What is the added value and impact of participating in a COST Action?

Our experience

Institute of Microbiology of the Czech Academy of Sciences

Laboratory of Biotransformation

Nitrile and phenol biotransformation group **(Ludmila Martínková)**

COST Actions

D25 „Applied biocatalysis. Stereoselective and environmentally friendly reactions catalysed by enzymes“; **2001-2006**

CM0701 „Cascade chemoenzymatic processes – new synergies between chemistry and biochemistry“; **2006-2011**

CM1003 „Biological oxidation reactions – mechanisms and design of new catalysts“; **2011-2015**

CA15106 „C-H activation in organic synthesis“; **2016-2020**

D25 2001-2006 Applied biocatalysis.
Stereoselective and environmentally friendly reactions catalysed by enzymes

WG Nitrile- and amide-hydrolyzing enzymes as tools in organic chemistry

WG meeting
Biotrans symposium 2005 Delft, NL

Supported by project OC D25.001 Nitrile- and amide-hydrolyzing enzymes as tools in organic chemistry (Ministry of Education, CZ; ca. 30,000 €)

D25 Applied Biocatalysis

Events, benefits …

Working group meetings and action workshops

optionally in conjuction with international symposia

WG Kick-off meeting Stuttgart 2002

Action workshops at **Biotrans 2003 Olomouc and Biotrans 2005 Delft**

international symposia on biocatalysis; >500 participants

support by COST: **„COST-Day“**

WG meeting at **Multistep enzyme-catalyzed processes**

2006 Graz

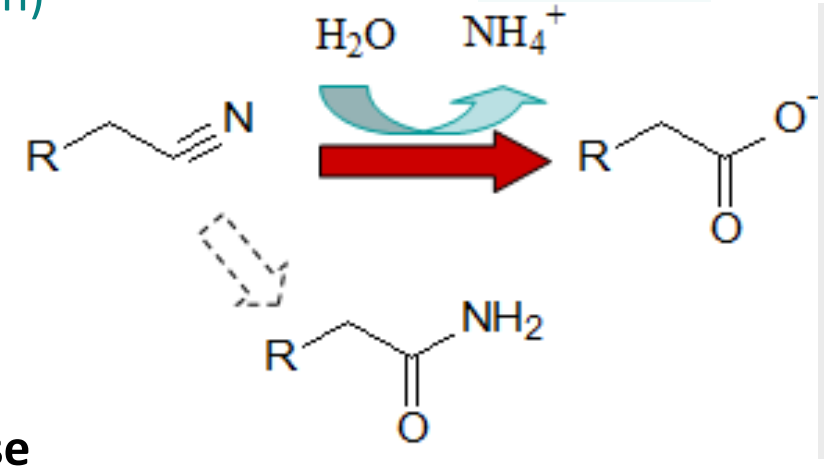
D25 Applied Biocatalysis

Events, benefits …

STSMs (= short-term scientific missions) of students

Veronika Mylerová from Prague to **CNR Catania**, Inst. of Biomolecular Chemistry **2002** (2 weeks)
Gudrun Fischer-Colbrie from **TU Graz** to Prague **2002** (2 weeks)
Margit Winkler-Preiml from **TU Graz** to Prague **2003** (2 weeks)
Ondřej Kaplan from Prague to **Univ. L´Aquila 2004** (1 month)

Nitrilases from bacteria, fungi, plants
Use: preparation of **fine** and **pharmaceutical chemicals**
Benefits: **environment-friendly**, **stereoselective** enzymes



Research at the **frontier of biology and chemistry**
Integration of groups with **chemical and biological expertise**

CM0701 2007-2011 Cascade chemoenzymatic processes – new synergies between chemistry and biochemistry

WG Cascade reactions at the nitrile group

WG meeting
Prague 2009

Supported by project
COST OC09046
Cascade chemoenzymatic reactions of nitriles
(Ministry of Education, CZ; ca. 53,000 €)

CM0701 Cascade Chemoenzymatic Processes

Events, benefits …

Working group meetings and action workshops optionally in conjuction with international symposia

Kick-off Action Workshop 2008 Como

WG meeting 2009 Prague

Biotrans* 2009 Bern

b UNIVERSITÄT BERN

Action Workshop
in conjuction with **Biotrans* 2011 Giardini Naxos, Sicily**

*International symposia on biotransformation and biocatalysis with >500 participants

CM0701 Cascade Chemoenzymatic Processes

Events, benefits …

Summer School of Biocatalysis 2009, 2011 Certosa di Pontignano

Conference Centre of the **University of Siena**

STSMs (= short-term scientific missions) of students

Anna Malandra from **Univ. L´Aquila** to Prague **2009** (6 months)

Marcella Spampinato from **CNR Catania** to Prague **2009** (6 weeks)

Bronislava Uhnáková from Prague to **BOKU Vienna 2010** (6 weeks)

Alena Petříčková from Prague to **Univ. Stuttgart 2010** (3 months)

Integration of **expertise in biology and chemistry**

Combination of enzymatic and chemical reactions to produce fine chemicals and pharmaceuticals

CM0701 Cascade chemoenzymatic processes

2 successive STSMs (6 months) to Anna Malandra

(University of L´Aquila, IT; supervisor Prof. Maria Cantarella)

2007-8 Erasmus internships at the Institute of Microbiology, Prague

2008 Anna **started her PhD.** in L´Aquila;

2009 April - Earthquake in L´Aquila

2009 July – Dec Anna **continued her PhD. in Prague (STSMs)**

2010 and after returning to L´Aquila

2011 received her PhD.

2017 returned to Prague as **postdoc**

(Prof. Šebo´s lab; Inst. Microbiol., since May 2017)

L´Aquila, 6 April 2009

Nitrilases in filamentous fungi: a success story

prior to our study: **two fungal nitrilases known** (not sequenced)

⇨ enzyme hyperinduction - sequence determination - database mining
- overprodution in *Escherichia coli*

➡ **over 20 fungal nitrilases characterized**

(from *Aspergillus*, *Fusarium* etc.)

Aspergillus niger (MicrobeWiki)

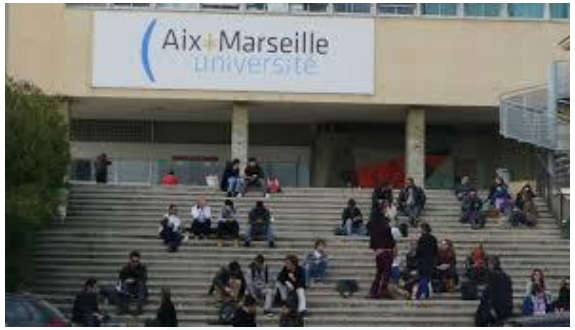
cooperations - construction of **artificial enzyme variants** – with **Univ. Stuttgart**
testing in **continuous reactors** – with **Univ. L´Aquila**
applications in **organic synthesis** – with **TU Graz**, **Univ. Clermont-Ferrand**

JOINT PUBLICATIONS

- Šnajdrová R, Mylerová V, Crestia D, Nikolaou K, … Martínková L, 2004. *J Mol Catal B-Enz* 29, 227-232
- Winkler M, Martínková L, … Klempier N, 2009. *Tetrahedron* 61, 4249-4260
- Martínková L, … Malandra A, Cantarella M, 2009. *Biotechnol Adv* 27, 661-670
- Malandra A, Cantarella M, … Martínková L, 2009. *Appl Microbiol Biotechnol* 85, 277-284
- Winkler M, … Klempier N, Martínková L, 2009. *J Mol Catal B-Enz* 59, 243-247
- Petříčková A, Sosedov A, … Stolz A, Martínková L, 2012. *J Mol Catal B-Enz* 77, 74-80
- Kaplan O, … Pasquarelli F, … Martínková L, 2013. *Mol Biotechnol* 154, 996-1003
- Rinágelová A, … Pasquarelli F, Cantarella M, Martínková L, 2014. *Proc Biochem* 49, 445-450

***Fusarium* sp.** (vetbook.com)

CM1003 2011-2015 Biological oxidation reactions – mechanisms and design of new catalysts



Supported by project: COST LD12049

Characterization and application of fungal non-heme oxidases

(Ministry of Education, CZ; ca. 80,000 €)

WG Oxidation of phenols and related substrates by type 3 dicopper sites

Working group meetings in conjuction with international symposia

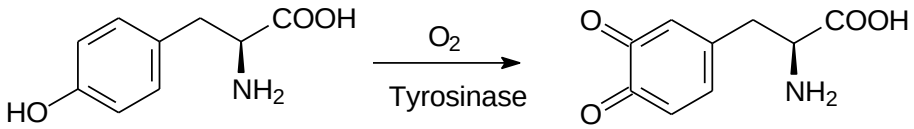
Int. Symposium on Applied Bioinorganic Chemistry 2011 Barcelona

Int. Conference on Bioorganic Chemistry 2013 Grenoble

STSM **Eva Marková-Böhmová** from Prague to **University Aix-Marseille 2016 (3 months)**

Using tyrosinase prepared by us with substrates and inhibitors synthesized by the host lab

Tyrosinases as models for testing inhibitors of hyperpigmentation

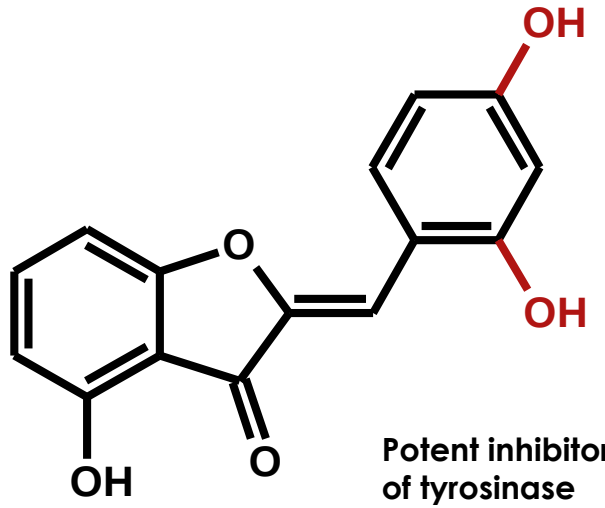


L-Tyrosine L-Dopaquinone

Tyrosinase from ***Polyporus arcularius*** prepared in *E. coli* with high yields

Aurons (plant flavonoids and analogues) tested for inhibition effects on this enzyme

Polyporus arcularius
Mycoweb; mushroomcollecting.com



Potent inhibitor of tyrosinase

Snapdragons: contain aurons
(Growveg.com)

JOINT PUBLICATION

Marková E, Kotik M, Křenková A., Man P, Haudecoeur R, Boumendjel A., Hardré R., Mekmouche Y, Courvoisier-Dezord E, Réglier M, Martínková L, 2016.
***Agric Food Chem* 64, 2925-2931.**

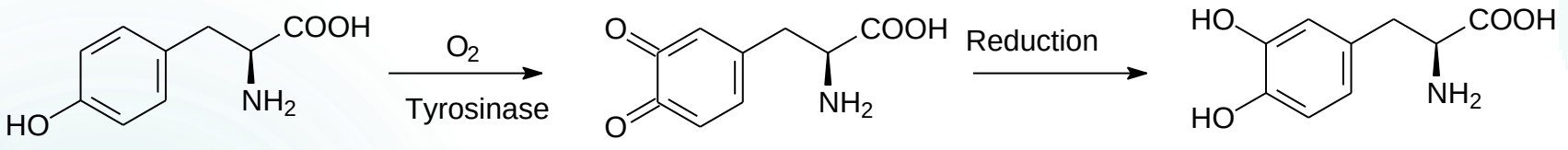
CM15106

2016-2020 C-H Activation in Organic Synthesis

WG C-Heteroatom bond formation via C-H activation

Application for support from program Inter-Excellence (Ministry of Education, CZ) submitted 2017

Our contribution: exploiting expertise in **tyrosinases – use for C-O bond formation**

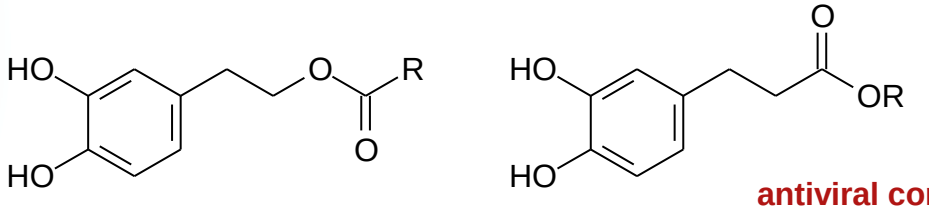


L-Tyrosine

L-Dopaquinone

3,4-Dihydroxy-L-phenylalanine (L-Dopa)
treatment of Parkinson´s disease

Analogously



antiviral compounds

Benefits: access to the **state-of-the-art methodology**, use of tyrosinases in combination with **chemical reactions** proposed by partners

Ongoing collaborations

from previous Actions - examples

TU Graz, Institute of Organic Chemistry – **Dr. Norbert Klempier**
exchange of enzymes and substrates, joint publication*

TU Graz, Institute of Molecular Biotechnology – **Dr. Margit Winkler**
joint project application (Austria Science Fund – Czech Science Foundation)
submission 16 March 2018

University of L´Aquila – **Prof. Maria Cantarella**, **Dr. Agata Spera**
student and staff exchange in Erasmus

University of Marseille – **Dr. Marius Reglier**
preparing H2020 project application
(tyrosinases as inhibition models)

*Wilding B, Veselá A.B, Perry JJB, Black GW, Zhang M, Martínková L, Klempier N, 2015. *Org Biomol Chem* 12, 7803-7812

Acknowledgements

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Laboratory of Biotransformation (head **Prof. V. Křen**)
Institute of Microbiology of the CAS

Institute of Microbiology CAS

National partners:
University of Chemistry and Technology Prague
Charles University

COST partners:
University **L´Aquila**, University **Stuttgart**, TU **Graz**, BOKU **Vienna**, University **Aix-Marseille**, University **Clermont-Ferrand**, University **Oviedo**, CNR **Catania**, University **Debrecen** *etc.*

Thank you for listening!