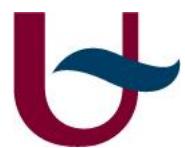


**IT-DED<sup>3</sup>**  
**MSCA-ITN-ETN-2017 Recruitment Event**  
**24 May 2018**

Muhammet TANC

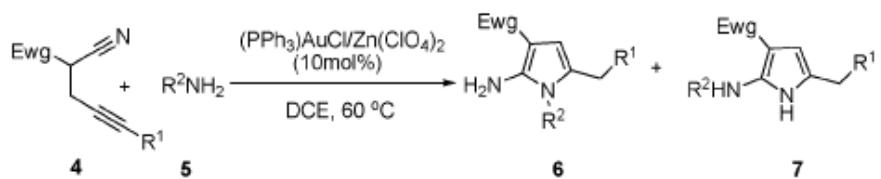


University of Antwerp  
Medicinal Chemistry





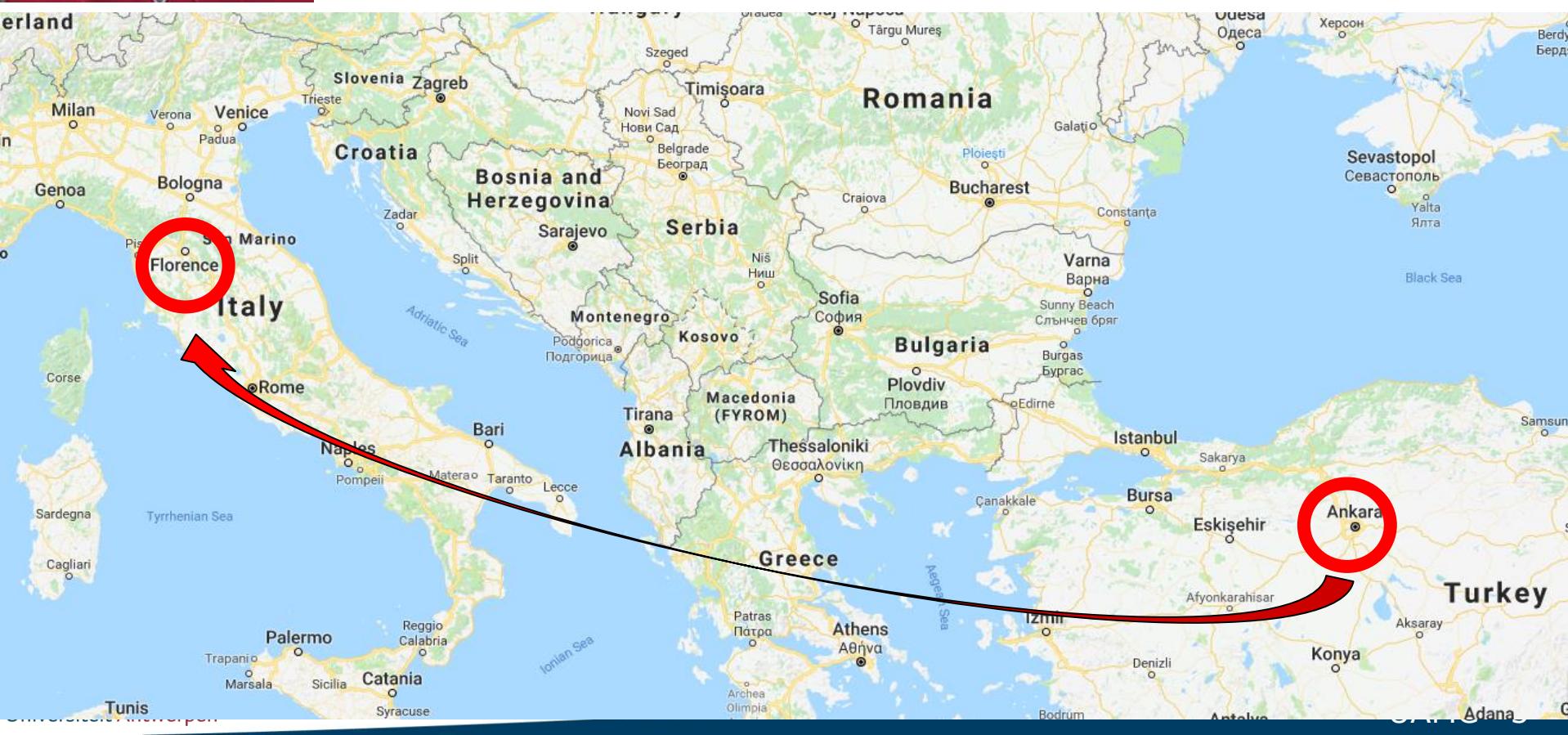




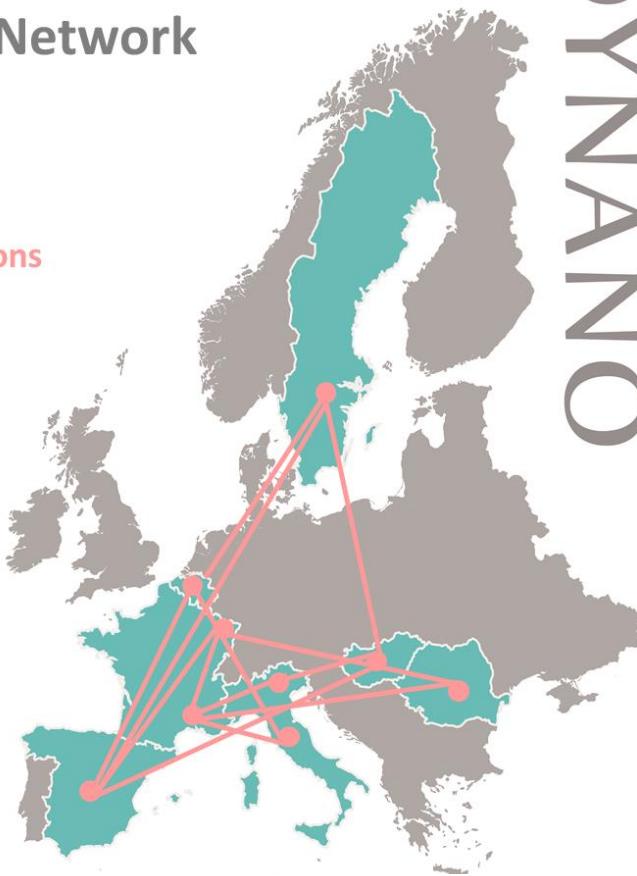
**Scheme 2** Au(I)/Zn(II)-catalyzed sequential inter/intramolecular hydroamination reaction of 4-yne-nitriles with amines.

**Table 1** Efficiency of the transition-metal catalysts for the transformation of 4a with aniline 5a to 6aa<sup>a</sup> and 7aa<sup>a</sup>

Entry	Catalyst <sup>a</sup>	Conditions	Yield <sup>c</sup> (%)
1	$\text{Zn}(\text{ClO}_4)_2$	80 °C, 12 h	Trace
2	PTSA	80 °C, 12 h	—
3	$\text{AgSbF}_6$	60 °C, 8 h	—
4	$\text{AuCl}_3$	60 °C, 8 h	—
5	$(\text{PPh}_3)\text{AuCl}$	60 °C, 8 h	—
6	$(\text{PPh}_3)\text{AuCl}/\text{AgSbF}_6$	60 °C, 6 h	58
7	$\text{AuCl}_3/\text{AgSbF}_6$	60 °C, 8 h	—
8	$\text{AuCl}_3/\text{Zn}(\text{ClO}_4)_2$	60 °C, 5 h	—
9	$(\text{PPh}_3)\text{AuCl}/\text{Zn}(\text{ClO}_4)_2$	rt, 12 h	40
10	$(\text{PPh}_3)\text{AuCl}/\text{Zn}(\text{ClO}_4)_2$	60 °C, 5 h	65, 70 <sup>b</sup>
11	$(\text{PPh}_3)\text{AuCl}/\text{Zn}(\text{ClO}_4)_2$	90 °C, 3 h	68
12	$(\text{PPh}_3)\text{AuCl}/\text{Zn}(\text{OTf})_2$	60 °C, 5 h	63
13	$(\text{PPh}_3)\text{AuCl}/\text{AgClO}_4$	80 °C, 8 h	61 <sup>d</sup>



# The DYNANO Global Network



Active  
collaborations

DYNANO



BELGIUM  
FRANCE  
HUNGARY  
ITALY  
ROMANIA  
SPAIN  
SWEDEN

- 11 Research
- 3 Industrial
- 1 Associate

## PARTNERS

### A strong consortium!

DYNANO's challenging objectives will be reached thanks to a strong multidisciplinary consortium of 15 partners with high-level expertise from all over Europe. First-class research groups are working hand in hand with innovative industrial companies to reach DYNANO's scientific goal and train a new generation of skilled scientists.

Confidential

# Carbonic Anhydrases (CAs)



$\alpha$  -CAs Bacteria, algae, cytoplasm of green plants, protozoa animals – including vertebrates

$\beta$  -CAs - Bacteria, algae, chloroplasts of mon-/dicotyledons

$\gamma$  -CAs - Archaea, Bacteria

$\delta$  -CAs - Cd or Zn enzymes from marine diatoms

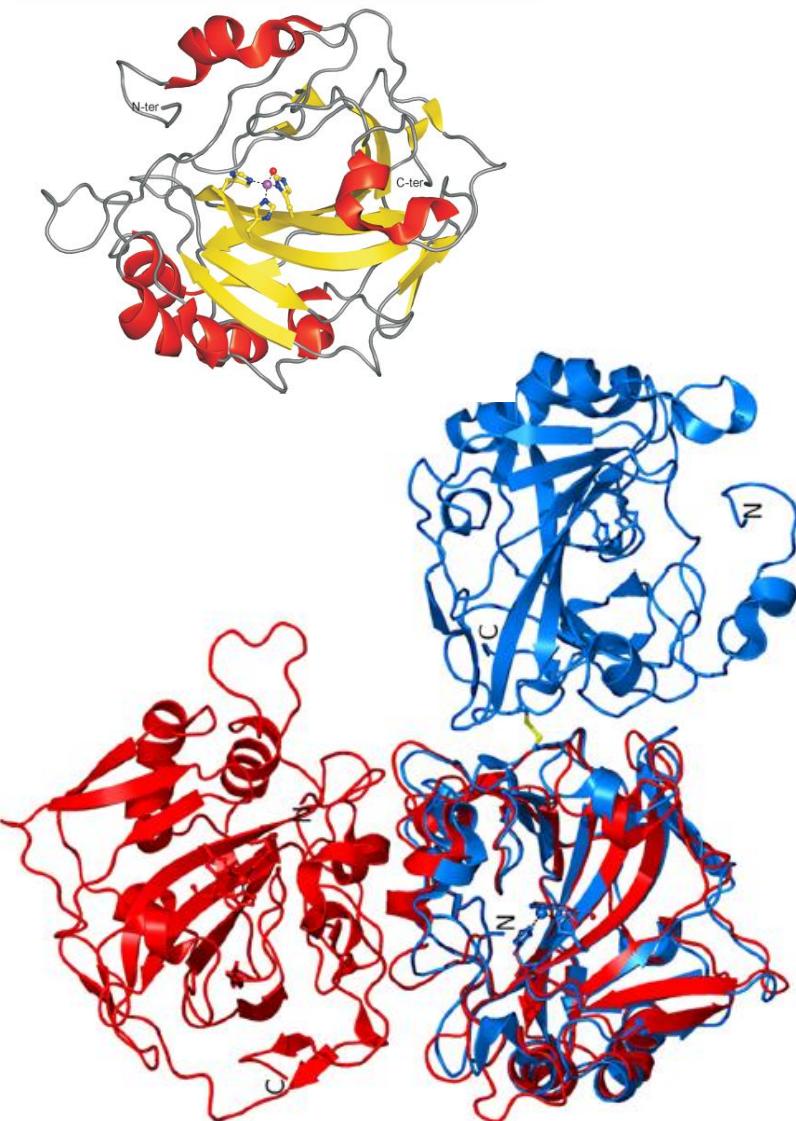
$\zeta$  -CAs - Marine diatoms and algae

$\eta$  -CAs - *Plasmodium falciparum*

$\theta$ -CAs - Thylakoid luminal marine diatoms

*Nature Rev. Drug Discov.* **2012**, 11, 709  
*Bioorg. Med. Chem. Lett.* **2014**, 18, 4389  
*Proc. Natl. Acad. Sci.* **2016**, 113, 9828

# Carbonic Anhydrases (CAs)



Isozyme	Sub-cellular localization
CA I	cytosol
CA II	cytosol
CA III	cytosol
CA IV	plasma membrane
CA VA	mitochondria
CA VB	mitochondria
CA VI	secreted (saliva/milk)
CA VII	cytosol
CA VIII	cytosol
CA IX	transmembrane
CA X	cytosol
CA XI	cytosol
CA XII	transmembrane
CA XIII	cytosol
CA XIV	transmembrane

*Nature Rev. Drug Discov.* **2012**, *11*, 709

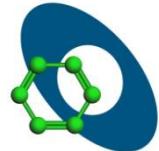
Confidential



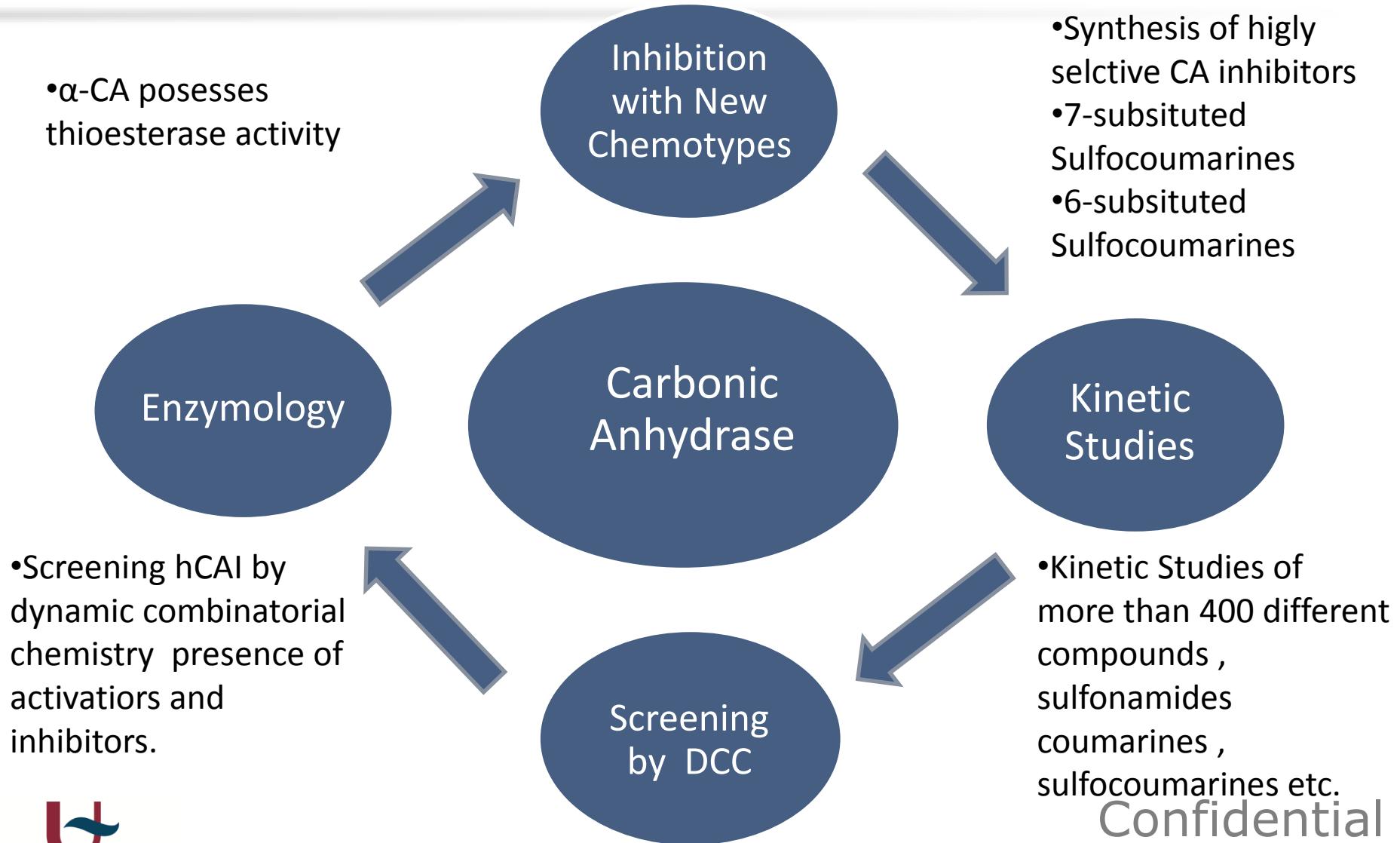
# Therapeutic applications of CAIs and CAAs

- CA I : Alzheimer
- CA II : Glaucoma, Osteoporosis, CAIs diuretics
- CA IV : Glaucoma, CAIs diuretics
- CA VA, VB : Obesity
- CA IX : Cancer
- CA XII : Cancer , CAIs as diuretics
- CA XIV : CAIs as diuretics
- Infections caused by protozoa , fungi and bacteria





# Approaching Carbonic Anhydrase



# Academia or Industry ?



## THE PLANS:



THE PLAN YOU  
TELL YOUR  
ADVISOR

: "I'M GOING TO BE A  
PROFESSOR AT A MAJOR  
RESEARCH UNIVERSITY  
AFTER I GRADUATE."



THE REAL  
PLAN

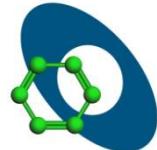
: LOOK FOR CAREER  
ALTERNATIVES.



THE SECRET  
PLAN

: BECOME A  
BAKER/ROCKSTAR/WRITER.

# DYNANO after PhD



- Marta Abellan Flos, **Supervisor:** Stéphane Vincent
- Industry - Academia



- Xabier Osteikoetxea Veleze **Supervisor:** Buzás Edit
- Industry



- Susanne Schneider **Supervisor:** Jean-Marie Lehn
- Industry



- Romina Crasneanu **Supervisor:** Mihai Barboiu
- Secret Plan

- 5 ESR's out of 12 follow a path outside of academia



# What I did...



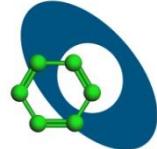
The screenshot shows a web browser window with the following details:

- Header: "has problems." (redacted)
- Logo: European Commission
- Title: "European Commission  
Research & Innovation - Participant Portal  
Proposal Submission Forms"
- Section: "Horizon 2020"
- Text: "Call: H2020-MSCA-IF-2016  
(Marie Skłodowska-Curie Individual Fellowships)"
- Text: "Topic: MSCA-IF-2016"
- Text: "Type of action: MSCA-IF-EF-ST  
(Standard EF)"
- Text: "Proposal number: 753221"
- Text: "Proposal acronym: ONCOPHAGY"

Novel Atg4B-inhibitors and dual [Atg4B-Carbonic Anhydrase] inhibitors for interfering with cytoprotective mechanisms of cancer cells in the acidic tumor micro-environment



# Autophagy



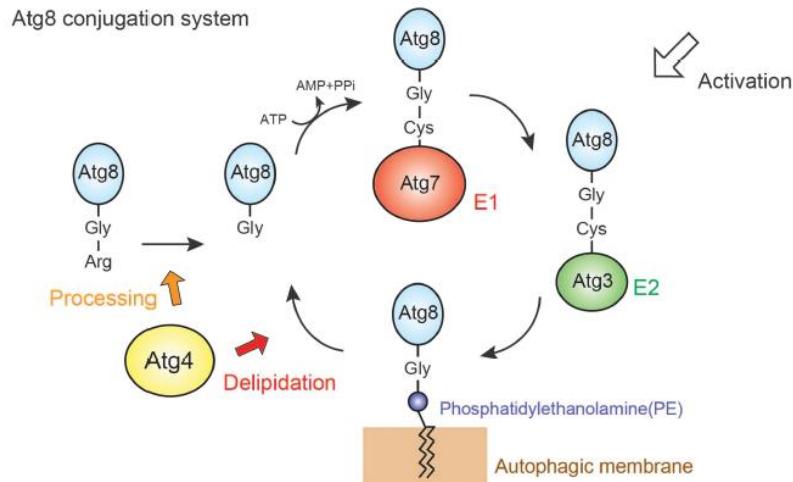
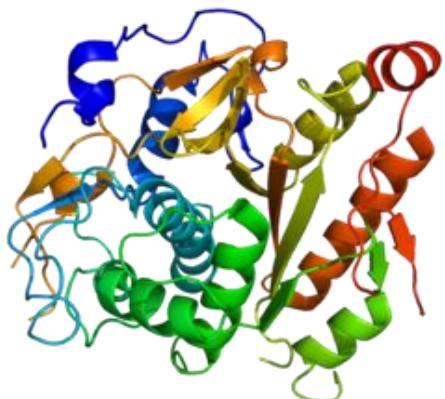
- Autophagy is an intracellular recycling process of cytosolic proteins and organelles
- Conserved in eukaryotes
- Maintaining cellular homeostasis
- Degradation also targets pathogenic microbes
- Dysfunction can play role in diseases such as infection , neurodegenerative diseases and cancer.

*Cancer Metastasis Rev.* **2014**, 33, 823-833,  
*J. Antibiot.* **2017** 71, 72-78

Confidential



# Targeting Atg4B

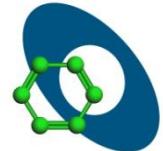


- Tumor cells activate autophagy to produce nutrients in cell
- Most of autophagy inhibitors act in a non-specific manner
- Processing Atg8 precursors by Atg4 highly specific
- Atg4B exhibits higher activity than the other homolog

Figure 1 Basic mechanism of autophagy. (a) Membrane dynamics of autophagy. (b) Atg8 and Atg12 conjugation systems essential for autophagy.



# MSCA Fellowship



- Excellence in Science , Pushing limits
- Mobility
- Networking



# Marie Curie Alumni Association (MCAA)



The screenshot shows the homepage of the MCAA website. At the top, there is a navigation bar with links for HOME, ABOUT US, CHAPTERS & GROUPS, EVENTS, NEWS, JOBS, and BLOG. To the left of the main content area is a sidebar with a logo consisting of four stylized human figures in red, green, blue, and yellow, and the text "MARIE CURIE ALUMNI". The main content area features a large banner with a background image of laboratory glassware. A dark overlay box contains the text "Welcome to the Marie Curie Alumni website!". Below this, there is a brief description of the association's purpose, followed by two calls to action: "An Association providing high-quality services to enhance research and professional collaboration." and "Find out about our activities! Join us!".

## MCAA: A global network of researchers



### Vision

We envision a future in which knowledge will be used to benefit society.



### Mission

We support, and contribute to, the advancement of knowledge for a global, diverse, and informed society.



### Strategy

MCAA connects researchers throughout Europe, and around the world, to enable international transdisciplinary collaborations.



### Goals

Enhance the flow of knowledge across different countries, sectors of the economy, and scientific disciplines





# THANK YOU

