

Regione Piemonte - CIPE 2007

**Developing white and green technologies
by converging platforms from biology and
information technology towards
metagenomics**

BioBits

Biotechnology -ICT

Ordine del giorno del 16 gennaio 2009

Piano organizzativo

Piano finanziario (cenni)

Piano scientifico

Prossime scadenze

**Dead lines-- 30 gennaio
febbraio-Marzo**

Identificazione di compiti/responsabili

Commissione coordinamento e Controllo

Costituzione ATS

BANDO CIPE 2007 bando regionale per progetti di ricerca industriale e/o di sviluppo sperimentale per l'anno 2007 nell'ambito delle "Converging Technologies" ha l'obiettivo di favorire la collaborazione tra atenei, imprese piemontesi ed enti di ricerca pubblici e privati su progetti di ricerca nell'ambito di alcune aree tematiche considerate strategiche per lo sviluppo del territorio regionale. La Regione Piemonte attraverso questo strumento intende realizzare una politica volta a sostenere lo sviluppo e il consolidamento di un'economia regionale basata sulla conoscenza e sull'**innovazione**.

Area tematica	n° id progetto	Acronimo proposta progettuale	Responsabile ricerca	Contributo approvato (€)
Cognitive Sciences - ICT	17	ICT4LAW	Gianmaria AJANI	2.344.095,00
Cognitive Sciences - ICT	10	PIEMONTE	Luca CONSOLE	1.375.872,00
Biotechnology - ICT	15	BIO_THER	Lorenzo SILENGO	3.236.250,00
Biotechnology - ICT	9	BioBITs	Paola BONFANTE	2.059.030,00
Nanotechnolgy, New materials - ICT	32	NANOCONTACT	Adriano ZECCHINA	3.250.065,00
Biotechnology - Nanotechnology	26	NanoIGT	Silvio AIME	2.736.087,00

Che cosa abbiamo proposto di fare?

Our project will integrate Biology and Information Technology platforms applying them to a soil Metagenomics system.

The goal is to identify new molecules relevant for agrochemical industries. The study will start from a complex biological system, consisting of three levels: i) populations of uncultivable bacteria living inside a symbiotic, arbuscular mycorrhizal fungus (AMF), ii) AMFs which associate to plant roots and originate the most widespread symbiosis in the plant kingdom, and iii) plant roots.

This tripartite system will be investigated as a source of undescribed molecules/metabolic pathways, and will also be analysed with simulation tools. AMFs are fundamental in projects of sustainable agriculture, they furnish a better mineral nutrition and are considered crucial means for improving the plant health increasing pathogen resistance.

In addition to this widely recognised aspects, AMFs could also be exploited as a still unknown resource to promote green (agriculture) and white (industrial) biotechnologies.

Will annotate the bacterial genes in order to identify candidate proteins/enzymes of industrial relevance; will investigate the behaviour of such systems by considering them as biological computing units and by developing models for their simulation;

Will define the metabolic pathways that in planta lead to bioactive molecules (strigolactones) which are active on the fungal/bacterial system (but are also useful in the biocontrol of plant pests);

Will produce synthetic more active analogues of such molecules.

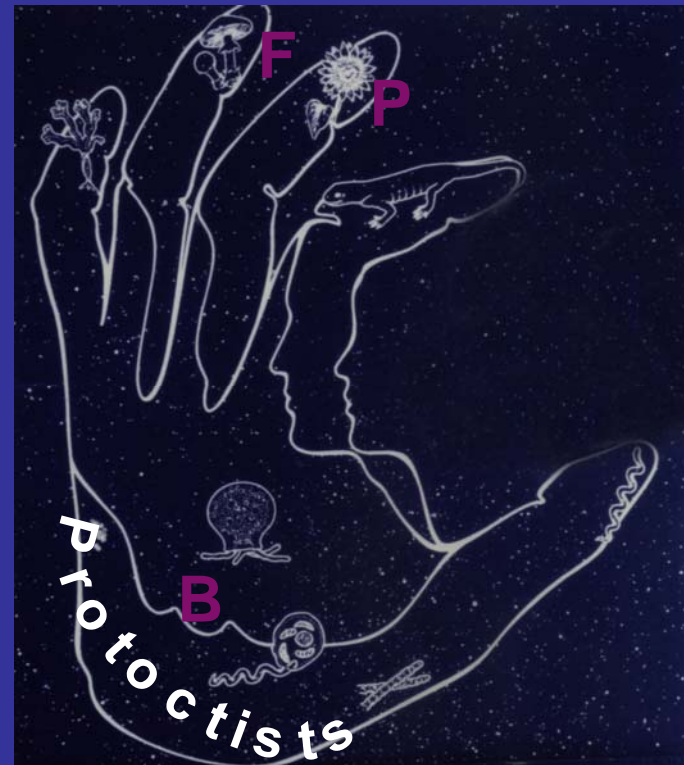
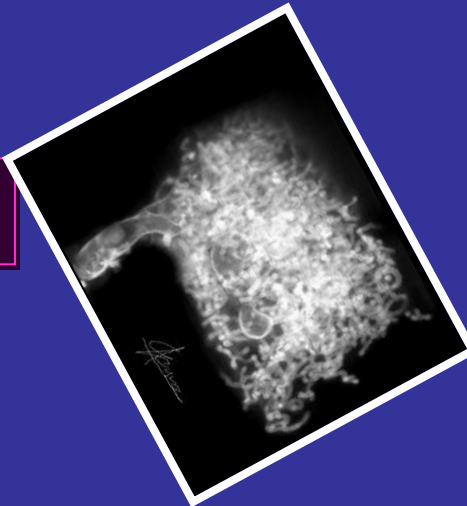
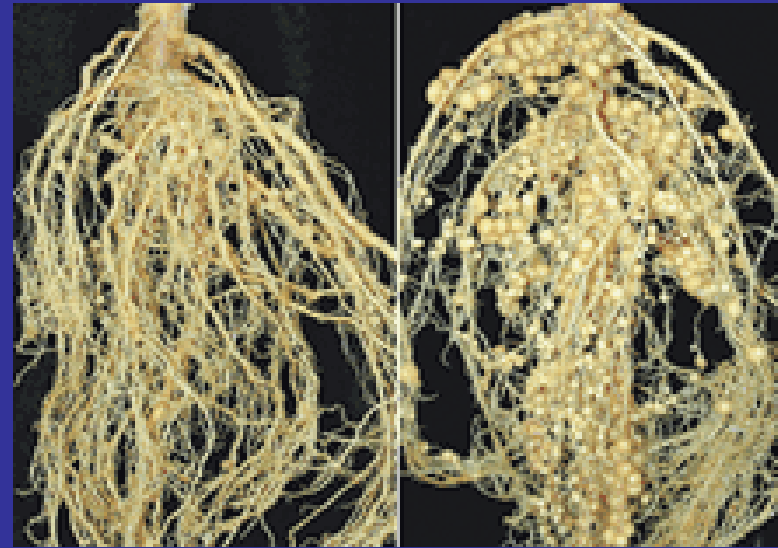
Interactions in action

Plants

Mycorrhizae

Symbiont fungi

Endobacteria



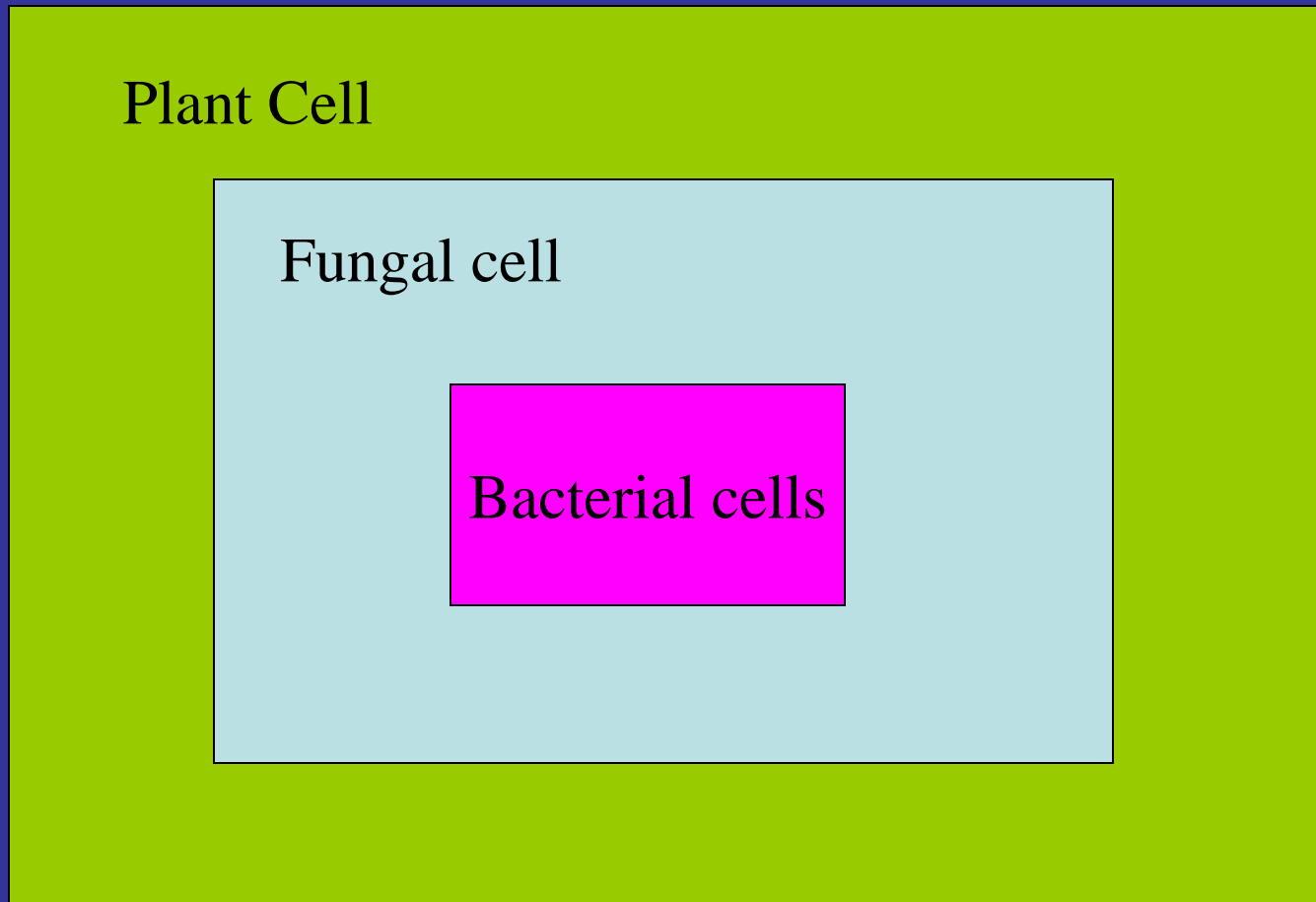


Fig.1 The three boxes illustrate the tripartite complex system which is investigated by using metagenomics/ informatics/chemical approaches

II budget....

Bando ricerca 2007 - Elenco costi richiesti

Acronimo: ***BioBITS***

Costo richiesto dal Proponente: **Dipartimento di Biologia Vegetale**

Università di Torino: 1.251.013,00 €

Costo richiesto dal Coproponente: **C C SI VALLE D'AOSTA S.R.L.:**

33.200,00 €

Costo richiesto dal Coproponente: **GEOL SAS DI CIBRARIO OTTAVIO E**

C.: 601.120,00 €

Costo richiesto dal Coproponente: **ETICA srl:** 166.620,00 €

Costo richiesto dal Coproponente: **Isagro Ricerca Srl:** 991.871,00 €

Costo richiesto dal Proponente aggiuntivo: **Dipartimento di chimica
generale ed organica applicata:** 678.308,00 €

Costo richiesto dal Proponente aggiuntivo: **Dipartimento Colture arboree:**

148.742,00 €

Costo richiesto dal Proponente aggiuntivo: **Dipartimento di Informatica:**

684.490,00 €

Costo richiesto dal Proponente aggiuntivo: **Consiglio Nazionale delle**

Ricerche - Istituto Protezione Piante : 53.634,00 €

Costo richiesto dal Proponente aggiuntivo: **Dipartimento di Informatica:**

242.969,00 € 1 of

		BUDGET		
Ente/Azienda + Referente	TIPO Proponente Proponente Aggiuntivo Co-Proponente Soggetto Aggiuntivo	Imputabile al contributo regionale	Imputabile al co- finanziamento	TOTALE
Dipartimento di Biologia Vegetale Univ. Torino	Proponente	546.617,62 - 135,06= 546.482,56	234.264,69 - 31,98 = 234.232,71	780.715,27
Dipartimento di Chimica generale e Organica applicata Univ. Torino	Proponente aggiuntivo	296.379,89	127.019,95	423.399,84
Dipartimento di Informatica Univ. Torino	Proponente aggiuntivo	299.081,06	128.177,59	427.258,65
Dipartimento di Colture Arboree Univ. Torino	Proponente aggiuntivo	64.991,32	27.853,42	92.844,74
Consiglio Nazionale delle Ricerche	Proponente aggiuntivo	23.434,83	10.043,50	33.478,33
Dipartimento di Informatica Univ. Piemonte Orientale	Proponente aggiuntivo	106.162,87	45.498,37	151.661,24
Centro colture sperimentali Valle d'Aosta	Coproponente	14.402,79	6.320,64	20.723,43
Etica srl	Coproponente	65.522,64	38.481,55	104.004,19
Geol Sas di Cibrario Ottavo	Coproponente	240.140,22	105.078,87	345.219,09
Isagro Ricerca srl	Coproponente	402.431,82	246.694,05	649.125,87
	TOTALE	2.059.030,00	969.400,65	3.028.430,65

-135,06 sono gli arrotondamenti di excel e li toglierà al capofila
- 31,98 idem

Distribuzione dell'ottenuto

- Domande:
- Rimodulazione?
- Che cosa sottrarre ancora
- Overhead 5% da parte dell'Ateneo
- Overhead % da parte Dip biol ?

**BANDO REGIONALE PER PROGETTI DI RICERCA INDUSTRIALE E/O DI SVILUPPO SPERIMENTALE PER L'ANNO 2007
NELL'AMBITO DELLE "CONVERGING TECHNOLOGIES"**

1° monitoraggio al 31 dicembre 2008

BioBITS	titolo	Developing White and Green Biotechnologies by Converging Platforms from Biology and Information Technology towards Metagenomics			codice intese	RV/01/6BI
Responsabile progetto	Paola BONFANTE					
Ente	UNIVERSITA' DEGLI STUDI DI TORINO					
contributo regionale (€)	2.059.030,00	cofinanziamento (€)	969.400,65	costo totale progetto (€)	3.028.430,65	
previsione di inizio e fine progetto	<i>data inizio</i>	2-feb-2009	<i>data fine</i>	31-dic-2011		
CRONOPROGRAMMA DI SPESA COMPLESSIVO						
	da realizzare				costo totale progetto	
	2009	2010	2011			
previsione di spesa totale per anno (€)	1.000.000,00	1.500.000,00	528.430,65		3.028.430,65	
					<i>firma responsabile</i>	

Modalità di erogazione

Acconto del 30%

Pagamento intermedio del 50% (al ragg. del 60% delle spese compreso il cofinanziamento)

20% a saldo alla rendicontazione finale

Next steps

30 gennaio 2009 : riunione per
verbalizzare l'inizio

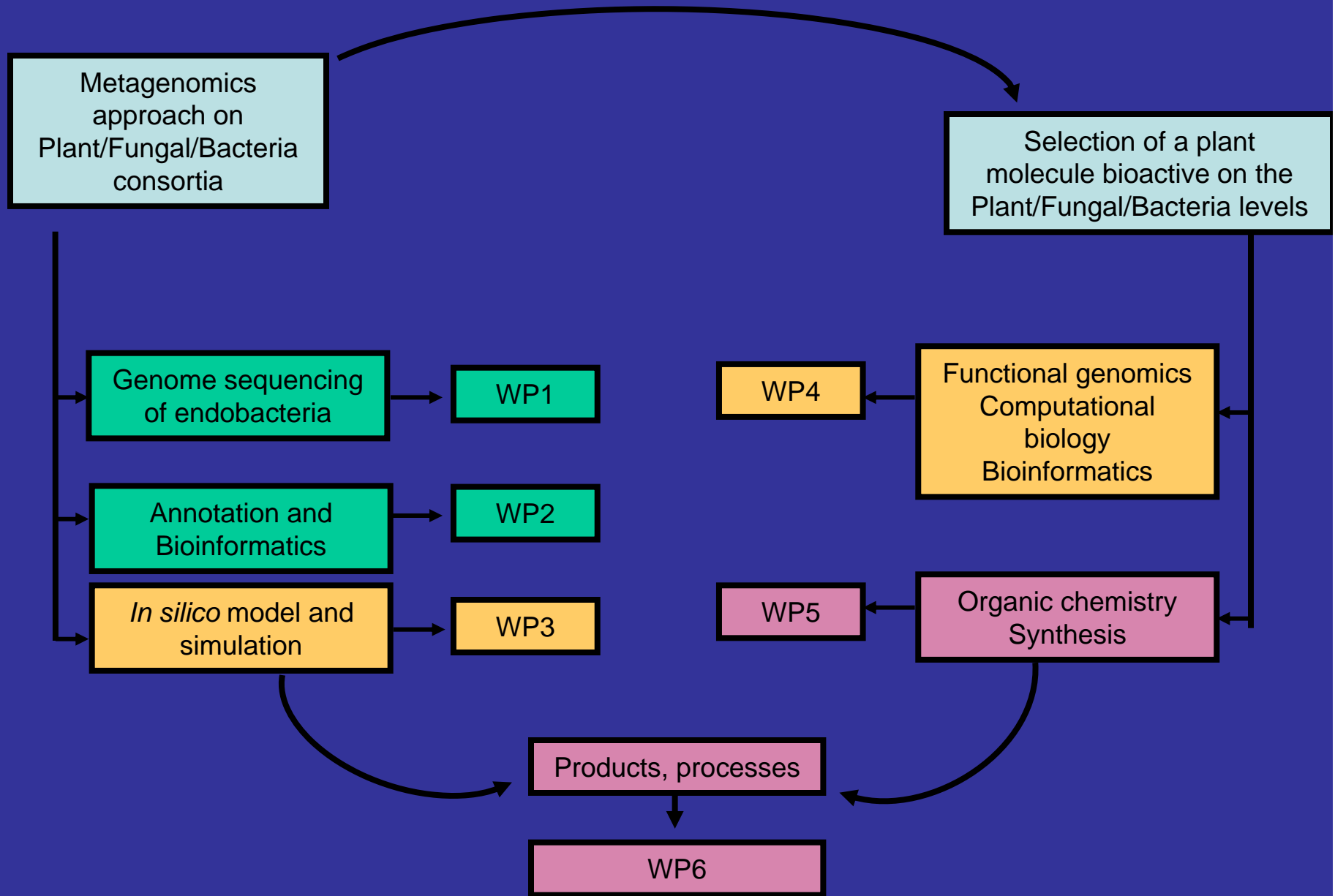
ATS entro febbraio

Definizione del consiglio di
gestione Consiglio...

Organizzazione scientifica

1. WP Dip Biol, P. Bonfante
2. WP Dip Biol, L. Lanfranco
3. WP Dip Infor, M. Coppo
4. WP Geol, G. Ranghino
5. WP Dip Chimica, C Prandi
6. WP Isagro, F. Pellacini

METABIOTICS scientific, technological & industrial strategy



Color code for Scientific outcomes: WP1,2 (Green); Technological outcomes: WP3, 4 (orange) Industrial outcomes : WP5, 6 (purple)

Work Package: A metagenomics approach to sequence the genome of
Candidatus glomeribacter gigasporarum

NUMBER: 1

RESPONSIBLE: PAOLA BONFANTE

STARTING MONTH: 1

ENDING MONTH: 12

The following activities are planned within the WP1:

- 1) Generation of DNA sequence data from *Candidatus Glomeribacter gigasporarum* genome by Sanger sequencing of selected fosmid clones from the *Gigaspora margarita* genomic library
- 2) Development of a protocol for the isolation of purified bacterial cells and the whole genome amplification (WGA) of bacterial DNA
- 3) Generation of sequence data through the innovative 454 sequencing platform on the WGA DNA
- 4) Hybrid assembly of Sanger and 454 sequences and gap closure by computer assisted and manual approaches.

Endobacteria

Participants:

Dipartimento di Biologia Vegetale, Università Torino

Istituto Protezione Piante - CNR Torino



A genomic approach to understand *Gigaspora margarita* / *Candidatus Glomeribacter gigasporarum* association



S. Ghignone,

J. Jeongwon, M. de Jong, P. Lammers
New Mexico State University, Las Cruces NM-USA

F. Celestini, P. Piffanelli
CERSA Genomics Platform, Lodi, Italy

The strategy

36,000 primary recombinant clones
average insert size: 35 Kbp
1095 prim clones were end sequenced
Database sequence similarity searches
using BLASTX



1. Fosmid library construction
Screening



2. Validation process
3. Retrotransposition
4. Fosmid sequencing
5. Partial Assembly- Sanger
approach

- Bacterial isolation
- WGA
- 454
- General Assembly

- ❑ Design of PCR primers specific to one end reading
- ❑ PCR assays using DNA from B + and B- spores
- ❑ Validation of 68 fosmids out of 1095 screened

Work Package: Candidatus Glomeribacter gigasporarum genome annotation and selection of candidates genes of biotechnological interest

NUMBER: 2

RESPONSIBLE: LUISA LANFRANCO

STARTING MONTH: 3

ENDING MONTH: 36

The WP2 comprises the following tasks:

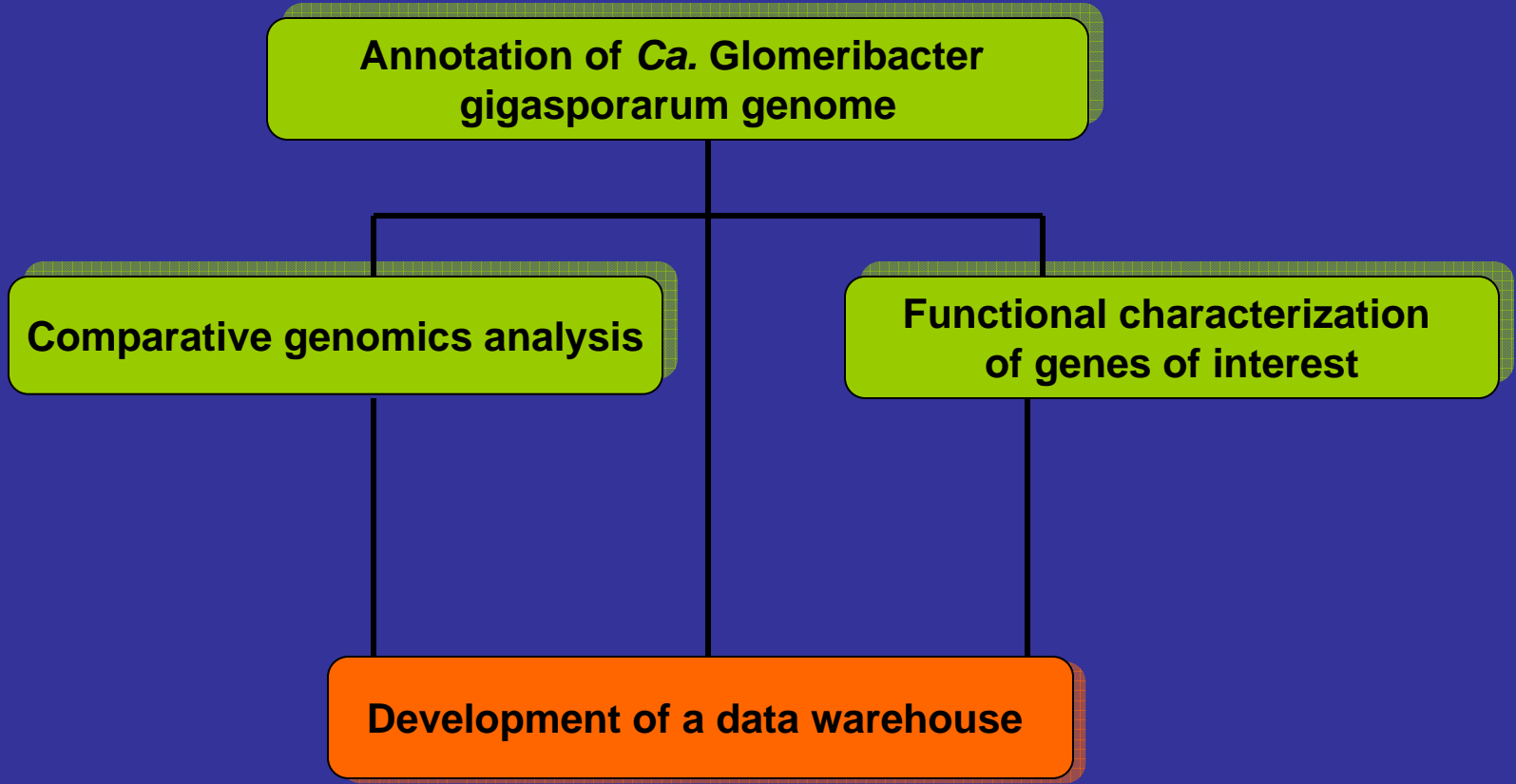
- 1) Annotation of the bacterial genome (automated annotation + manual curation)
- 2) Comparative analyses with genomes from free-living and endosymbiont bacteria
- 3) Characterization of genes of biotechnological interest by means of gene expression profiles along the different steps of the fungal life cycle and/or complementation assays.
Potential candidates: genes related to vitamin B12 biosynthesis
- 4) Development of an experimental data warehouse to manage *Ca. G. gigasporarum* genomic sequences, annotation, functional data and comparative analyses.

Partecipants:

Dipartimento di Biologia Vegetale Università Torino / Istituto Protezione Piante - CNR Torino

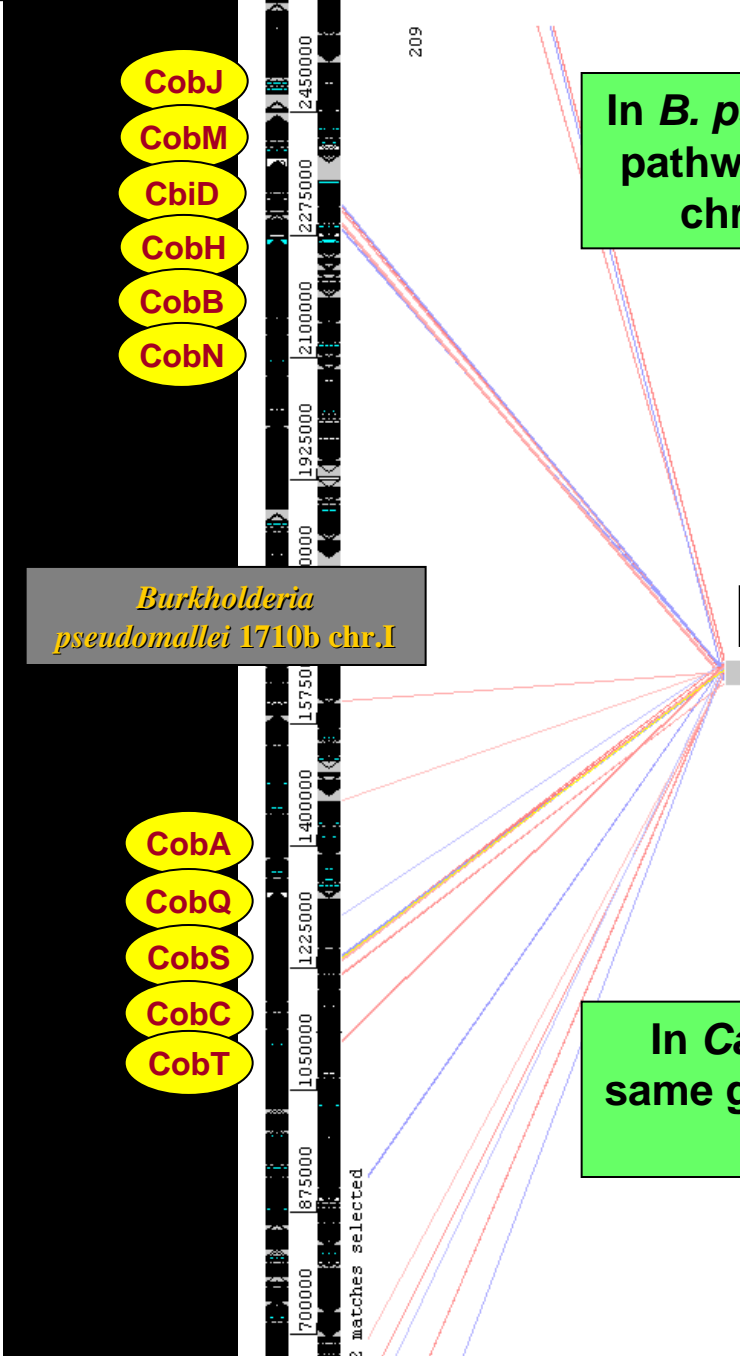
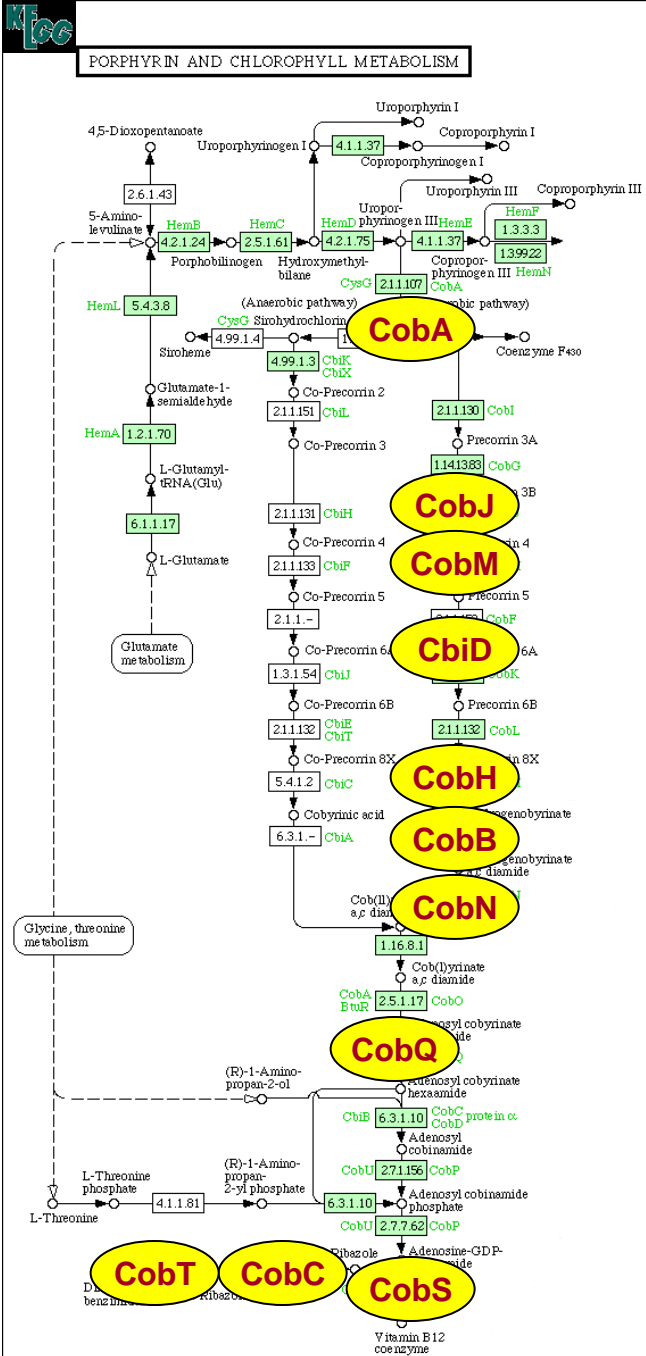
Dipartimento di Informatica, Università Torino / ETICA

Interaction with WP3



-  DBV / IPP-CNR
-  DI - ETICA

Fosmid 167: Vitamin B12 pathway



In *B. pseudomallei* Vitamin B12 pathway genes are located on chr. 1 within aprox 1 Mb

Ca. G. gigasporarum fos. 167

In *Ca. G. gigasporarum* the same genes are grouped within 33kbp

Work Package: In Silico Modeling and Simulating Biological Systems

Number: 3

Responsible: Mario Coppo

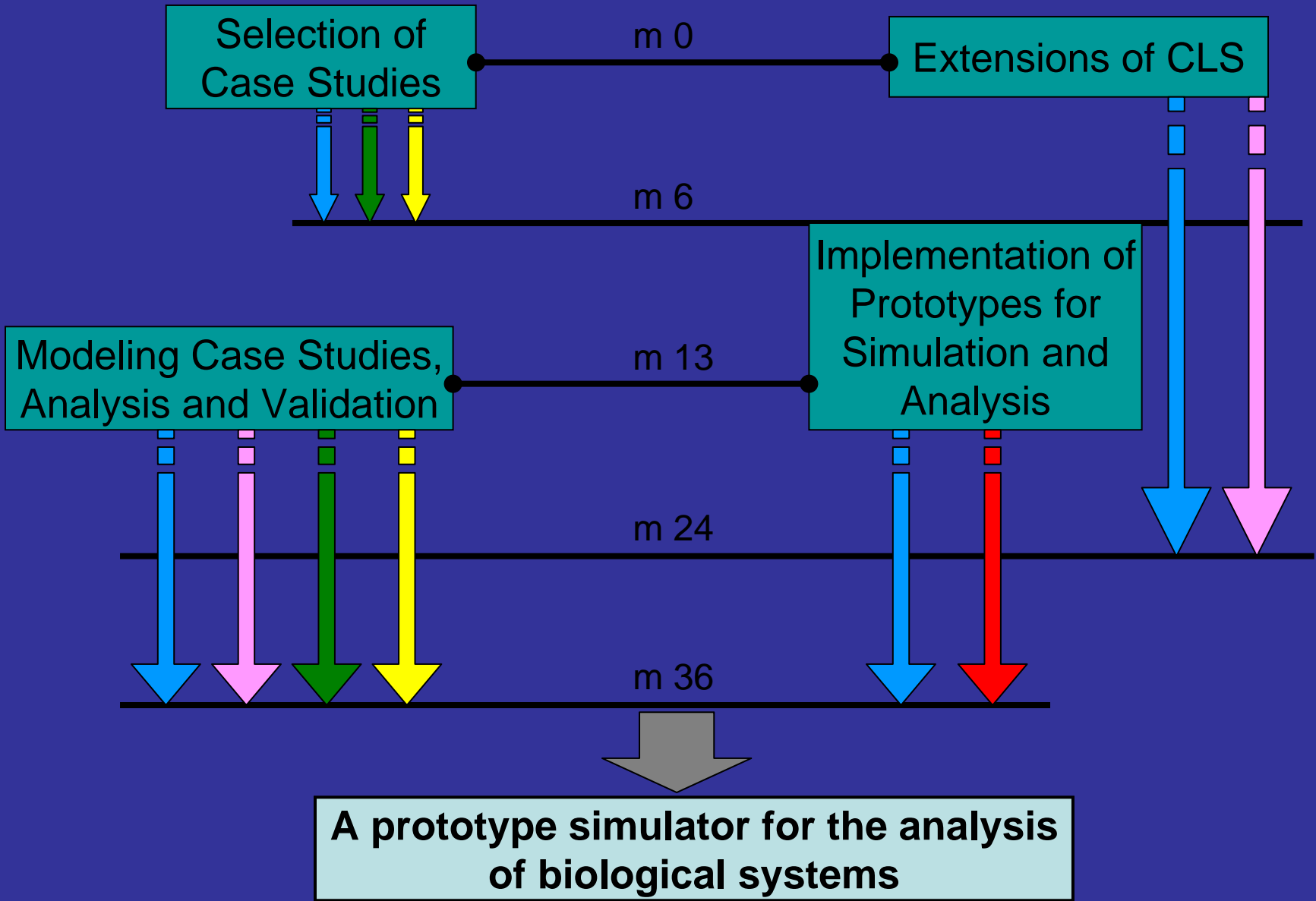
Starting month: 0



Ending month: 36




The WP3 comprises the following tasks:

- 1) **Selection of Case Studies** (months: 1-6): single out a significant set of biological interactions and situations that we will model with the aim of determining which of their aspects are particularly relevant for description, analysis, and simulation.
- 2) **Extensions of CLS** (months: 1-24): develop models, provided with analysis and simulation tools, capable of dealing with complex behaviors of biological systems and representing emerging properties.
- 3) **Modeling Case Studies, Analysis and Validation** (months: 13-36): the activity of modeling will cause a feed-back giving rise to the necessary tuning of the extensions proposed in point 2). This activity will be carried on together with the biologists involved in the project, in order to continuously check whether our in silico results conform with the standard ones known from the in vivo or in vitro experiments.
- 4) **Implementations of Prototypes for Simulation and Analysis** (months: 13-36): we will complete prototypes for the execution and simulation of our specifications, as well as those for the analysis of their behaviors.

Participants: Dipartimento di Informatica (To e AI), Dipartimento di Biologia Vegetale, Dipartimento di chimica generale ed organica applicata, ETICA srl.



 Dip. Informatica (Torino)
 Dip. Informatica (Alessandria)

 Dip. Biologia Vegetale
 Dip. Chimica generale ed organica applicata
 ETICA srl.

Work Package: Biological and structural study of a plant product: biosynthesis and activity elucidation and bioinformatics study, aiming at the discovery of synthetic compounds with desired properties

NUMBER: 4

RESPONSIBLE: GRAZIELLA RANGHINO

STARTING MONTH: 1 **ENDING MONTH:** 36

The following activities are planned:

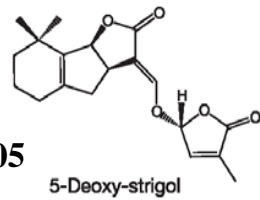
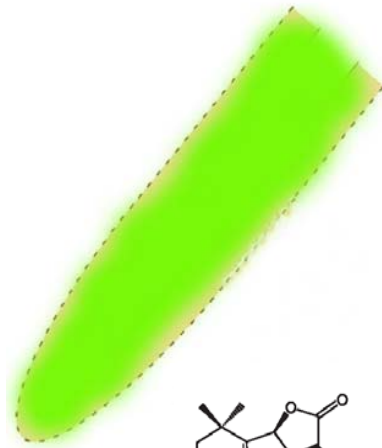
WP 4.1 identification of genes involved in the biosynthetic pathway:

WP 4.2 validation of the role in strigolactone biosynthesis of the genes identified at wp1

WP 4.3 By means of computational biology define the 3D structure of the receptor and the binding features of the natural ligand and of analogs suitable for the synthesis

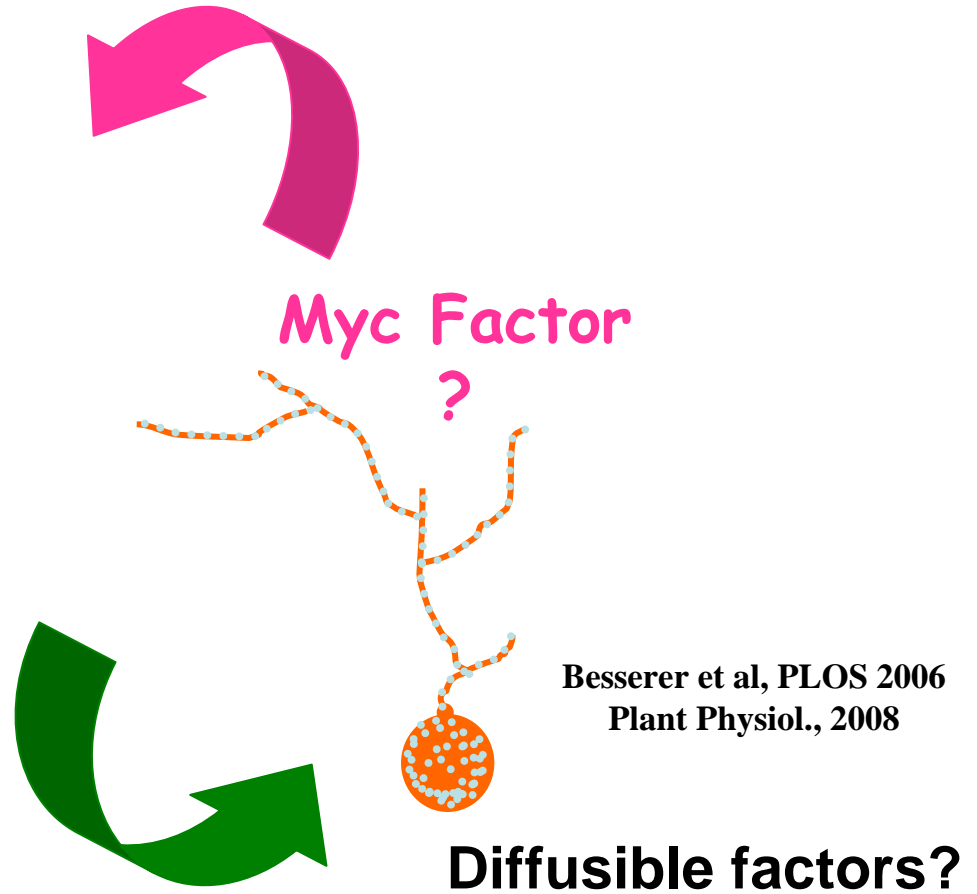
PARTICIPANTS:

- Dipartimento di Biologia Vegetale Università di Torino,
- Dipartimento Colture arboree,
- GEOL SAS DI CIBRARIO OTTAVIO E C.,
- Isagro Ricerca Srl



Akiyama et al., Nature June 2005
Plant sesquiterpenes induce
hyphal branching in AM fungi

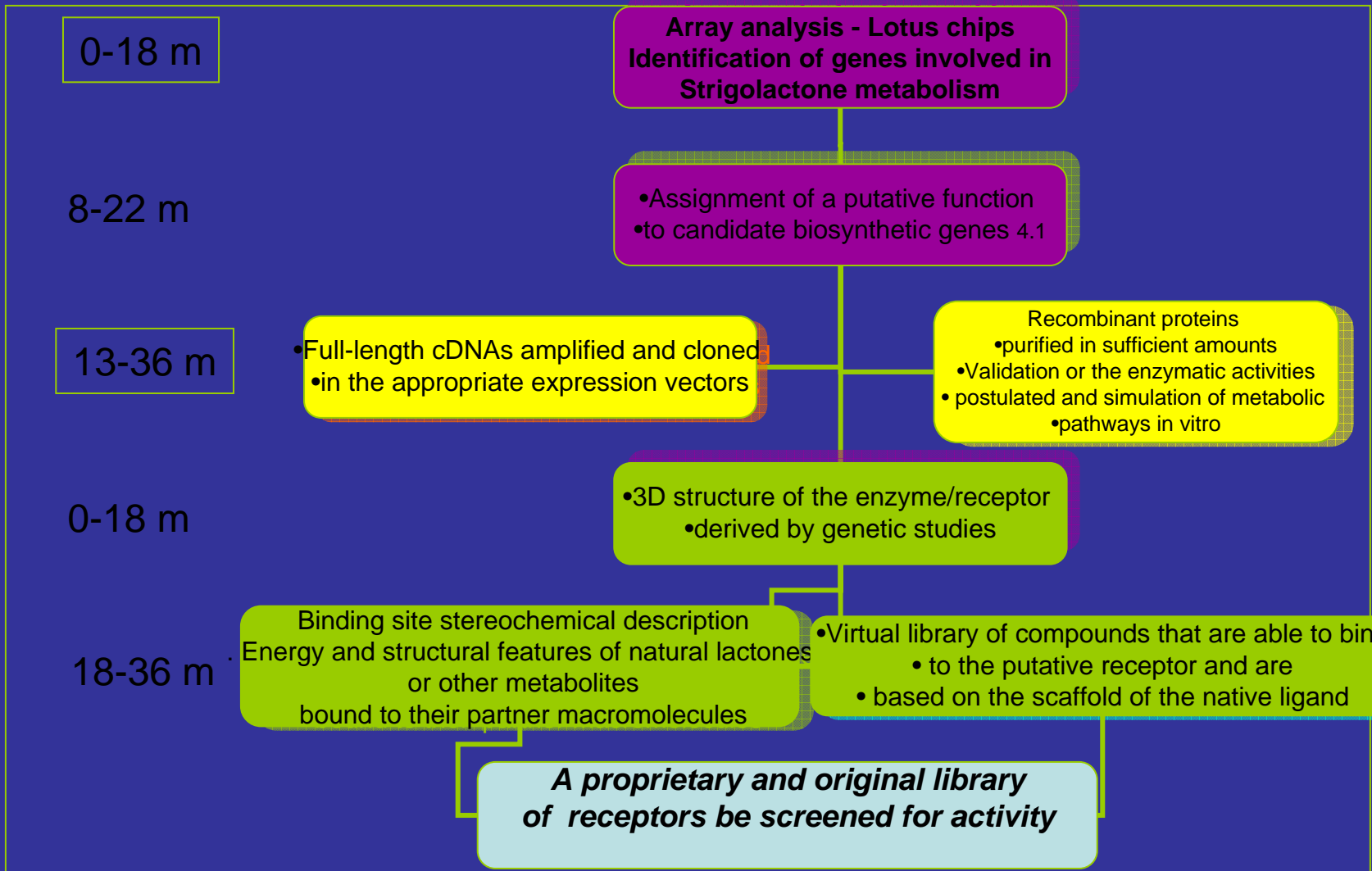
Gomez-Roldan et al., Nature 2008
Strigolactone inhibition of shoot branching



Besserer et al, PLOS 2006
Plant Physiol., 2008

Signalling events in the rhizosphere

- **Results and deliverables:**
- 4.1 List of genes involved in the biosynthetic pathway leading to strigolactone production
- 4.2.1: Assignment of a putative function to candidate biosynthetic genes provided by activity 4.1
- 4.2.2 Full-length cDNAs amplified and cloned in the appropriate expression vectors
- 4.2.3 Recombinant proteins purified in sufficient amounts
- 4.2.4 Validation of the enzymatic activities postulated at 4.2.1, and simulation of metabolic pathways in vitro.
- 4.3.1 3D structure of the enzyme/receptor derived by genetic studies
- 4.3.2. Binding site stereochemical description. Energy and structural features of natural lactones or other metabolites bound to their partner macromolecules;
- 4.3.3. Virtual library of compounds that are able to bind to the putative receptor and are based on the scaffold of the native ligand



 DBV

 D.CA-P

 Geol

Work package 5

Responsabile: **Cristina Prandi** Dip. Chimica Generale e Chimica Organica 11m
partecipanti: Barbero Margherita, Annamaria Deagostino Dip. Chim. Generale e
Chimica Organica 11+11m
Andrea Genre (1m), Mara Novero (1m)

WP 5a 0-18m production of a first generation of analogues of natural strigolactones

WP 5b 18-22m biological tests on fungal germination

WP 5c 22-36 development of the new molecules on industrial scale (WP6)

WP 5d 18-36 will use bioinformatics proprietary package (WP4) in order to perform a screening of possible candidate molecules to be synthesized by WP6 and production of a second generation of analogues.

WP 5e 22-36 will use bioinformatics to investigate molecule interactions (WP2).

DELIVERABLES: A proprietary and original library of compounds to be screened for activity

0-18 m

1° generation of analogues
CP, MB, AD

18-22 m

Biological tests on Fungal
Germination AG, MN

22-36 m

Industrial Scale production
WP6

screening of possible candidate
molecules WP4

18-36 m

production of a second generation
of analogues

22-36 m

Biological tests

molecule interactions at
the receptor site
AT WP2

*A proprietary and original library
of compounds to be screened for activity*



Work Package: Checking the green/white biotechnological potentialities of BioBits

Number: 6

Responsible: Franco Pellacini

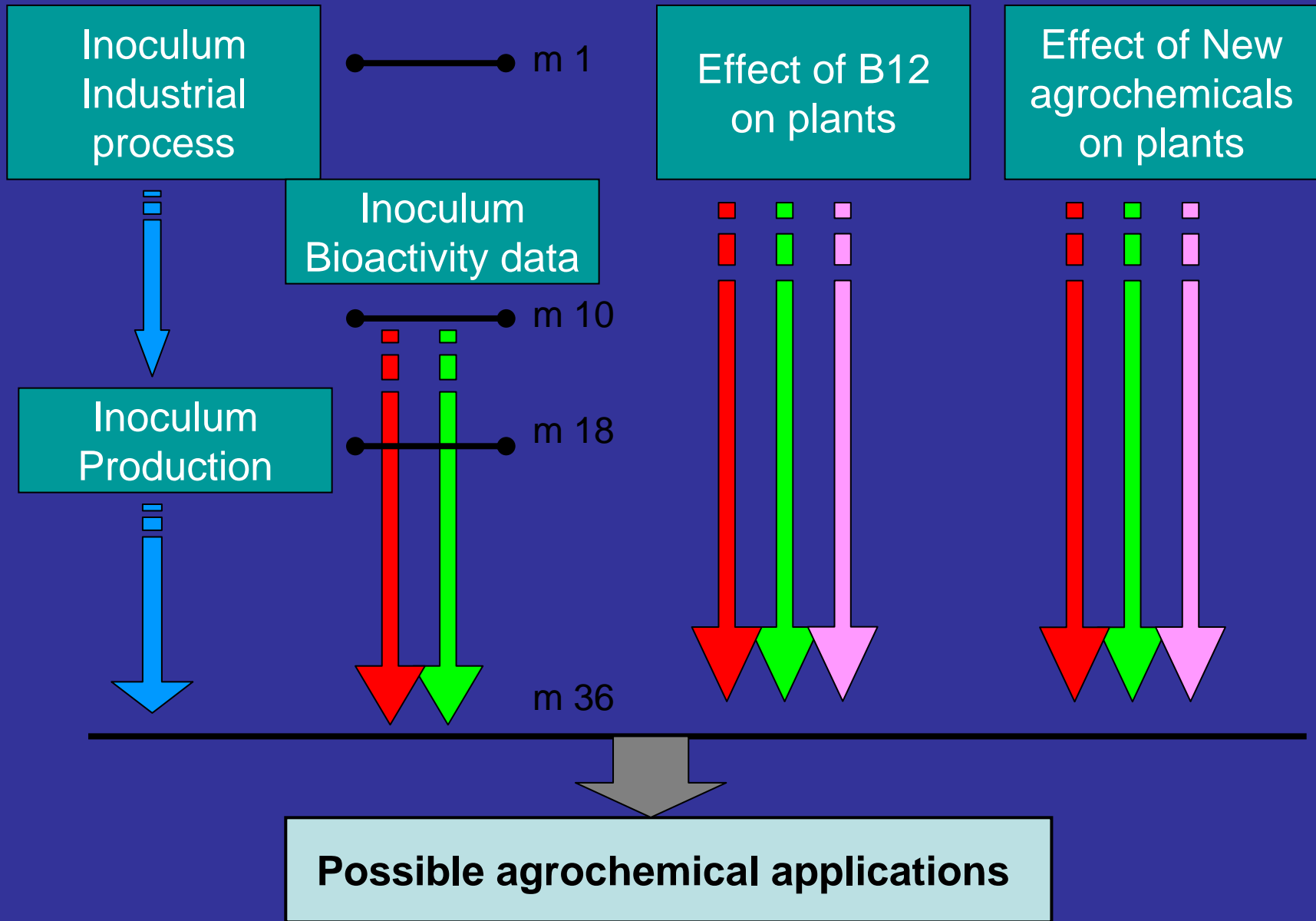
Starting month: 1

Ending month: 36

The WP6 comprises the following tasks:

1. to evaluate the impact of the endobacteria on the growth parameters of the mycorrhizal plant;
2. to evaluate the impact of the added Vit B12 on some health plant parameters;
3. to investigate the impact of strigolactone-like molecules (both of natural origin as well as synthetic analogues, as resulting from WP5) on the mycorrhizal success and on plant health;
4. to check the effects of such molecules on germination of weeds plants.

Participants: Isagro Ricerca Srl; CENTRO COLTURE SPERIMENTALI VALLE D'AOSTA S.R.L; Dipartimento di Biologia Vegetale Università di Torino; Dipartimento di chimica generale ed organica applicata



Centro colture sperimentali valle d'aosta s.R.L)

Dip. Biologia Vegetale

Dip. Chimica generale ed organica applicata

Isagro Ricerca Srl

1. Verbale
2. Segreteria tecnica-scientifica
3. Materiale per riunione del 30
3. Nomina Commissione
4. ATS
5. Primi BO dal 1 febbraio