



Bratislava, SK, 2017

## Current state of biotechnology and prospects in Croatia

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**Objective:**

The overall objective of the Workshop is to further promote:

Research and Innovation Smart Specialization Strategy (RIS3)

focus on CEE countries in the field of Biotechnology

industrial biotechnology, biobased industries and bioeconomy, environmental, agro-food biotechnology up to medicinal and pharma biotechnologies

**Agenda:**

- 1) Short review of biotechnology development in Croatia with European context
- 2) Educational and research biotechnology centers in Croatia
- 3) Industrial biotechnology in Croatia
- 4) Croatia partner in EU research projects
- 5) Innovation in Croatia biotechnology projects
- 6) Conclusion
- 7) References

## **Short review of biotechnology development in Croatia within European context**

Institutional development of biotechnology in Croatia started around 1955 with development of pharmaceutical company Pliva. Scientific impetus with European context is due to Croatian chemistry Nobel laureates L. Ružička and V. Prelog.

In 1956 initially Food Technology and Biotechnology Department was a part of Technology Faculty which in 1980 became a separate faculty institution of University of Zagreb.

**In 1967 started a doctorate level study in Biotechnology and Food Technology (among the first in Europe).**


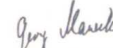
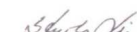

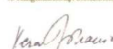
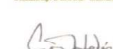

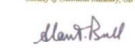
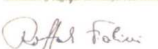
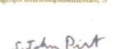


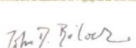

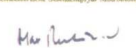
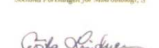
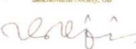
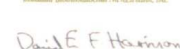






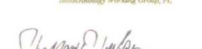

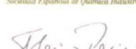









# 1978 Croatia is a cofounder of EU Federation on Biotechnology



Prof. Vera Johanides

The undersigned Societies are agreed that a friendly collaboration in the field of biotechnology in Europe, and the interests of their members, can be well served by the establishment of a European Federation of Biotechnology.

The undersigned technical and scientific societies, through their appointed representatives, have therefore decided to found jointly a European Federation of Biotechnology. They are further agreed that the Federation is to be established on the basis of the statutes which have been accepted at the inaugural meeting of the Federation held on the same day.

 Arbeitsgemeinschaft Biotechnologie, D	 Gesellschaft Deutscher Chemiker, D	 Novak Biotechnik Sektang - Forschungsgruppe für mikrobiol. N	 Society of Chemical Industry, GB
 Association of European Societies for Microbiology, TU	 Forschungsinstitut für Mikrobiologie, S	 Schweizerische Gesellschaft für Lebensmittelwissenschaft und Technologie, CH	 Society for General Microbiology, GB
 Associazione Italiana di Ingegneria Chimica, I	 Institute of Biology, GB	 Schweizerische Gesellschaft für Mikrobiologie, CH	 Seneca Församling för Mikrobiologi, S
 Biochemical Society, GB	 Institut für Biochemie No. 1, DE	 Schweizerischer Chemikerverband, CH	 Seneca Reinigungsvers. für Mikrobiologie, S
 Biotechnology Working Group of the Hungarian Academy of Sciences, H	 Institute of Petrology, GB	 Schweizerischer Ingenieur- und Architektenverein - Fachgruppe für Vordrucktechnik, CH	 Seneca Reinigungsvers. für Mikrobiologie, S
 Biotechnology Working Group, PL	 Institution of Chemical Engineers, GB	 Societät Papieren de Quilmes Industriell, E	 Verein Österreichischer Lebensmittel- und Biotechnologen, A
 Dutch Engineering - Koninklijke Ingenieurs, NL	 Koninklijk Instituut van Ingenieurs, NL	 Societä Chimica Italiana - Sezione Lombardia, I	 Verein für Lebensmittel- und Biotechnologie in Berlin im Institut für Lebensmittel- und Biotechnologie, D
 DGB - DGB Deutsche Gesellschaft für chemische Industrie, D	 Koninklijke Nederlandse Chemische Vereniging, NL	 Societä Chimica Italiana - Sezione Lombardia, I	 FED Gesellschaft Verfahrenstechnik und Chemingenieurwesen, D
 Formenverarbeitungsgruppen, DE	 Niederlande Vereniging voor Microbiologie - Section of Technical Microbiology, NL	 Societä Chimica Italiana - Sezione Lombardia, I	 Division of Microbial and Biotechnological Technology of the American Chemical Society, USA - Corresponding Member

On the occasion of the 1st European Congress of Biotechnology, Interlaken, 25 September 1978

# Educational and research biotechnology centers in Croatia



## Zagreb

Faculty of food technology and biotechnology  
Faculty of chemical engineering and technology  
Research Institute Ruđer Bošković  
University Biocenter

## Osijek

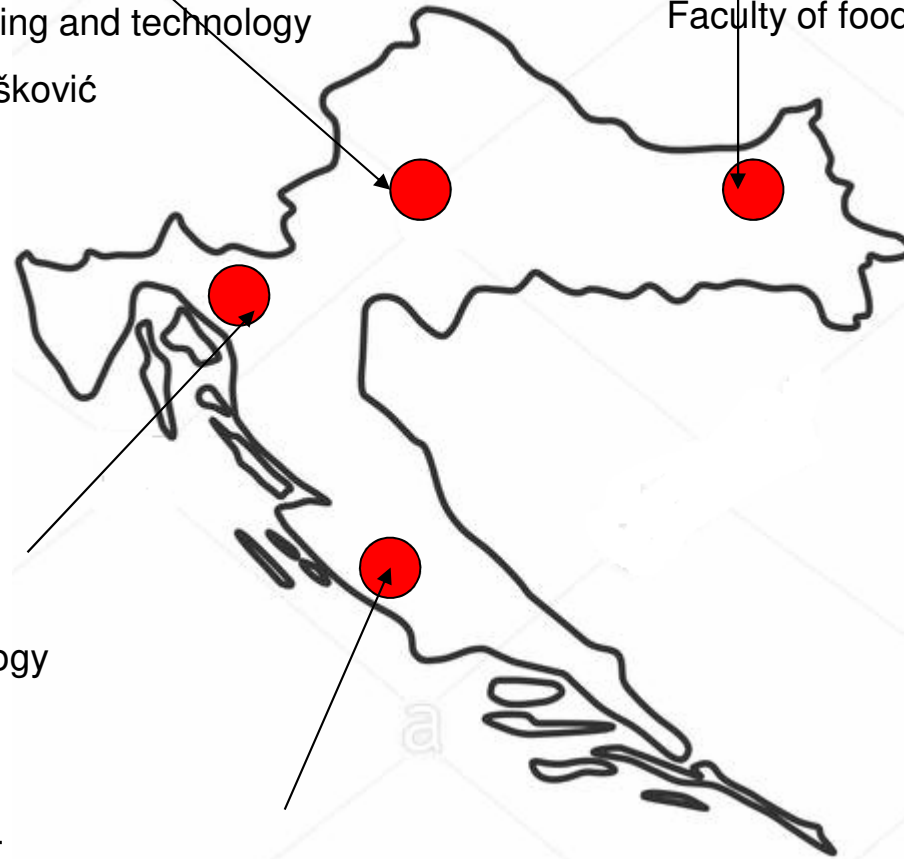
Faculty of food technology

## Rijeka

Faculty of medicine  
Department of biotechnology

## Split

Faculty of chemical technology



Croatian university and research institutions in biotechnology



University of Zagreb



Faculty of Food Technology and  
Biotechnology

**over 4500** diploma engineers (4-5 years program)  
**over 400** obtained scientific master degree (Bologna program)  
**over 70** obtained specialist master degrees  
**over 450** PhD degrees

# Industrial biotechnology in Croatia



Pliva, member of TEVA



Biocentre (University Zagreb)

## Pliva development

**1953** - THE START OF **VITAMIN C** PRODUCTION , BASED ON IN-HOUSE PATENTED TECHNOLOGY,

**1959** - START OF **OXYTETRACYCLINE** AND **VITAMIN B6** PRODUCTION

**1968** - PLIVA'S **OXYTETRACYCLINE PRODUCTION** PLANT RECEIVES **APPROVAL BY FDA**

**1980** - PLIVA'S ORIGINAL MACROLIDE ANTIBIOTIC **AZITHROMYCIN** IS PATENTED

**1988** - **AZITHROMYCIN** IS LAUNCHED UNDER PLIVA'S BRAND NAME **SUMAMED**

**1991** - **AZITHROMYCIN** IS LAUNCHED UNDER PFIZER'S BRAND NAME **ZITHROMAX** ON US AND WESTERN EUROPE MARKETS

**2008** - PLIVA BECOMES A MEMBER OF THE **TEVA** GROUP, THE LARGEST WORLD GENERIC PHARMACEUTICAL COMPANY

**2011** - A NEW INVESTMENT CYCLE, THE NEW PRODUCTION FACILITY FOR ACTIVE PHARMACEUTICAL INGREDIENTS , THE EXPANSION OF PRODUCTION CAPACITIES FOR ORAL SOLID FORMS AND INJECTIONS

## Biocentre, opened 2016 (EU regional development program)

Start-up companies, research, incubator, biotransfer, education





**Hospira Zagreb** - member of Pfizer group

**Nivestim** (**filgrastim**) is 175 amino acid protein – recombinant methionyl human granulocyte-colony stimulating factor (r-metHuG-CSF)

*E. coli* recombinant technology



## Production of sugar, ethanol and feed in Croatia



Virovitica sugar company

- companies: Sladorana, Viro, and Sugar factory Osijek
- annual sugar production in, Croatia is **370000** tones

## Production of wine, spirits and vinegar in Croatia

- Wine production** [Agrokor vina (Vina Belje, Vina Laguna), Badel 1862, Badel d.o.o., Vinoplod etc; 21000 ha of vineyards) –
- 1.3 million hL; 75 % red and 25 % white wines)

## Yeast production in Croatia



**Pliva Kvasac a Lesaffre company**

- since 1999. - the part of Lesaffre group
- Yeast biomass production – molasses containing medium, fed batch process,
- annual production capacity 16.000 t (fresh and dry active yeast)

## Beer production in Croatia

**6 industrial breweries**

(located in Zagreb, Karlovac, Koprivnica, Daruvar, Osijek and Buzet) and  
cca. over 30 craft brewers

- world largest beer companies  
in Croatia: Molson Coors, Heineken and Carlsberg

## Biofuels production in Croatia



Biogas plant - Vrbovec,- 2 MW

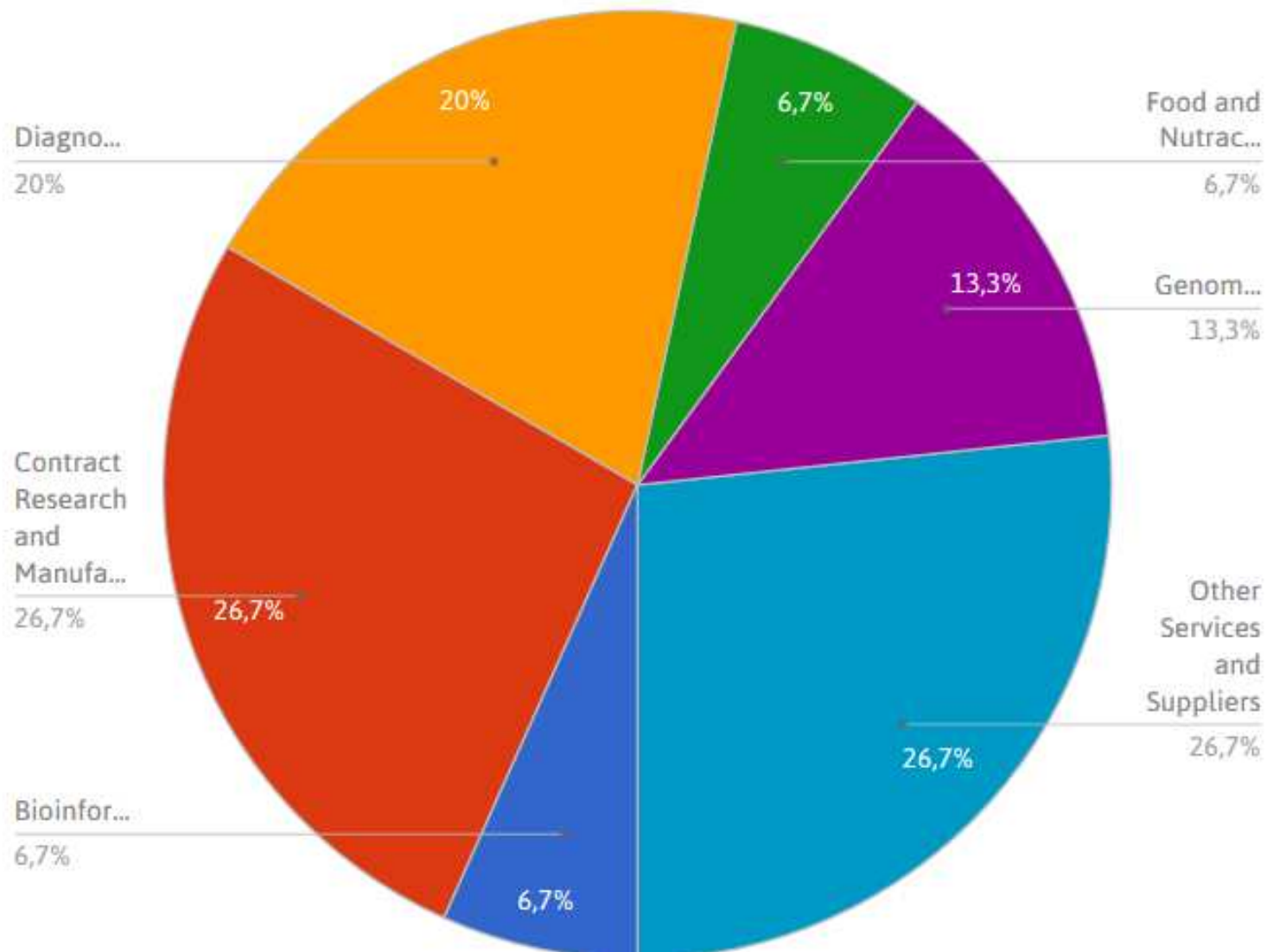
- **bioethanol** production from starch and lignocellulose containing raw materials – in development stage
- **biodiesel** production from vegetable oils (Biodizel Vukovar – capacity 35000 t (stopped production))
- **biogas** production from relatively wide range of renewable feedstocks

## Blue biotechnology (marine biotechnology)



- 35 companies registered for fish farming on 63 locations at Adriatic sea (Zadar and Split-Dalmatia county),
- 4 companies registered for tuna farming on 10 locations.
- 124 registered shellfish farmers on a total of 280 locations

## Biotech Companies in Croatia



## Croatia partner in EU research projects

### Industrial biotechnology and food technology

Projects:

**Program:** SEE-ERA.NET/Leonardo da Vinci:

Raising the Awareness on Healthy Food and Healthy Eating Among Children

Partners: Croatia, Spain, Turkey

**Program:** IPA component IIIC Operational program

Sour cherry Marasca (*Prunus cerasus* var. Marasca) as an ingredient for functional food

**Program:** Program with innovative concept (POC)

Development of rotational tube bioreactor

**Program:** European Framework Projects (FP7)

Biotechnological conversion of carbon containing wastes for eco-efficient production of high added value products

Partners: Croatia, Austria

**Program:** European Framework Projects (FP7)

AmyloEnzymes Captured by Targeted Metagenomics (AMYLOMICS)

Partners: Danmark, Croatia

**Program:** SEE-ERA.NET Plus Joint Call, ERA 195/01

**Project:** Conservation and standardisation of traditional technologies of fermented milk products based on autochthonous lactic acid bacteria

Partners: Croatia, Slovenia, Serbia

**Program:** European Framework Projects (FP7)

**Project:** Processing Raw Materials into Excellent and Sustainable End products while Remaining Fresh (PRESERF)

**Program:** Tempus

**Project:** Improving Academia – Industry Links in Food Safety and Quality

**Program:** Bilateral Croatia-Austria

**Project:** Novel bioethanol production from cellulose

**Program:** Structural EU development front

**Project:** Application of innovative technologies for isolation of bioactive components



### ***COST Projects:***

**Suzana Rimac Brnčić** - POSITIVE - Interindividual variation in response to consumption of plant food bioactives and determinants involved FA 1403 (2014-2018)

**Swen Malte John** - Development and Implementation of European Standards on Prevention of Occupational Skin Diseases, 28. 05. 2013. do 27. 05. 2017.

**Mladen Brnčić** - Food waste valorisation for sustainable chemicals, materials & fuels (EUBis), Od 22.11.2012 do 21.11.2016.

**Mladen Brnčić** - Expert Judgment Network: Bridging the Gap Between Scientific Uncertainty and Evidence-Based Decision Making, Od 23.09.2013 do 22.09.2017.

**Mladen Brnčić** - Valorisation of lignocellulosic biomass side streams for sustainable production of chemicals, materials & fuels using low environmental impact technologies, Od 15.05.2014 do 14.05.2018.

**Anet Režek Jambrak** - „A European Network For Mitigating Bacterial Colonisation and Persistence On Foods and Food Processing Environments”, COST Action FA1202 (2012-2016)

**Anet Režek Jambrak** - „Network on technology-critical elements - from environmental processes to human health threats”, COST Action TD1407 (2015-2019)

**Anet Režek Jambrak** - „Mathematics for industry network (MI-NET)” COST Action TD1409 (2015-2019)

**Anet Režek Jambrak** - „European network for algal-bioproducts (EUALGAE)” ESSEM COST Action ES1408 (2015-2019)

**Anet Režek Jambrak** - „A European Network for Foodborne Parasites (Euro-FBP)” FA COST Action FA1408 (2015-2019)

Electrical discharges with liquids for future applications, 2015.-2018.

TD1408 Interdisciplinarity in research programming and funding cycles, 2015.-2019.

**Jurica Žučko** - Harmonising standardisation strategies to increase efficiency and competitiveness of European life-science research, 21.03.2016.-20.03.2020.

**Damir Ježek** - CA15118 „Mathematical and Computer Science Methods for Food Science and Industry“, 11.04.2016.-10.04.2020.

**Mladen Brnčić** - CA15136 „European network to advance carotenoid research and applications in agro-food and health“, 18.04.2016.-17.04.2020.

## **EU social program**

MICRO-AA

Application of microreactors for determination of antioxidant activity of Croatia wild plants

## **European Commission Horizon 2020 Programme: CARBAZYMES**

total budget of 8,2M€. Implementation the biocatalytic synthesis of Active Pharmaceutical Ingredients (APIs) and bulk chemicals by using a broad platform of unique C-C bond forming enzymes.

**Partners:** Croatia, Germany, Spain

## **European regional development fund**

“Development of innovative process of agricultural waste biological treatment in biogas production – ProBioTech”

## EU Projects “**Biotechnology in medicine**” (Rijeka)

"Strengthening adaptive immunity via innate immunity: enhancing the CD8 T cell response by using the NKG2D ligand expressed in a herpes virus vector (StAdvInn) "EU FP7ERC-2012-AdG\_20120314-Ideas, 2013. - 2018.

**EURAP** “Driving re-investment in R&D and responsible antibiotic use”, Inovative Medical Industry (IMI), 2014.-2017.

„**UHCE**” - Urban Health Centre Europe: integrated health and social care pathways, early detection of frailty, management of polypharmacy and prevention of falls for active and healthy ageing in European cities“, European Commision, 2014.-2017

## Molecular medicine (IRB)

**MultiCaST**: A multidisciplinary approach to discover selective drugs targeting cancer stem cells: The role of potassium transport

**DAAD**: Alzheimer’s disease – the role of cholesterol on processing and localization of APP family members

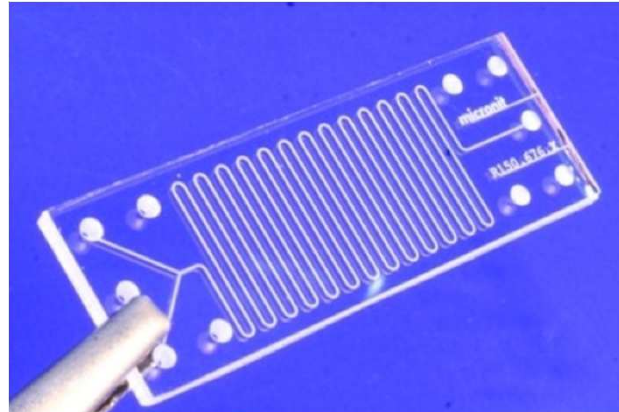
## **BIOXYARN**

In vitro evaluation of the biocompatibility of nanofibrous yarns from an oxidative stress perspective

# Innovation in Croatia biotechnology projects

## Long range objective:

Micro-bioreactors for integration of enzymatic transformations with coenzyme regeneration and product separation



## Project: **CARBAZYMES**

The CARBAZYMES project is a 48-month collaborative project funded by the European Commission under the Horizon 2020 Programme with grant agreement number 635595 and a total budget of **8,2 M€**. During its course, the project will implement the biocatalytic synthesis of Active Pharmaceutical Ingredients (APIs) and bulk chemicals by using a broad platform of unique C-C bond forming enzymes.

**Potential for cooperation:** integration of enzyme multistep transformations, bioactive component separations, multiphase reactions, selectivity and control

## Conclusions

- 1) Dominant scientific biotechnology related projects in Croatia are funded and guided through EU cooperation.
- 2) Main fields of the projects are:
  - enzyme reaction engineering
  - molecular medicine
  - functional foods
  - biofuels
  - environment protection
- 3) Croatia expertise in micro reactor biotechnology has potential for EU cooperation and development of new biotechnology processes with main application in pharma industry.

## References

- 1) B. Šantek, European biotechnology congress, Dubrovnik, 2017, Croatia
- 2) Đ. Vasič Rački, Z. Findrek, Univ. Zagreb, FKIT <http://carbazymes.com/>
- 3) M. Tišma, University of Osijek, PTFOS,
- 4) University of Rijeka, Department of biotechnology <https://www.biotech.uniri.hr/en/>
- 5) Institute Ruđer Bošković, Zagreb, <http://www.irb.hr/eng/Research/Divisions/Division-of-Molecular-Medicine>