Getting health allies from agriculture enemies

In recent years, research in nanotechnologies has demonstrated that nanometer-sized particles constructed using a wide array of materials (e.g. metals, lipids, polymers, proteins) can offer answers to unmet questions concerning drug/vaccine delivery. Ideally, these systems should prevent the off-target distribution of a drug allowing to use the minimum efficient dose, and in the case of vaccines, should also be needle-free and heat stable. These goals are not trivial to achieve as they imply the possibility to control the drug/vaccine release in terms of rate, time and place. Nanoparticles have at least one dimension ranging between 1-100 nm, can be used to deliver drugs/vaccines through various routes and have the potential to improve the overcoming of biological barriers and the access to cells and sub-cellular compartments. They can be constructed using top-down (lithography) or bottom-up (exploiting self-assembly properties of the material) approaches.

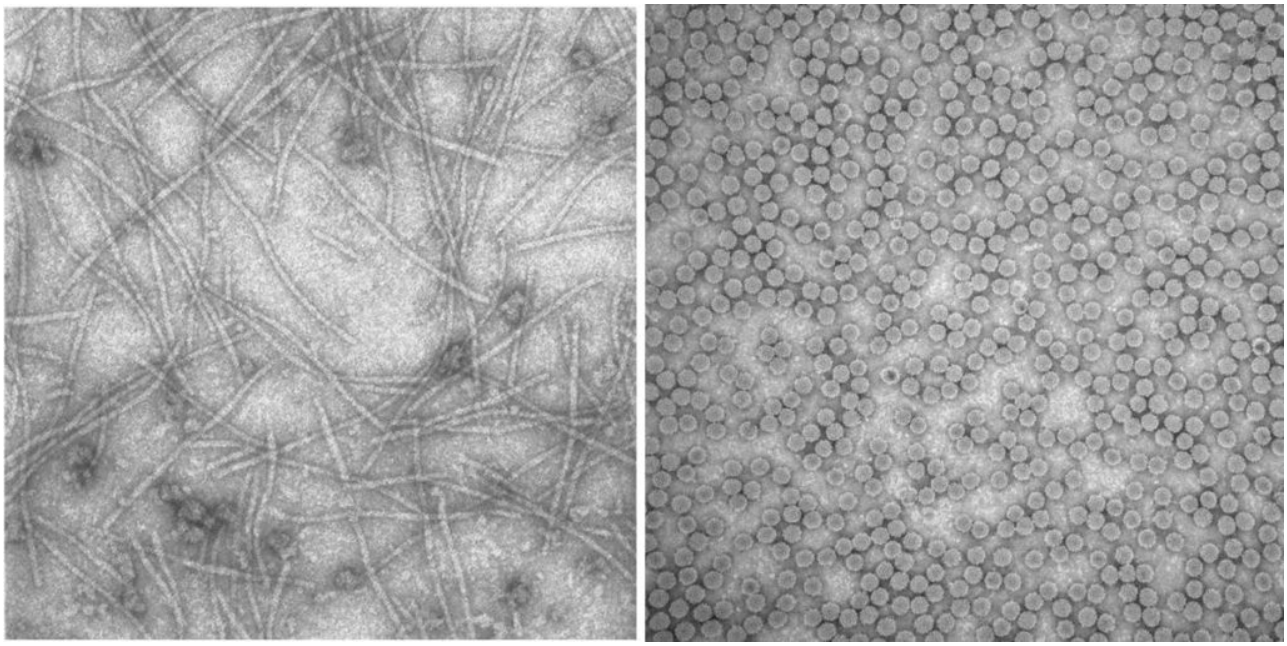

Fig. 1. Transmission electron microscopy images of purified Potato virus X (left) and Tomato Bushy Stunt virus (right).

The research focused on the construction, production, and structural and functional characterization of nanoparticles is strongly multidisciplinary. Just think that even viruses are considered as nanoparticles because of their structural features, and are explored as carriers for drug/vaccine delivery. This may seem a madness as we are used to associate viruses to diseases. Indeed viruses, made of a DNA or an RNA genome protected by a protein capsid, are obligate intracellular parasite that exploit and kill cells for their reproduction inducing different types of

pathologies. Nevertheless, each virus has developed highly specific strategies to parasite the cells it has adopted as host. In other words, each virus is able to infect only a very restricted number of cell types (often only one) within a very restricted number of living species (often only one). Moreover, to get empty viral capsids unable to replicate, is by now quite easy. All these aspects allows to circumvent the problem of disease induction by viruses and to make allies of these enemies.

Plant virus nanoparticles (pVNPs) might represent an ideal delivery tool in terms of biocompatibility and biodegradability. They have evolved to use plants as their reproductive hosts, and to this aim, have developed infection strategies very different from those adopted by their animal counterparts, so that if injected into animals they behave as unreplicative nanobjects. Moreover, they offer a wide range of shape diversity, are easy to be chemically/biologically engineered on both the surface and/or the internal cavity of the capsid, are easy, safe and rapid to be produced at low costs in plants.

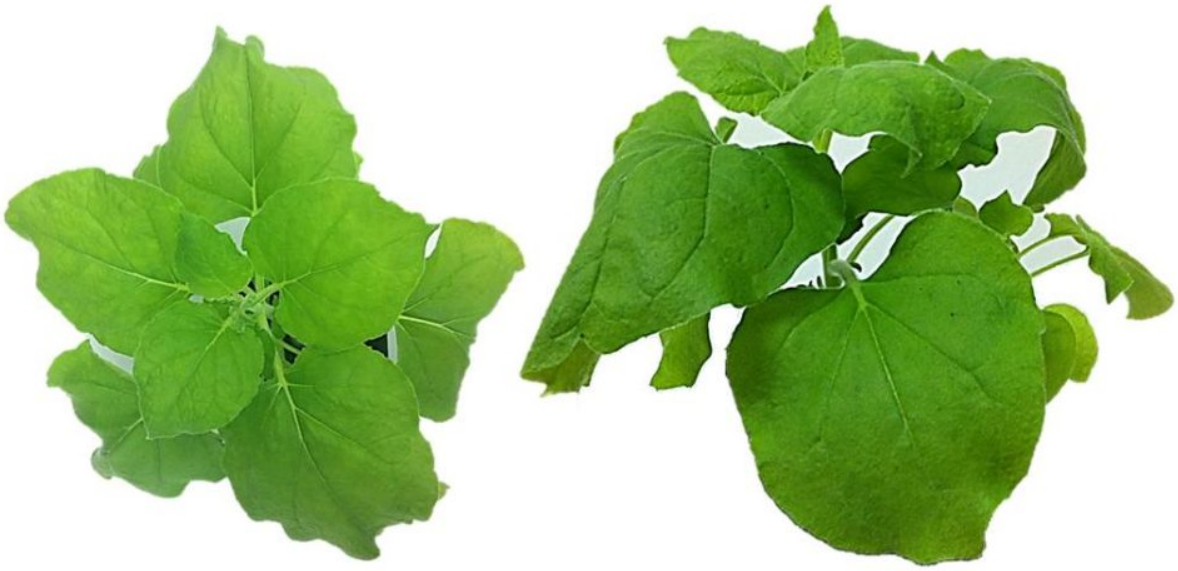

Fig. 2. Nicotiana benthamiana plant top (left) and side (right) view.

In this perspective, we are exploring the potential for biomedical applications of two structurally different plant viruses, the filamentous Potato Virus X (PVX) and the icosahedral Tomato Bushy Stunt Virus (TBSV) that we produce inoculating the tobacco-relative *Nicotiana benthamiana*. In previous studies, we have defined how, by biotechnology interventions, we can produce particles carrying antigens for vaccination purposes, and demonstrated that these particles work excellently in activating different types of immune responses (innate and adaptive, humoral and cell-mediated). Because intrinsic toxicity cannot be taken for granted, we have also verified that PVX and TBSV are neither toxic nor teratogenic. To complete the picture, more recently we observed

that, when injected in mice, these structurally robust pVNPs do not induce alterations of tissues architecture, although having different behaviors in terms of persistence in the blood stream and biodistribution, probably as a function of their shape and surface characteristics. Overall, these information sets a solid ground reference for future testing of pVNPs designed to answer to specific health challenges, and there is no reason to suppose these nanoparticles will not progress rapidly contributing to widen the number of devices available to face evolving issues in biomedicine.

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Publication

A biodistribution study of two differently shaped plant virus nanoparticles reveals new peculiar traits.
Lico C, Giardullo P, Mancuso M, Benvenuto E, Santi L, Baschieri S
Colloids Surf B Biointerfaces. 2016 Dec 1