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Plant virus capsids as biotemplates for nanomaterials and their use in nanotechnology

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Bio-nanotechnology is the fusion of biology and nanotechnology, which takes advantage of biomaterials to create materials and devices on the nanoscale level. Biomaterials such as DNA, RNA, proteins, and viruses are used as building templates for nanomaterials. Of the many biomaterials used for building nanomaterials, viruses are of particular interest to the nanotechnology field because of their highly uniform structures, small size, and ability to self-assemble. Viruses are protein shells that assemble from self-similar protein subunits into capsids with precise three-dimensional (3D) structure. The genetic material is located in the interior of the capsid as circular, single-stranded or double-stranded fragments. Enveloped viruses contain a bi-lipid layer on the exterior that provides targeting specificity to the virus. Plant and bacteria viruses (bacteriophages or phages) are other types of viruses that are not pathogenic to animals that make them amenable for use in material science. Plant viruses have been genetically and chemically modified for broad uses from vaccines to nanomaterials. The variety of nanomaterials generated in rod-like and spherical viruses is highlighted for tobacco mosaic virus (TMV), Cowpea chlorotic mottle virus (CCMV), and mosaic virus (CPMV). Functional biohybrid nanomaterials find applications in biosensing, memory devices, nanocircuits, light-harvesting systems, and nanobatteries.

Applications of Plant viruses in nanotechnology

Tobacco Mosaic Virus

Tobacco mosaic virus (TMV) is a classic example of a rod-like plant virus consisting of 2,130 identical protein subunits arranged helically around genomic single-RNA strand. Native TMV particle is 300 nm long and 18 nm in diameter, with a 4-nm cylindrical cavity along the central core. It has been shown that the surface properties of TMV can be manipulated chemically or genetically without disrupting the integrity and morphology of TMV capsids. The polar outer and inner surfaces of TMV have been exploited as templates to grow metal or metal oxide nanoparticles such as iron oxyhydroxides, CdS, PbS, gold, nickel, cobalt, silver, copper and iron oxides, and silica in many studies.

Cowpea mosaic virus

Cowpea mosaic virus (CPMV) is a member of the comovirus group of plant viruses. The structure of CPMV has been determined to 2.8 A° resolution. The virus particles are 30 nm in diameter and display icosahedral symmetry formed by 60 copies of a subunit with two different proteins. With its icosahedral protein coat shape, it is capable of exterior display and encapsidation of molecules which enables cowpea mosaic virus as a powerful non-invasive imaging tool and as a delivery system for therapeutics. Cowpea mosaic virus-based nanomaterials have uses as biosensors in antibody microarrays. CPMV labeled with binding molecules which are analyte specific, such as DNA, antibodies, or peptides, and which are simultaneously labeled with fluorescent dyes have a niche in immunoassay use. This function takes advantage of the multiplexing capability of CPMV, to conjugate CPMV with more than one moiety at one time. Antibody microarrays are one such application of multiplexing, where the normal tracer molecules are substituted for EF-CPMV scaffolds conjugated with fluorescent dyes and antibodies simultaneously. Another application of Cowpea mosaic virus-dye complex is in vivo imaging. The CPMV-A555 nanoparticle that was first chemically conjugated to fluorescent dyes by NHS ester chemistry, was more successful than the dye alone at dispersing to all blood vessels, and did not aggregate. Over a period of 72 hours, the CPMV-

A555 was excreted and no toxic effects were noted. Fluorescently labeled CPMV can also be used as an imaging probe to visualize the vasculature and blood flow in living mice which enabled the ability of labeled CPMV to image the vasculature of tumors.

Cowpea chlorotic mottle virus

Cowpea chlorotic mottle virus (CCMV) is a member of the bromovirus group of the Bromoviriedae family. The CCMV genome consists of three unique single-stranded, Positive sense RNA molecules that are encapsidated separately. The capsid is composed of 180 identical protein subunits (20.3 kDa each) that form a 28.6 nm diameter icosahedral shell. A recent study by Comellas-Aragone's is a good example of the synthesis of biohybrid nanostructured materials based on viruses. They were able to functionalize the exterior of CCMV with polyethylene glycol (PEG) and entrapped polystyrene sulfonate (PSS) in the interior of the capsid after the self-assembly of the PEG-modified capsid. This expands the possibilities for the generation of new types of virus-hybrids nanomaterials. Trevor and Young are the pioneers in the use of CCMV as a nano-container. They have reported the mineralization of polyoxometalate species, the encapsulation of anionic polymers, the encapsulation of iron oxide (Fe_2O_3) particles, and the reduction and symmetry directed synthesis of gold nanoparticles. Engineered plant virus capsids have been developed for cell-targeted delivery of therapeutic activity. CCMV has also been recently used as a combined cell-targeted, therapeutic delivery system.

The use of plant viral capsids for materials chemistry at the nanoscale provides a number of unique advantages. Protein cages are biological in origin and, as such, are amenable to genetic manipulation and large-scale production. The monodispersity, chemical specificity, and the three dimensional character of viruses bring unique capabilities for the organization of materials in the nanoscale. Reports in which viral constructs are individually addressed for determining conductance, switching capabilities, memory effects, elasticity, and stability have demonstrated the usefulness of these types of materials at the nanoscale. As the field of bionanotechnology continues to grow, new research discovers, or designs, novel applications for virus platforms, as well as new hurdles to overcome. One such hurdle for virus-based nanotechnology is in the ability to with-stand more extreme conditions, such as pH, temperature, and organic solvents. Therefore, the discovery of novel viruses from more extreme environments that may be naturally tolerant of extreme conditions is important to the future. Genetic modification creates more resilient viral particles is also a potential research topic for the future. Novel methods for mass production of viral particles for self-assembly are also necessary in future. The ability to scale-up current and future applications, in economical ways, can play a large role in the growth of the field.

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