



PROJECT PERIODIC REPORT

Grant Agreement number: 222716

Project acronym: SMARTCELL

Project title: Rational Design of Plant Systems for Sustainable Generation of Value-Added Industrial Products

Funding Scheme: Large collaborative project

Date of latest version of Annex I against which the assessment will be made:
29th October, 2008

Periodic report: 1st 2nd 3rd 4th

Period covered: from 1 January 2009 to 30 June 2010

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¹ Usually the contact person of the coordinator as specified in Art. 8.1. of the Grant Agreement.

² The home page of the website should contain the generic European flag and the FP7 logo which are available in electronic format at the Europa website (logo of the European flag: http://europa.eu/abc/symbols/emblem/index_en.htm logo of the 7th FP: http://ec.europa.eu/research/fp7/index_en.cfm?pg=logos). The area of activity of the project should also be mentioned.

Declaration by the scientific representative of the project coordinator

I, as scientific representative of the coordinator of this project and in line with the obligations as stated in Article II.2.3 of the Grant Agreement declare that:

- The attached periodic report represents an accurate description of the work carried out in this project for this reporting period;
- The project (tick as appropriate)³:
 - has fully achieved its objectives and technical goals for the period;
 - has achieved most of its objectives and technical goals for the period with relatively minor deviations.
 - has failed to achieve critical objectives and/or is not at all on schedule.
- The public website, if applicable
 - is up to date
 - is not up to date
- To my best knowledge, the financial statements which are being submitted as part of this report are in line with the actual work carried out and are consistent with the report on the resources used for the project (section 3.4) and if applicable with the certificate on financial statement.
- All beneficiaries, in particular non-profit public bodies, secondary and higher education establishments, research organisations and SMEs, have declared to have verified their legal status. Any changes have been reported under section 3.2.3 (Project Management) in accordance with Article II.3.f of the Grant Agreement.

Name of scientific representative of the Coordinator: Kirsi-Marja Oksman-Caldentey

Date: First version submitted 31.8.2010 to the Commission.

Second version submitted 9.11.2010 to the Commission

Third version submitted 4.3.2011 to the Commission

Fourth version submitted 7.4.2011 to the Commission

Fifth version submitted 18.4.2011 to the Commission

For most of the projects, the signature of this declaration could be done directly via the IT reporting tool through an adapted IT mechanism.

³ If either of these boxes below is ticked, the report should reflect these and any remedial actions taken.

1 PUBLISHABLE SUMMARY



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Project coordinator: Dr. Kirsi-Marja Oksman Caldentey
VTT Technical Research Centre of Finland

Project website address: <http://www.smart-cell.org/>

1.1 A summary description of project context and objectives

The overall scientific objective is to gain a thorough understanding and exploitation of the extraordinary complexity of the biochemical capacity of plants. This can be done by means of the developed enabling technologies which facilitate rational pathway engineering of plants and plant cells towards desired secondary metabolites systematically in a predictable and reproducible way. These enabling technologies include multigene transformation technologies and developing metabolomics and bioinformatics tools to handle huge data sets which have been and will be generated in the course of the project. Important element is also to establish and optimize large-scale production platforms for plants and plant cell cultures. The specific aims for the first reporting period were:

- to collect candidate genes for the fast track transformation experiments
- to discover and validate new genes in the isoprenoid and TIA pathway (partly)
- to develop multigene transformation techniques for tobacco with four fast track candidate genes
- to establish relevant analytical platforms for targeted and non-targeted chemical analyses
- to evaluate and optimise the production platforms for tobacco and *Catharanthus* (partly)
- to establish scale-up and down-stream systems for plants and plant cells (partly)
- to standardise data formats and data processing and to establish experimental data repository
- to ensure a widespread dissemination of results
- to comply with biosafety and regulatory issues
- to ensure the proper handling of IPR and create an IP database which will help to inform FTO strategies for SmartCell (partly)

- to grant access rights to project members and subsequently to additional third parties, including SMEs
- to organize training school for post-docs and PhD students

1.2 A description of the work during the first reporting period

In general, the SmartCell project has advanced according to the work plan with some minor deviations which are explained and justified in part 2 of this periodic report. The collaboration between partners has been active and three project meetings have been organized.

The terpenoid pathway engineering is divided in two themes: a fast track leading to 10-hydroxygeraniol and an advanced track leading to secologanin. By the end of the first reporting period the set of suitable genes leading to 10-hydroxygeraniol have been identified. Those genes are transformed into tobacco plant in different combinations by novel multigene particle bombardment transformation techniques. A large number of transformants are currently being analysed at molecular and metabolic level. Additionally these genes have been inserted into tobacco *via Agrobacterium rhizogenes* to lead hairy root cultures. Also their analysis is currently on the way. The attempts to discover all the missing genes from 10-hydroxygeraniol to secologanin have been started and the deep sequencing of our target plant of, *Catharanthus roseus*, has been designed and is currently in process. Besides of discovering functional genes the Consortium has studied the potential function of regulatory and transporter genes. To modify the terpenoid structures also some genes coding for terpenoid decorating enzymes have been discovered and functionally tested. By screening and functionally categorizing genes at structural, regulatory and transport levels a comprehensive knowledge base of how terpenoid indole alkaloid biosynthetic pathway operates in plants will be developed in the course of the SmartCell project.

The SmartCell partners have also developed several analytical platforms to profile terpenoid formation and content in different control and transgenic plants and plant cell and tissue cultures. Chromatographic (UPLC-MS, GC-MS) and spectrometric (NMR) methods as well as basic methods for flux analysis are now available for targeted and non-targeted use of analyzing terpenoid end products and their intermediates. To be able to handle huge data sets which are and will be generated during the project the data formats and data processing have been standardized and the experimental data repository has been established. Also the work for the database for repository of secondary metabolite data has been started.

The development of IPR strategy and safety regulation for transgenic material is in progress. So far no exploitable results towards patenting have been obtained. A first training workshop was organized in conjunction with the Neuchatel meeting on May 27th, 2010. The topic of the workshop was “Green Cell Factory” and was open to all SmartCell scientists as well the scientists from the hosting partner.

Substantial efforts have been made forwards large scale production of plants and cultivated plant cells and tissue in various types of bioreactors. Novel disposable *e.g.* wave-type bioreactors have been tested as well as conventional bioreactors. In connection to optimize large-scale production of plant cell cryopreservation techniques to different cell lines are now in process. The case study component *i.e.* manufacturing valuable terpenoids, 10-hydroxygeraniol and/or secologanin in an optimized large-scale system gives SmartCell a unique opportunity to directly make the transition from fundamental science to application. This part of the project will only start on month 37.

1.3 The expected final results and their potential impact and use

The **SmartCell** project addresses the specific issues for using plants as green factories for sustainable non-food products. It focuses in developing enabling technologies for plant-based products in rationally engineered plants and plant cells, especially for pharmaceuticals and speciality chemicals. This in turn will impact environmental improvement and sustainability, economic advancement and international competitiveness. Especially plant genomics and metabolomics (WP1 – WP5) are included in **SmartCell** to improve the productivity and composition of plant raw materials to known and new high-value added products. The expected impact for Europe is to exponentially increase our knowledge on molecular, biochemical, genetic and physiological aspects of plant metabolic pathways at the systems level for the rational, efficient and sustainable production of important compounds for industrial use. A major component of this exercise is the generation, protection and exploitation of Intellectual Property as well as taking into account the regulatory and biosafety issues as discussed in WP9.

The cutting edge of basic plant research is rapidly evolving from understanding the function of single genes to studying networks of genes that control complex biological processes such as production of metabolites in plant cells at the systems level (WP4, WP5 and WP8). For long-term exploitation an integrated database, compound library, cell culture collection and a genebank available for academic and industrial communities will be established. The demonstration component (WP7), which will start on month 37, i.e. manufacturing terpenoid end products, 10-hydroxygeraniol and/or secologanin, in an optimised large-scale system (WP6) gives **SmartCell** a unique opportunity to embark on the transition from the fundamental science to applications, thus validating, within the lifetime of the project concepts, tools, tangible material and resources, and also IP and regulatory/biosafety aspects. After the project a “real life” genebank, metabolomics and pathway map databases, all created in a project, will be made available to the wider academic and industrial communities. Direct involvement of SMEs and large end-user companies in **SmartCell** will support the competitiveness of European industries, specifically those dealing with industrial applications of new technologies, processes and products.

1.4 The address of the project website

www.smart-cell.org