



## USING ROTAVIRUS VP6 TO PRODUCE PROTEIN COATED INORGANIC NANOPARTICLES

Liliana Carreño-Fuentes<sup>1</sup>, German Plascencia-Villa<sup>2</sup>, Laura Palomares<sup>1</sup>, and Octavio T. Ramírez<sup>1</sup>;

<sup>1</sup>Departamento de Medicina Molecular y Bioprocesos, Instituto de Biotecnología, UNAM, Cuernavaca, México, 62210; <sup>2</sup>Department of Physics and Astronomy Applied Engineering and Technology, UTSA, San Antonio, USA, 78249. lcarreno@ibt.unam.mx, tonatiuh@ibt.unam.mx

*Key words: Nanostructures, encapsulation, charge*

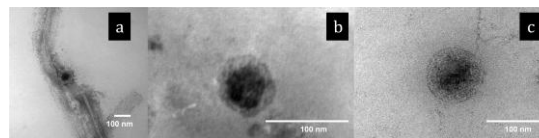
**Introduction** Protein cages that naturally self-assemble around nucleic acids or negatively charged cargo have been employed to encapsulate inorganic nanoparticles in their core<sup>1</sup>. Rotavirus VP6 assembles over VP2, which has no substantial charge in its surface, to form double-layered particles. In the absence of VP2, VP6 can assemble into nanotubes or spheres depending on the pH<sup>2</sup>. We have previously demonstrated that the intrinsic properties of VP6 allow the synthesis of metallic nanoparticles and nanowires on the external and internal surface<sup>3,4</sup> of VP6 nanotubes, but the capacity to encapsulate nanoparticles inside VP6 structures has not been explored.

Here, we developed strategies to induce the encapsulation of neutral magnetic FeOX nanoparticles or negatively charged gold nanoparticles.

**Methods.** VP6 was produced in the insect cell baculovirus system as previously described<sup>3,4</sup>. The supramolecular structures of VP6 were disassembled with CaCl<sub>2</sub> and reassembled by dialysis at different pH in the presence of aspartic capped gold nanoparticles of 40 nm in diameter or FeOx nanoparticles of 70 nm. Functionalizations were analysed by TEM (Jeol JEM-1011) and STEM (BF, DF, EDS) (HITACHI FE-SEM S5500) to determine encapsulation.

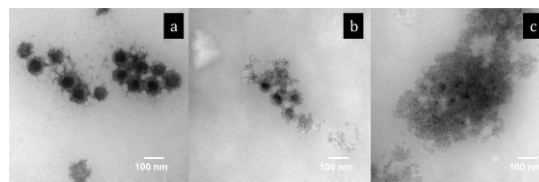
**Results** Reassembly at two different pH was tested. At pH 7.5, VP6 assembled into nanotubes of 80 nm, as previously observed in the absence of VP2<sup>2</sup>. Nanoparticles enclosed by VP6 were observed in the nanotubes. Also, spheres of 80-100 nm (figure 1) encapsulating the two types of nanoparticles tested, were also observed. Elemental analysis (EDS) corroborated the presence of gold or iron in the core of the formed nanostructures. In accordance with the literature, only nanotubes were observed in control experiments without nanoparticles at pH 7.5. Therefore the formation of spheres at this pH, not previously observed in the absence of VP2, was most likely directed by

the size and shape of the nanoparticle, and not by nanoparticle charge.



**Fig.1** Inner functionalization of VP6 nanostructures.at pH 7.5. a)Nanoparticle encapsulated in a nanotube, b) Sphere with gold nanoparticle core. C) FeOx core.

When reassembly was carried out at pH 4.6 only spheres containing the metal nanoparticles were observed (Figure 2). Control experiments without nanoparticles only contained spheres, as previously observed<sup>2</sup>. EDS was performed on experimental samples with gold nanoparticles. Gold was found inside the produced nanostructures.



**Fig.2** Reassembly at pH 4.6. a) control; b) Gold nanoparticles; c) FeOx nanoparticles.

**Conclusions** Metal nanoparticles can direct the assembly of VP6 into structures only previously found with the inner VP2 core. The versatility and intrinsic capacity of VP6 to encapsulate different kinds of cargos was demonstrated.

**Acknowledgements** This work was financially supported by PAPIIT UNAM IT200113. We thank V. Hernández, and R. Pastor for technical assistance, A. Lecona, INSP Electron Microscopy unit and NIH RCMI Nanotechnology and Human Health Core and Kleberg Advanced Microscopy Center at UTSA.

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