragment is called

the a fragment while the larger

fragment is called b. complexes with

enzymatic ability are designated

with a bar drawn over them.

For example,

you can see C4b2a with a bar

over it indicating that it is C3.

Convertase . Next is the activation.

The complement activation may occur

by one of three possible pathways.

The classical pathway.

The alternative pathway or lectin pathway

The classical pathway is antibody dependent,

which means that it is activated by the

formation of an antigen antibody complex.

The antibody in question is usually

Immunoglobulin M or Immunoglobulin G.

The classical pathway involves

C1,C2,C3 and C4 proteins.

The initial activation steps results

in the formation of C5 and the final

steps of all three pathways is the

formation of the membrane attack complex.

Let us now go into the classical

pathway up on your screen.

You have a comprehensive vision.

Of what the pathway looks like,

it begins with the antigen antibody,

complex formation and it ends in

the formation of a pore in the

microbial plasma membrane .

Let us now take each step and go through

the steps in the classical pathway.

The first step.

The first component of this pathway is C1.

It exists as C1 q , r & s,

which are the subcomponents of this molecule.

It begins with the binding of C1q to,

the antigen antibody complex.

One molecule of C1r activates

auto catalytically and in turn

activates another molecule of C1r.

Together,

these then activate two molecules of C1 s.

Thus we have a functional

molecule of $C1qr^2s^2$.

We now go to Step 2.

The $C1s$ is responsible for cleavage

of the components $C2$ and $C4$. $C4$ is

cleaved into the smaller fragment $C4a$.

And a larger fragment $C4b$.

Likewise,

$C2$ is cleaved into smaller,

fragment $C2a$, and a larger fragment, $C2b$.

The components now bind in the order

of $C4B$ and $2A$ to form an enzymatically

active component called $C3$.

Convertase. $C3$ Convertase is

now involved in step three.

It is responsible for hydrolysis

of many more.

$C3$ molecules and it splits them into

the smaller fragment $C3a$ and the

larger fragment $C3b$. fragment C

$3B$ combines with the $C4B2A$ fragment

to form what we call $C5$ convertase.

As you can see on your screen,
this step three is the major amplification
step in the classical pathway, Step 4.

In step 4 the C3b component
which combines with C5, cleaves
the C5 into a smaller fragment
and a larger fragment. It is the
C5a and the C5b respectively.

Step 5 in Step 5 the C5b fragment
is responsible for binding to C6 and
this is the initiation of formation
of the membrane attack complex.

Subsequent to this one molecule of
C7 also attaches and is followed
by attachment of 1 molecule of C8.

The final step is the attachment
of multiple molecules of C9.

In order to enable the formation of a pore.

As you can see in the image,
you have a microbial cell that
has a pore formed in it.

The green colored structures
are C9 and the lighter colored
structures are C5B, C6, C7 and C8.

Let us now look at the membrane
attack complex in detail.

As you can see,
the membrane attack complex is
the formation of a pore in the
membrane of a microbial cell. due
to the formation of this pore.

Ions and small molecules can
freely pass through the cell.

This will cause a destabilization
of the osmotic pressure and will
result in lysis of the cell.

Now the regulation of the classical
complement pathway is very important.

That is because the components are
capable of attacking the host cells.

And may undergo spontaneous
inactivation if they are not

stabilized with other components.

We have the presence of regulatory proteins.

For example,

the C1 inhibitor which causes

the disassociation of $C1r^2s^2$ from C1q.

We can also have factor one,

which is a serine protease and HRF.

What we call the Homologous restriction factor,

which blocks the binding of C9.

To summarize this module,

the beginning of the classical pathway is

by the formation of an antigen antibody,

complex to which complement protein One binds.

This, in turn,

activates C2 and C4 cleaving them.

Into larger and smaller fragments

there is the formation of

a C3 convertase which will break C3

into larger and smaller fragments.

A combination of the larger fragment

of C3 leads us to the formation

of a C5 convertase C5 convertase

will cleave C5 into larger and smaller

fragments and C5b is responsible.

For initiating the formation of Mac

that is membrane attack complex along

with C6C7C8 and many molecules of C9.

For your references you can

refer to any of your

prescribed textbooks. Thank you.