Biotecnologie applicate

Transactiva:

Company history and technology overview

Trieste, 29th April, 2025

Sara Raccovelli, PhD, MBA

transactiva
MOLECULAR FARMING

Transactiva srl

Biotech R&D company - Innovative SME



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Biotech R&D company - Innovative SME

Udine
FVG - Italy

FRIULI innovazione®
innovAction platform

Company history

2001
Foundation year

First idea

2008
Udine Headquarters

FRIULI innovazione
innovAction platform

2019
Administration and shareholders change

2021 + 2023
Equity crowdfunding

AREA SciencePark

UNIVERSITAS STUDIORUM UTINENSIS

Vision: sustainable biopharmaceuticals

Standard bioreactors

Molecular Farming

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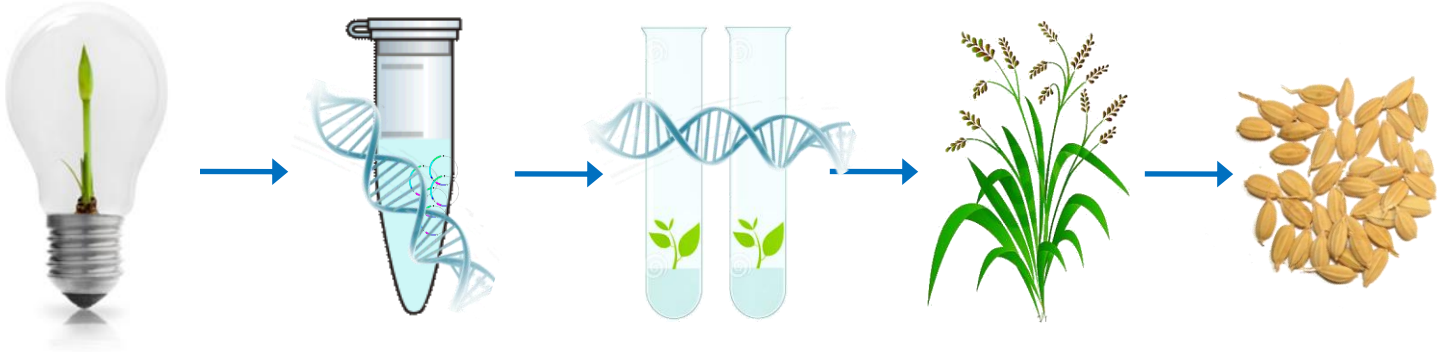
How? With Plant Molecular Farming



A multidisciplinary, sustainable technology
leveraging **whole plants** and **vegetal tissues**
as **bioreactors**
to obtain recombinant therapeutic **proteins**

Synergy of complementary expertise

TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

UNIVERSITÀ DEGLI STUDI DI TRIESTE

ISG
ISTITUTO DERMATOLOGICO SAN GALLICANO

International Centre for Genetic Engineering and Biotechnology

UNIVERSITÀ DEGLI STUDI DI UDINE

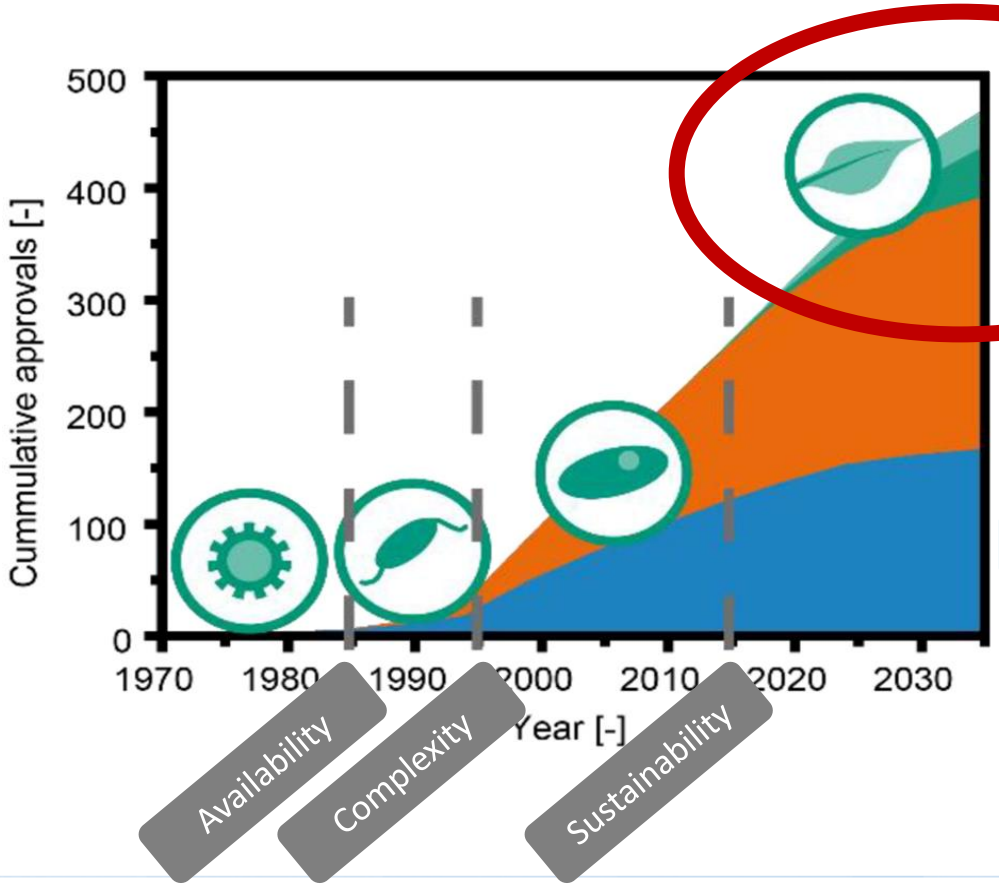
FRIULI innovazione
innovAction platform

BioHighTech Net 4.0

FRM
Farming Revolutionary Modules

PWD
INDUSTRIAL FILTRATION

The future of biopharmaceuticals



Plant-derived

Mammalian cell culture-derived

Microorganism-derived

Buyel, 2019

35+ year-old technology

Plant Molecular Biology 6:347–357, 1986

The expression of a nopaline synthase – human growth hormone chimaeric gene in transformed tobacco and sunflower callus tissue

Andrea Barta[1], Karin Sommergruber[1], Diana Thompson[1], Klaus Hartmuth[1], Marjori A. Matzke[2] & Antionius J. M. Matzke[2]
[1]*Institut für Biochemie, Universität Wien, Währingerstraße 17, A-1090 Wien, Austria*
[2]*Institut für Molekularbiologie, Akademie der Wissenschaften, Billrothstraße 11, A-5020 Salzburg, Austria*

Keywords: human growth hormone gene, plant transformation, polyadenylation signal, pre-mRNA

Production of antibodies in transgenic plants

Andrew Hiatt, Robert Cafferkey & Katherine Bowdish

Department of Molecular Biology, The Research Institute of Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, California 92037, USA

COMPLEMENTARY DNAs derived from a mouse hybridoma

NATURE · VOL 342 · 2 NOVEMBER 1989

Why isn’t it a golden standard yet?

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OGM?

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Molecular Farming

«The use of ***heterologous expression systems*** for the production of ***non-food***, ***non-feed***, ***non-fibre*** commodities like therapeutic molecules, fuels, biodegradable plastics, industrial and commercial proteins»

Molecular Farming

Molecular Pharming

Pharming

Plant Molecular Farming

Plant-based bioreactors for biopharmaceuticals

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Biopharmaceuticals / Biologics

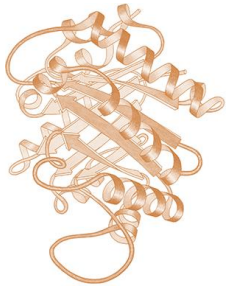
Therapeutic molecules whose production:

- can***not*** be achieved by simple ***chemical synthesis***
- require ***living organisms*** and innovative technologies

Proteins
Complex / multimeric
Biotechnology needed
Orphan drugs

→

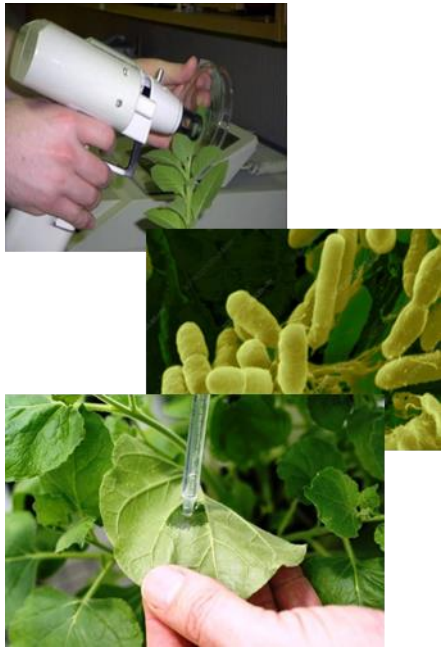
Enzymes
Antibodies
Vaccines
Hormones
…



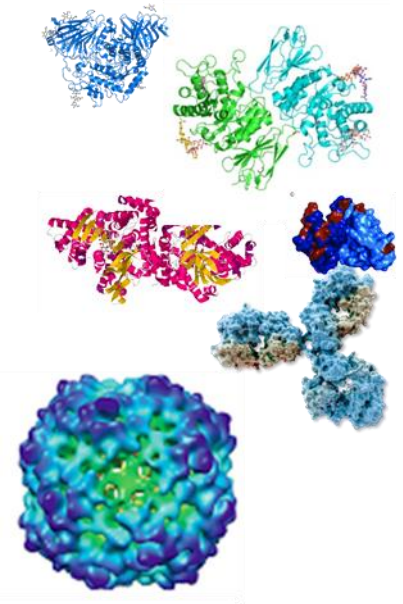
Extreme flexibility

Host species and target tissue

Transformation methods



Recombinant proteins



Examples of PMF-derived biologics

Product	Disease	Plant/expression system	Clinical trial stage	Company/Consortium
Antibodies				
Chimeric mAb (CaroRX)	Dental caries	Tobacco/ stable transformation	Phase 2	Planet Biotechnology
Idiotype IgG Based vaccine	Non-Hodgkin's lymphoma	*N. benthamiana*/ Agroinfiltration	Phase 1	Icon Genetics
Anti-HIV IgG	Prevention of HIV infection	Tobacco/ stable transformation	Phase 1	Pharma-Planta Consortium
Anti-Ebola IgG cocktail (ZMApp	Treatment of Ebola virus infection	*N. benthamiana*/ Agroinfiltration	Phase 2/3	Mapp Biopharmaceutical
IgG (ICAM1)	Common cold	Tobacco/ stable transformation	Phase 1	Planet Biotechnology
Radiolabeled anti-Ep-CAM IgG	Cancer treatment	Maize/ stable transformation	Phase 2	*NeoRx Corporation*
Vaccine antigens				
VLP-based Vaccine	Seasonal flu	*N. benthamiana*/ Agroinfiltration	Phase 3	Medicago
VLP-based vaccine (H5N1)	Pandemic flu	*N. benthamiana*/ Agroinfiltration	Phase 2	Medicago
Enzymes				
Glucocerebrosidase enzyme (ELELYSO)	Therapy of Gaucher's disease	Carrot/cell suspension culture	FDA Approved	Protalix Biotherapeutics
Alpha-galactosidase-A (Fabrazyme)	Therapy of Fabry disease	Tobacco/cell suspension culture	Phase 2	Protalix Biotherapeutics
Alpha-galactosidase-A (moss-aGal)	Therapy of Fabry disease	Moss cultures	Phase 1	Greenovation Biopharmaceuticals
Human deoxyribonuclease I (Alidornase alfa)	Treatment of cystic fibrosis	Tobacco/cell suspension culture	Phase 2	Protalix Biotherapeutics

Donini, Marusic, 2019

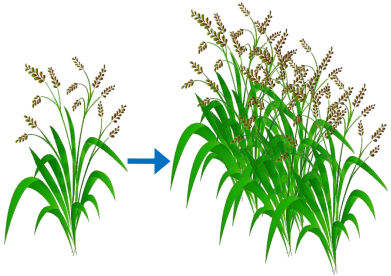
Molecular Farming: general advantages

↑ Safety

No batch loss
due to contamination

↑ Sustainability

Natural carbon-fixating source,
waste valorization,
circular economy approach



↑ Scalability

Intrinsically modular
and scalable
technology

↓ Spending

Reduce the upstream costs
for biopharmaceuticals

Technologies leveraged by Transactiva

1.  **STABLE** expression in **RICE**

2.  **TRANSIENT** expression in **TOBACCO**

3.  **STABLE** expression in cultured **CELLS**

Molecular Farming: specific advantages

Stable transformation (e.g. rice seeds)

✓ **Stability**
Natural reserve organ

✓ **Seed banking**
Stable, fully characterized line (analogous to a cell banking system)

✓ **Easy purification**
Low content of lipids and phenolic compounds

Transient transformation (e.g. tobacco leaves)

✓ **Quickness**
Production set-up in weeks, very suitable in case of emergency / crisis scenarios

✓ **Flexibility**
Easy to switch to other proteins

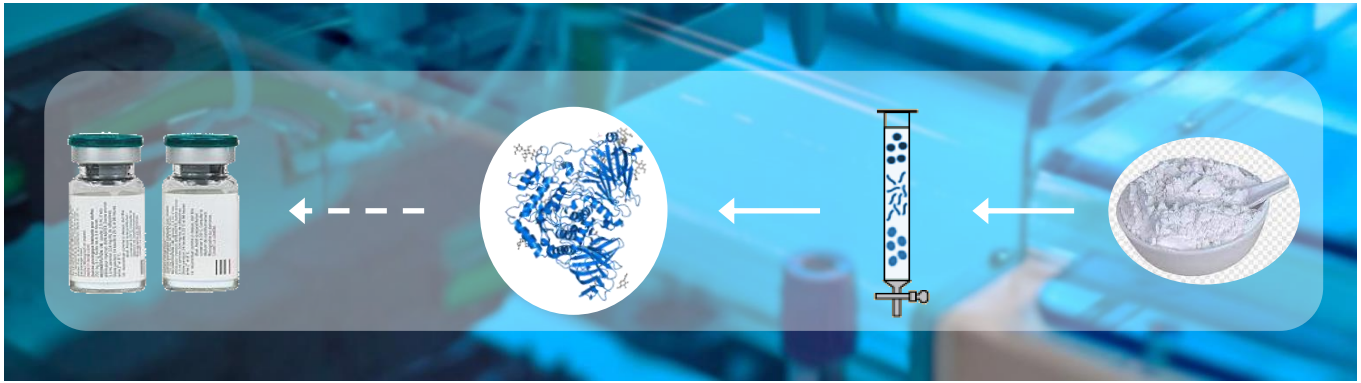
✓ **No GMO**
Transient transformation technology

Plant cell cultures (green fermenters)

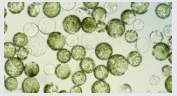
✓ **"Standard" bioreactor**
More similar to current CHO-based production technologies

✓ **cGMP-aligned**
Cells grow in a sterile and controlled environment

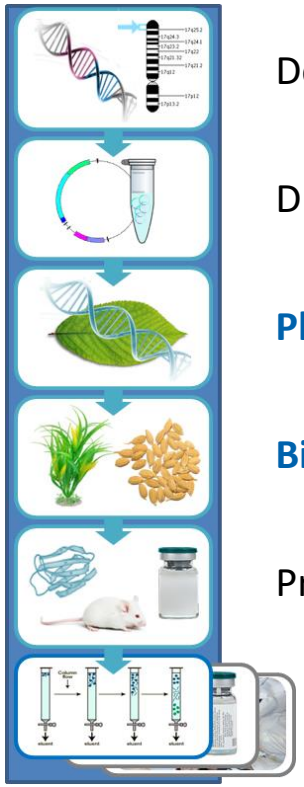
Plant Molecular Farming at a glance



Examples of industrial applications (pharma)

Company	Product / disease	Technology	Approval stage
PROTALIX Biotherapeutics	Elelyso® Gaucher disease		FDA U.S. FOOD & DRUG ADMINISTRATION 2012
Mapp Biopharmaceutical	Zmapp Ebola virus disease		TEMPORARY FDA U.S. FOOD & DRUG ADMINISTRATION 2014
medicago	Covifenz® COVID19 vaccine		Health Canada 2022
medicago	Seasonal flu vaccine		STOP Clinical phase 3 Waiting for approval
PROTALIX Biotherapeutics Chiesi	Elfabrio® Fabry disease		FDA U.S. FOOD & DRUG ADMINISTRATION 2023 EUROPEAN MEDICINES AGENCY
iBio PROTALIX Biotherapeutics KBio ICON GENETICS transactiva MOLECULAR FARMING			preclinical development

From idea to prototype: the pipeline



Definition of **target protein**

DNA **optimization** and handling

Plant biomass transformation

Bioreactor cultivation and expansion

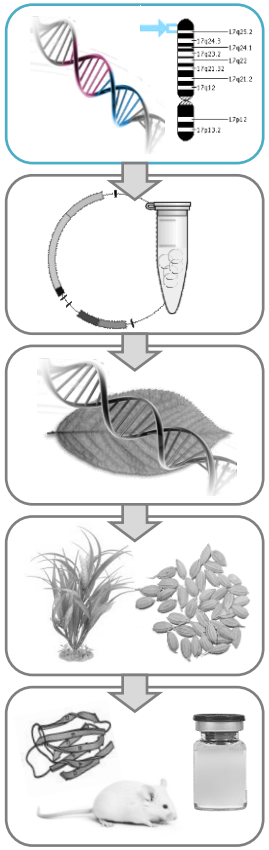
Preliminary **purification** and **characterization**

Proof of concept
Scalable prototype

Prototype is ready to be out-licensed to client pharma

The pipeline

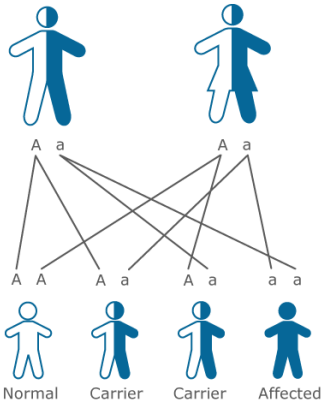
Definition of target protein

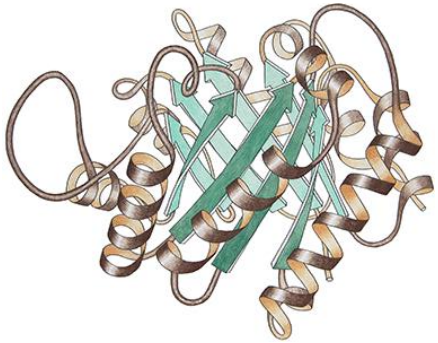


Recombinant protein

Strong industrial and therapeutic **interest**

Goal: selected by / together with pharmaceutical **partners**





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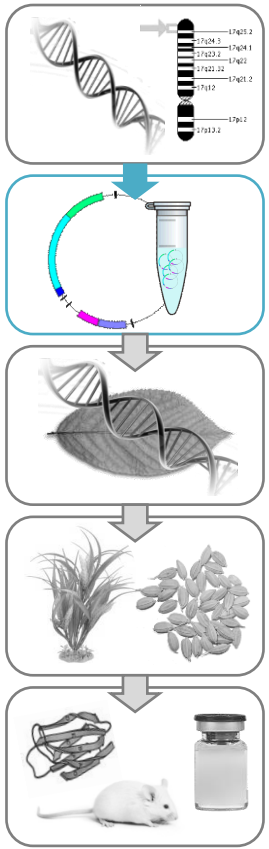
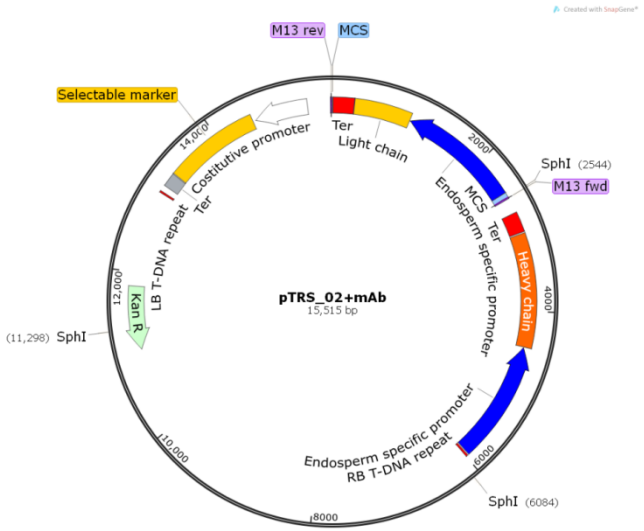
The pipeline

DNA optimization and handling

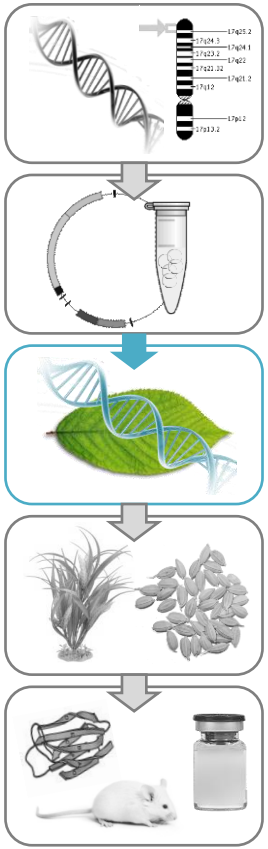


- **Plant** expression vector
- Gene optimization strategy for **high recombinant protein expression**

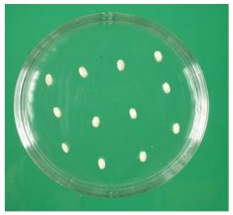


The pipeline

Plant biomass transformation

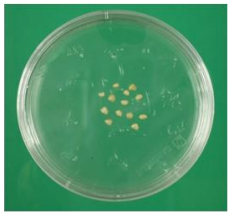


dehulling

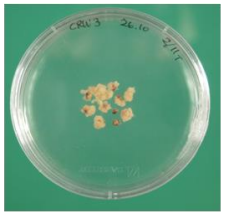


disinfection

germination

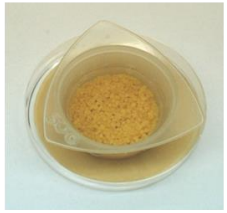


isolation of scutella

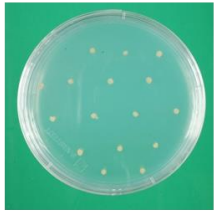


callogenesis

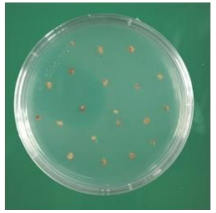
embryoids selection



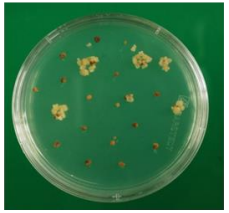
infection



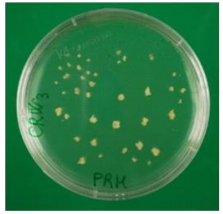
culture on CCM



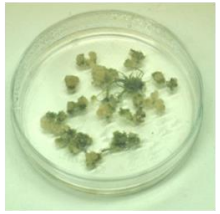
culture on SMI



culture on SMII



culture on PRM



regeneration

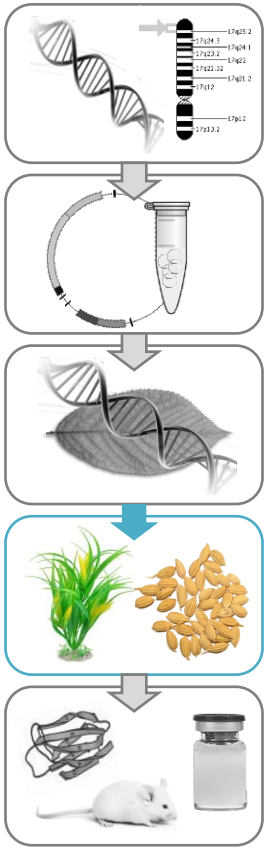
shoot differentiation

rooting

hardening and growth

The pipeline

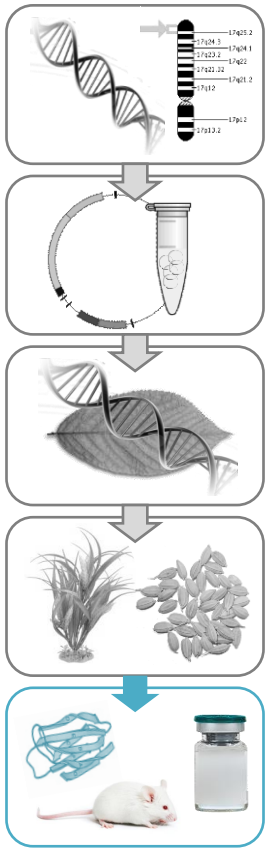
Bioreactor cultivation and expansion



- Plants regeneration and **selection**
- Growth in **confined environment**
- **Harvesting** and **primary processing** of the raw material
- Creation of a stable, **homozygous** line and a **seed banking system**

The pipeline

Preliminary purification and characterization

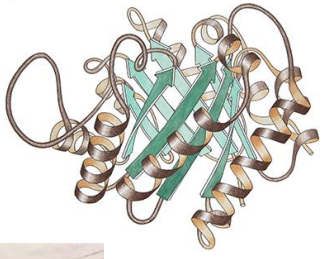


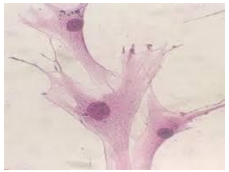
Setup of a scalable **purification** process

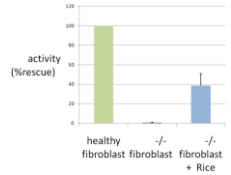
Biochemical characterization of the target molecule

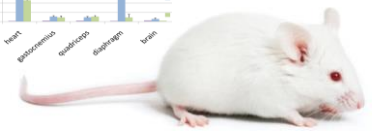
Development of **preclinical characterization** strategies

…for **PHARMA** applications

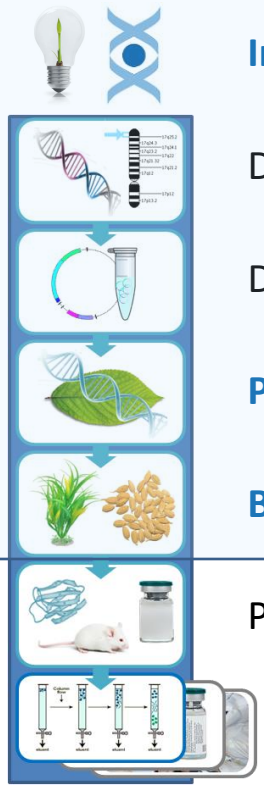








Course overview



Introduction: history of a biotech company / technology overview

Definition of **target protein**

DNA **optimization** and handling

Plant biomass transformation

Bioreactor cultivation and expansion

29/4/25

Preliminary **purification** and **characterization**

Next steps - out of the lab / **other applications** / exam simulation

Biotecnologie applicate

Company history and technology overview

Q&A

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