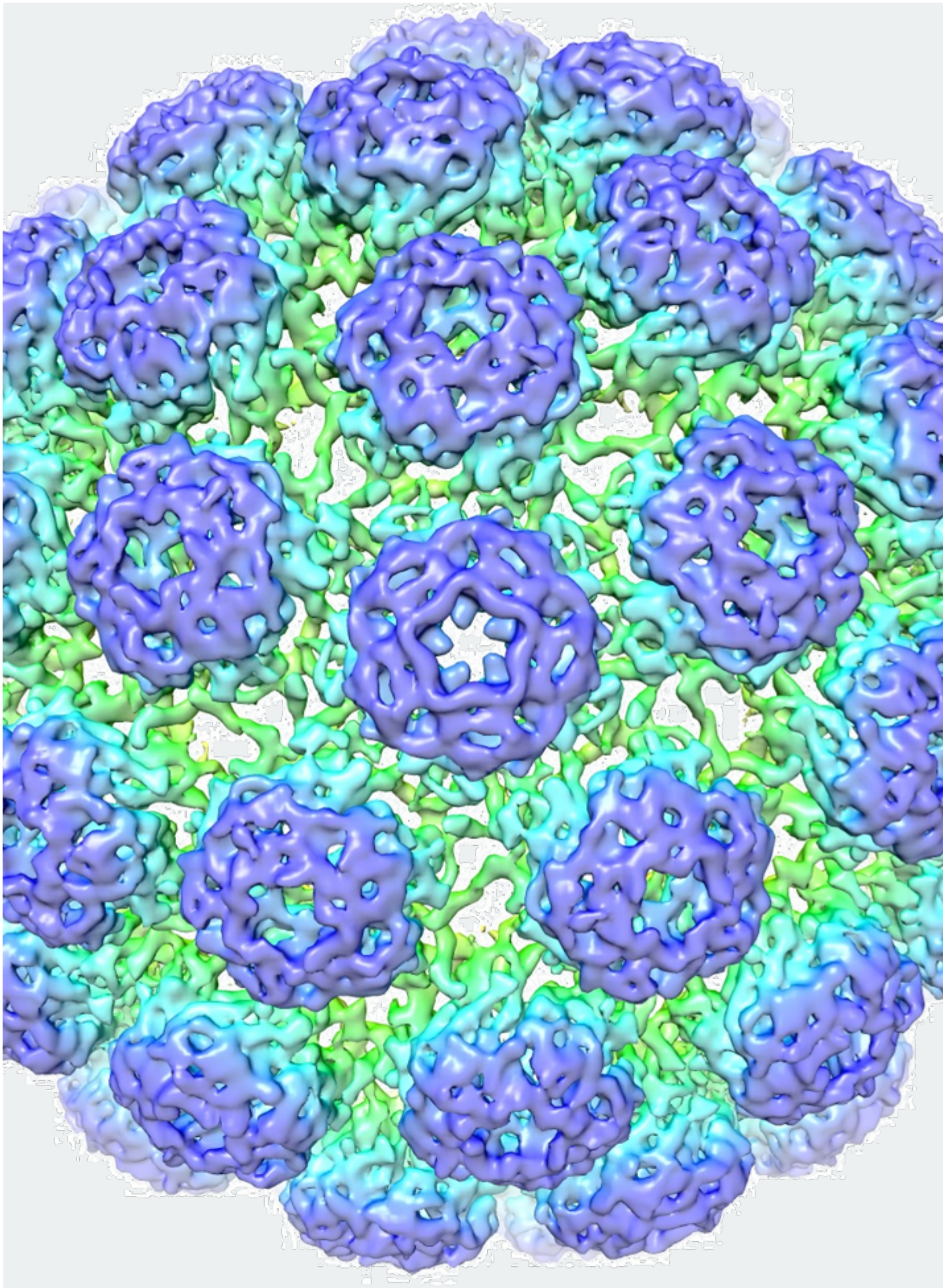
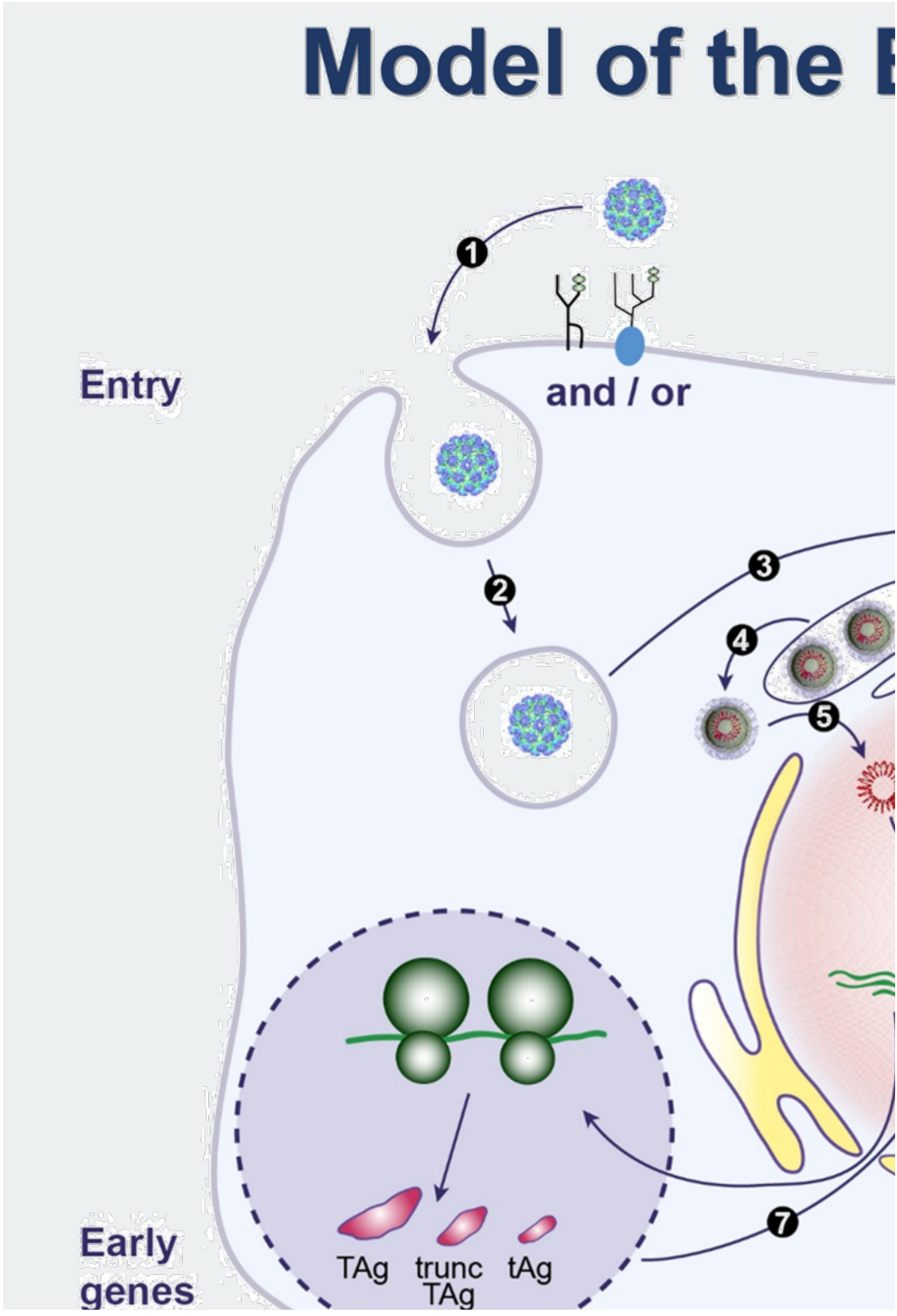
BK VIRUS

The BK virus was discovered in 1971 and is part of the *Polyomaviridae* family. It is a non-enveloped, circular, double-stranded human DNA virus, the primary infection of which occurs during the first ten years of life.



Virus BK (virus EM)

Virus BK *(cryo-EM)*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Pathogenesis

Primary infection with the BK virus generally occurs in childhood where approximately 50% of children aged 3-4 years have antibodies directed against this virus. It is often asymptomatic or can be associated with a small upper respiratory infection. Reactivations occur mainly in a context of immunosuppression, with a particular predisposition for kidney or bone marrow transplant patients.

• Tubular nephropathy affects approximately 1 to 10% of kidney transplant recipients and hemorrhagic cystitis affects approximately 5 to 15% of bone marrow transplant recipients. In kidney transplant recipients, progression of infection is associated with nephropathy leading to graft loss (up to 60% of infected patients). BK virus-associated nephropathy occurs on average between the 9th and 12th month after transplantation. Its prevalence is around 3 to 10% in transplant recipients.

• Hemorrhagic cystitis affects marrow transplant recipients, particularly in allogeneic transplants within 2 months following the transplant. In the most severe cases, hematuria can be responsible for the formation of clots and obstruction of the urinary tract, hemorrhages or even kidney failure.

Diagnosis

The diagnosis of BK virus infections is made by looking for viral DNA in urine and/or plasma. It is now recommended in the monitoring of transplant patients.

Treatment

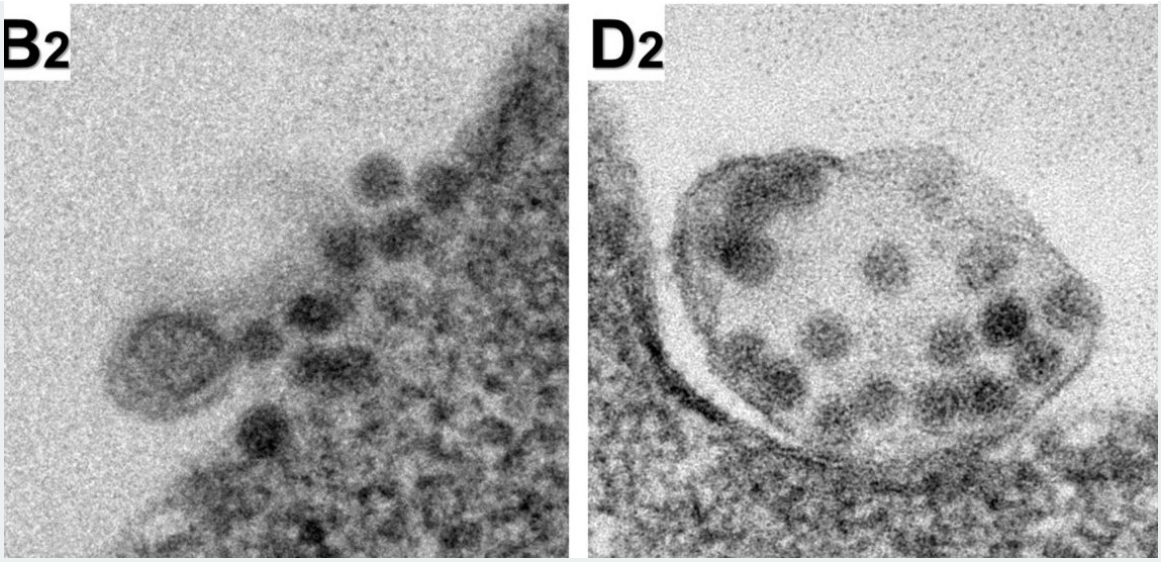
There is currently no specific antiviral treatment directed against BK virus. Indeed, this virus does not have a viral polymerase and uses the cellular machinery as much as possible to replicate. In the case of nephropathy in kidney transplant recipients, the first action consists of modulating immunosuppression in order to control the infection. Unfortunately, we also have to manage the risk of acute rejection that this creates. Different strategies make it possible to modulate immunosuppression: stopping a molecule, reducing the doses or even changing the molecule to an immunosuppressant of the same class or another class.

Research projects

• **Development and selection of potentially antiviral molecules (active against the BK virus) and practical tools (measurement of virus replication or study of the viral replication cycle)**

• **Clinico-biological studies**: study of risk factors for the development of BK virus nephropathy in pre-transplantation, development of a new BK virus detection tool and characterization of BK virus in cell culture and in transplanted patients

• **Fundamental studies:** study and characterization of the BK virus viral cycle (viral entry, replication, assembly) and identification of cellular dependence and restriction factors
Concerning the viral cycle, the team was able to show that the BK virus used extracellular vesicles to spread from one cell to another. This new mode of transmission is independent of the binding of the naked virus to sialic acids but remains sensitive to neutralizing Abs which target a later stage of viral entry. This new mode of virus secretion facilitates viral dissemination.



B2: Electron microscopy of naked BK virus on the surface of VERO cells
D2: Electron microscopy of quasi-enveloped BK virus on the surface of VERO cells.
Handala et al., Journal of Virology, 2020