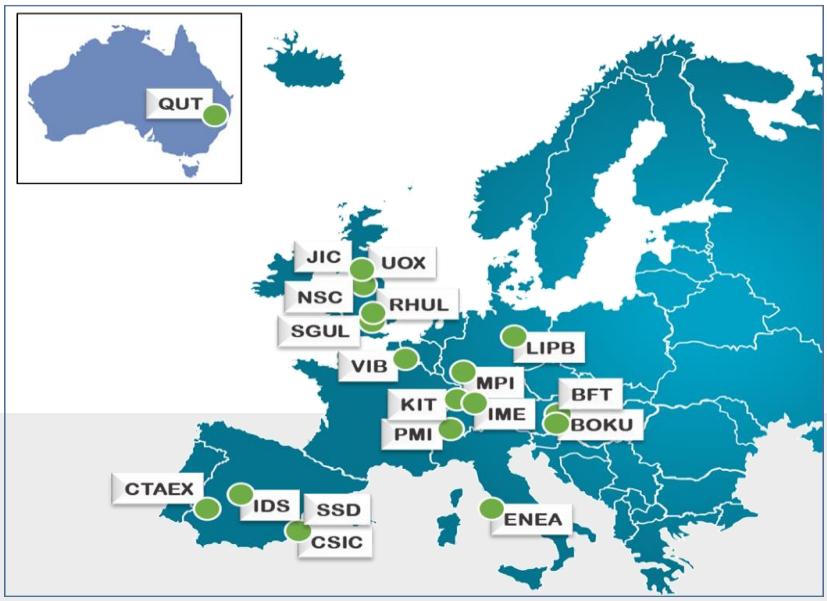
01/06/2019

Newcotiana

TOBACCO PLANTS AS BIOFACTORIES

NEWCOTIANA is a EU H2020 research and innovation action aimed at developing new tobacco-related crops for Molecular Farming using New Plant Breeding Techniques (NPBTs). NEWCOTIANA aims to modify the composition and therefore the use we make of tobacco plants, replacing smoking nicotine by added value substances used in medicine and cosmetics. During the project, we will develop elite plant varieties of the genus Nicotiana for the production of end-value chemicals including proteins and metabolites.

NEWCOTIANA involves private companies, universities and research centers from seven European countries and the Technological University of Queensland in Australia. Among other objectives, we aim to revalue the traditional cultivation of tobacco, providing it with new uses compatible with health and contributing to revitalize tobacco areas in decline with products of high added value. *Nicotiana tabacum* (cultivated tobacco) and *Nicotiana benthamiana* (Australian dwarf tobacco) will be used as broad Molecular Farming platforms.



Nicotiana benthamiana

is a close relative of cultivated tobacco (N. tabacum) indigenous to Australia. It has several wild ecotypes, and the laboratory strain (LAB) is originated from a Australian desert ecotype.

The use of plants as biofactories for production of added value chemicals as medicines or cosmetics is often known as Molecuilar farming. *Nicotiana benthamiana and Nicotiana tabacum* are the preferred plant species for Molecular Farming. *N. benthamiana* is particularly well suited for producing recombinant proteins in biocontainment due to its permissiveness to propagation of transient expression vectors and the high accumulation of recombinant products.

NEW PLANT BREEDING TECHNIQUES

In recent years, a group of New Plant Breeding Techniques (NPBTs) have emerged bringing unprecedented opportunities for Plant Biotechnology. In Newcotiana we will make use of four of these NPBTs:

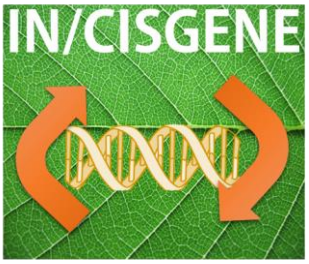
Site-Directed Nuclease (SDN)-mediated genome editing. This includes the popular CRISPR/Cas technique, which produces targeted modification of genomes induced by DNA breaks. SDNs are classified in: SDN1 induce small errors due to mis-reparation of DNA breaks; SDN2 is designed to introduce small editions encoded in a donor sequence that works as Homologous Recombination (HR) template; SDN3 introduces large transgenes at precise genome locations.

Cisgenesis and Intragenesis are genetic modification approaches where the DNA fragments used are restricted to those derived from sexually compatible species.

Agroinfiltration is a transient delivery of recombinant genes to plant cells to obtain recombinant gene expression without transmission to the offspring. *Agrobacterium tumefaciens* is used as a delivery vehicle and often involves a self-replicative genetic device to enhance extension and productivity.

Graft-mediated genome transfer across graft junctions creates new, non-transgenic synthetic crops with new chemotypes arising from the combination of the specialized metabolisms of the two different species, next to other agronomic features of interest.

A recent sentence of the European Court of Justice considers edited crops as GMOs. The ruling was contested by many scientific organizations. GMO status affect Newcotiana only partially, as our plants can be grown under confined conditions



The Nicotiana genus is especially amenable to the four NPBTs planned in our project. N. benthamiana carries a defective mutation that enhances its permissiveness to propagation of transient expression vectors via agroinfiltration. Nicotiana species are easily transformable using standard Agrobacterium-mediated techniques and, for yet unknown reasons, most (SSN) editing tools have shown exceptional efficiency levels in Solanaceae species including tobacco and *N. benthamiana*. Finally, graft-mediated horizontal genome transfer, a revolutionary breeding technique described as the tool to "produce new species without sex", has been optimized using Nicotiana species and offers extraordinary breeding possibilities for this genus. Together, NPBTs and Nicotiana are the ideal combination for innovation.

FIRST ANNUAL Newcotiana MEETING IN VALENCIA

The first Newcotiana annual meeting took place in Valencia, 5-6th March 2019 and was attended by 40 participants from EU and Australia.

During the meeting, delegates discussed the progress and future directions in the different workpackages in parallel sessions, and the conclusions were discussed in plenary sessions.

In WP1, delegates discussed the advances in the N. benthamiana genome project and presented the integration of the latest genome assembly in the collaborative Web Apollo genome browser. The new editing tools developed during the first 12 months were also discussed.

WP2 delegates updated partners on the progress made in identifying target genes for breeding protein biofactories.

During WP3 parallel meeting we discussed the advances in metabolite traits, with interesting results obtained in the accumulation of key added-value metabolites, and plans were made for best design of upscale activities in WP4, planned to start in year 2

WP5 and WP6 discussions were held jointly with representatives of Pharma-Factory a CHIC H2020 projects. This was a fruitful session where we put together our respective dissemination and communication strategies and discussed possible synergies and collaborations.

During the first annual meeting, Newcotiana organized jointly with Pharma-Factory project, an open workshop entitled "Plant Biofactories in the Genome Engineering Era", that received more than 100 external attendees.

Newcotiana OUTREACH and COLABORATION ACTIVITIES

During the first year of the project Newcotiana partners participated in an intense program of communication and dissemination activities. Here we present some of the most important ones.


Medicamentos y vacunas en las hojas de tabaco

Estudio de la otra cara del tabaco

El investigador Diego Orzáez lidera un proyecto en el que participa la UPV

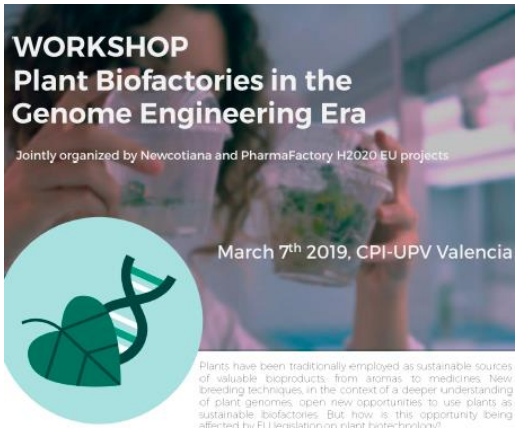
Australian tobacco may help treat disease

First Joint Press Release: Newcotiana in the News, TV, radio, newspapers around Europe and Australia.

Newcotiana presented at the Arts and Design festival in London 2018 with an innovative setup

Newcotiana was explained to the general public during the Night of Researchers in a joint experience with CHIC project

Meetings with stakeholders at the tobacco farming area in Extremadura, Spain



The Open Workshop "Plant Biofactories in the Genome Engineering Era" counted with top-class invited speakers as Lluis Montoliu and attracted public from academia and industry

Joint meetings and collaborations with PharmaFactory and CHIC projects