



Natural products in the fight against ageing and age-related diseases

Ioannis Trougakos

Professor, Group of "Ageing and Age-related Diseases"

<http://scholar.uoa.gr/itrougakos>

*Department of Cell Biology and Biophysics, Faculty of Biology
National & Kapodistrian University of Athens, Greece*

INNOVATIONS IN FOOD LOSS AND
WASTE MANAGEMENT



Ancona 23-25 January 2024

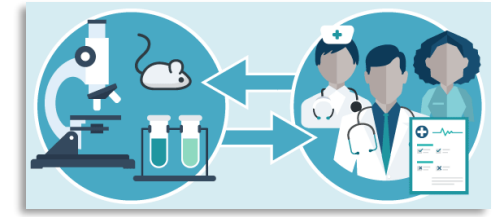
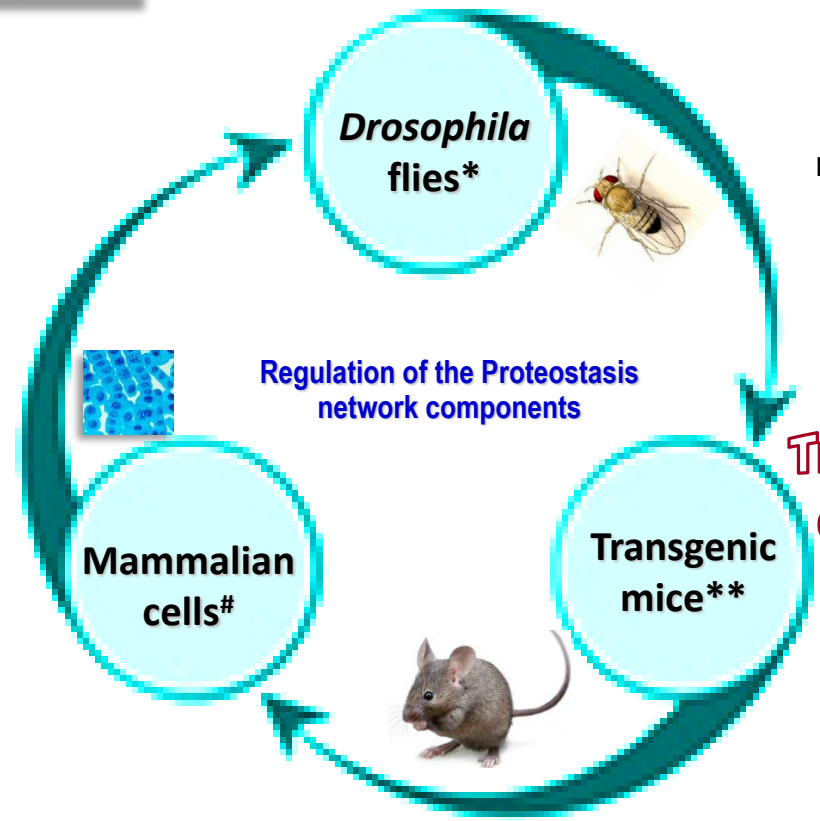


Group of "Ageing and Age-Related Diseases"

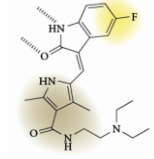
A multidisciplinary Systems Biology (cell-based, *in vivo* models) approach in order to understand:

- The different levels of regulation and cross-talk of the various proteostatic machineries
- The interaction, wiring and functional integration of PN with mitostasis and genomic integrity
- The systemic effects induced by tissue-specific loss of proteostasis
- The deregulation of proteostatic modules in *aging* and/or *age-related diseases*

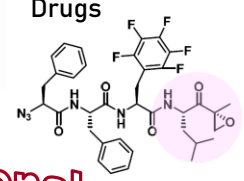
Cell
Organism
Cell/
Organism



Natural compounds



Drugs



Translational continuum



Human cohorts (e.g. cancer patients)

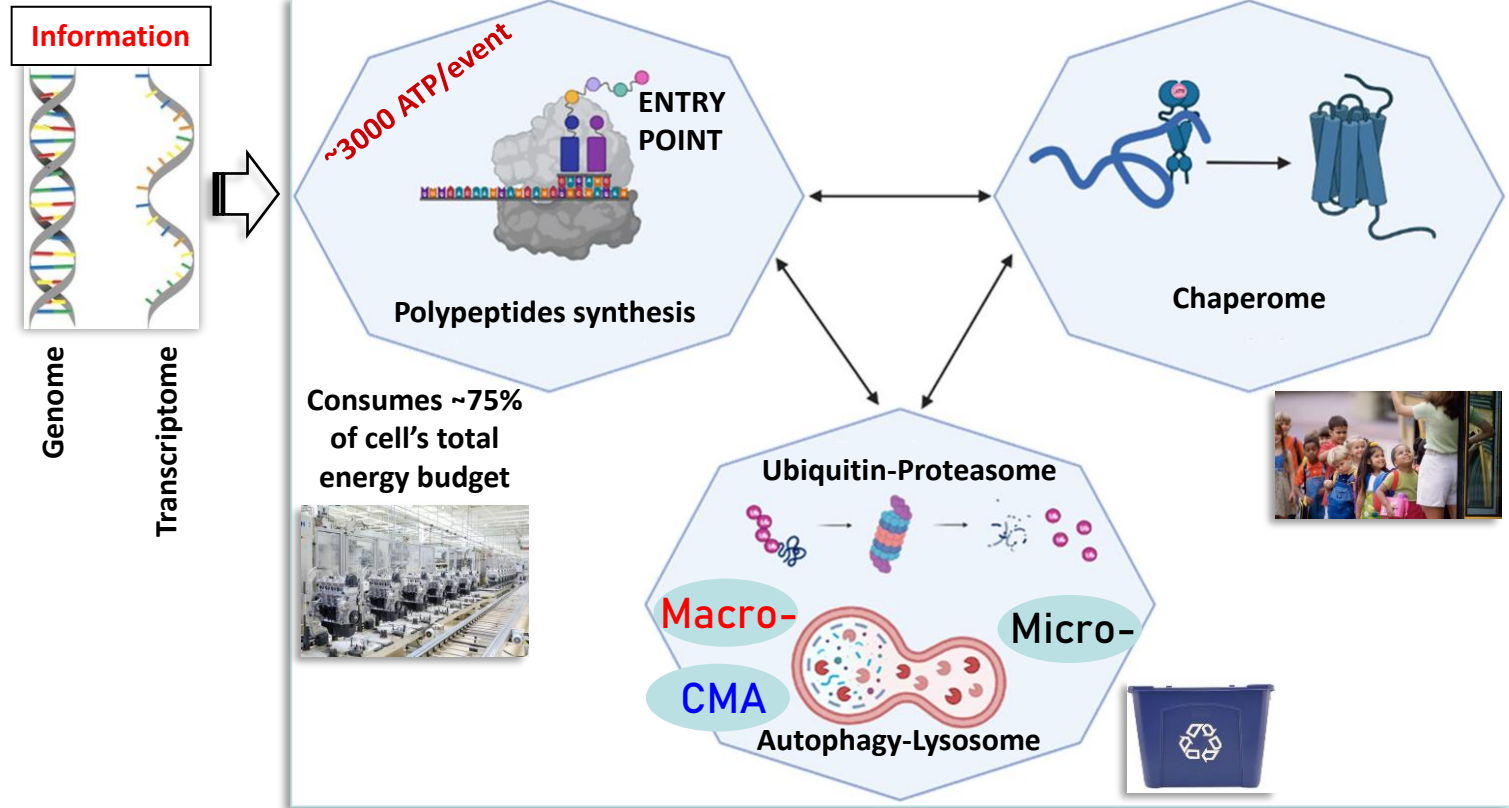
<http://scholar.uoa.gr/itrougakos/home>

* >320 Tg lines of proteostatic, mitostatic, genome stability genes, reporters, etc.
 # a biobank of numerous normal and cancer human or mouse/rat cell lines
 ** 4 Tg lines of CLU (molecular chaperone) ubiquitous or tissue-specific OE

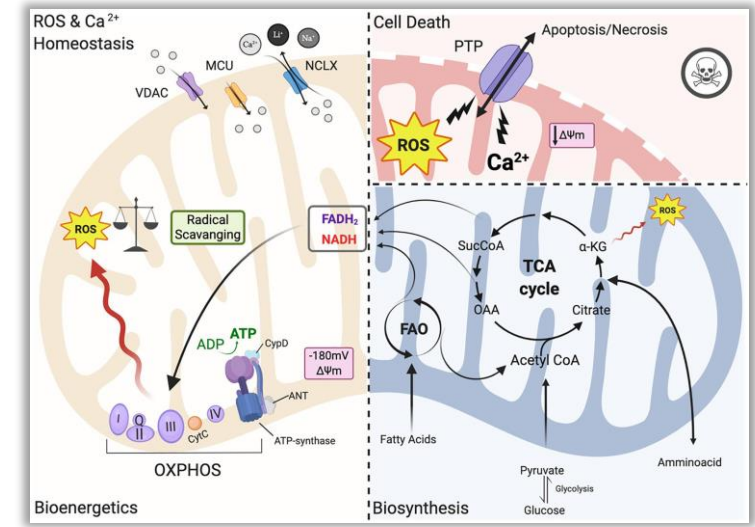


PROTEOSTASIS NETWORK (PN) and Proteome Damage Responses (PDR)

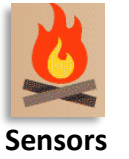
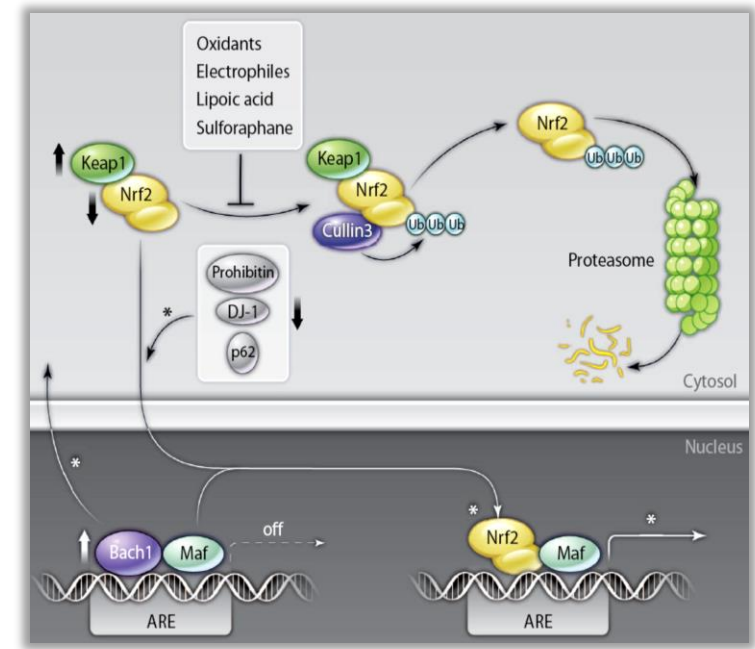
(a decision to *fold*, *hold*, or *degrade*)



Niforou et al. (2014). Redox Biol. 30, 323-332
 Gumeni and Trougakos (2016). Oxid Med Cell Longev. 4587691
 Gumeni et al. (2017). Int J Mol Sci. 18(10)
 Sklirou A, et al. (2018) Cancer Lett. 413, 110-121
 Tsakiri and Trougakos (2019). Int Rev Cell Mol Biol. 314, 171-237



Ramaccini et al. (2021). Front Cell Dev Biol. 12, 624216



Syktotis GP, Bohmann D. (2010). Sci Signal. 3, re3



"Nothing in Biology Makes Sense Except in the Light of Evolution"
 Theodosius Dobzhansky

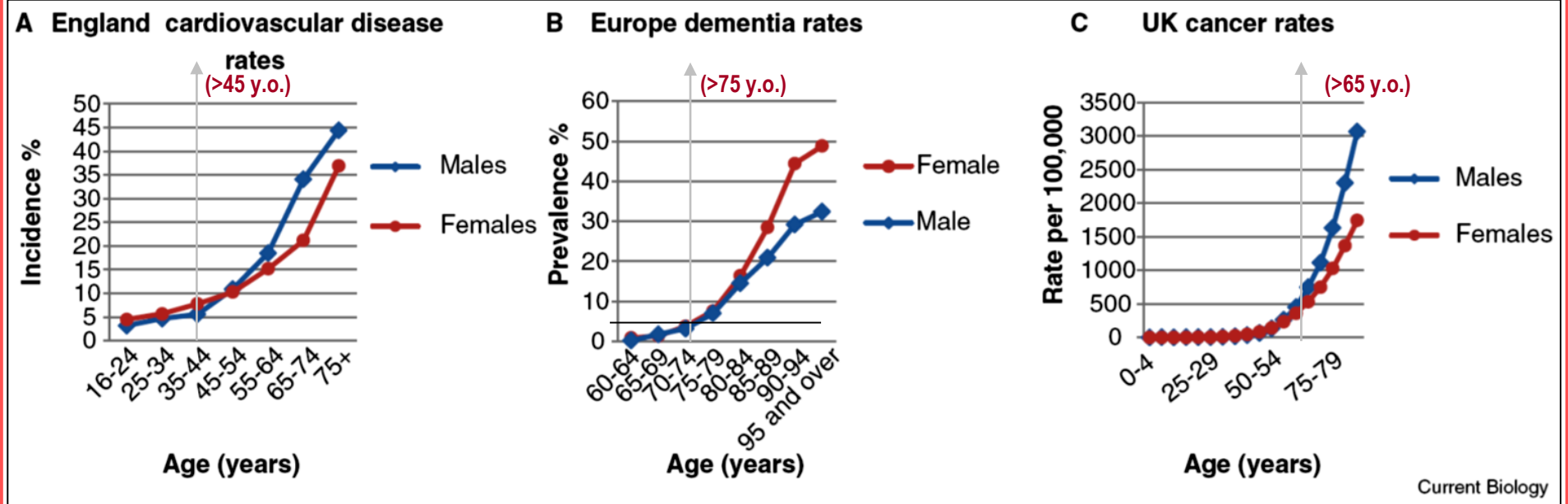
Ageing - an unnatural period of life

Stress responses
 (Fully Active)
 Survival

Reproduction
 (less tightly programmed as compared to construction)

Muscular

Aging is the primary risk factor for most major human pathologies



(A) Cardiovascular disease incidence in England in 2006 (source: British Heart Foundation 'Coronary heart disease statistics' 2010).
 (B) Dementia prevalence in EU countries in 2006 (source: Alzheimer Europe, 2009).
 (C) Age-specific mortality rates per 100,000 population, UK (source: Cancer Research UK).
 From: Niccoli and Partridge (2012). Curr Biol. 22, R741-52.

Age-Related Diseases
 (e.g., cancer, degeneration, diabetes, etc.)

Gorgoulis et al., (2018). J Pathol 246, 12-40.
 Trougakos (2019) Aging 11, 5289-5291.
 Trougakos (2023). In submission

No cell type is spared from ageing

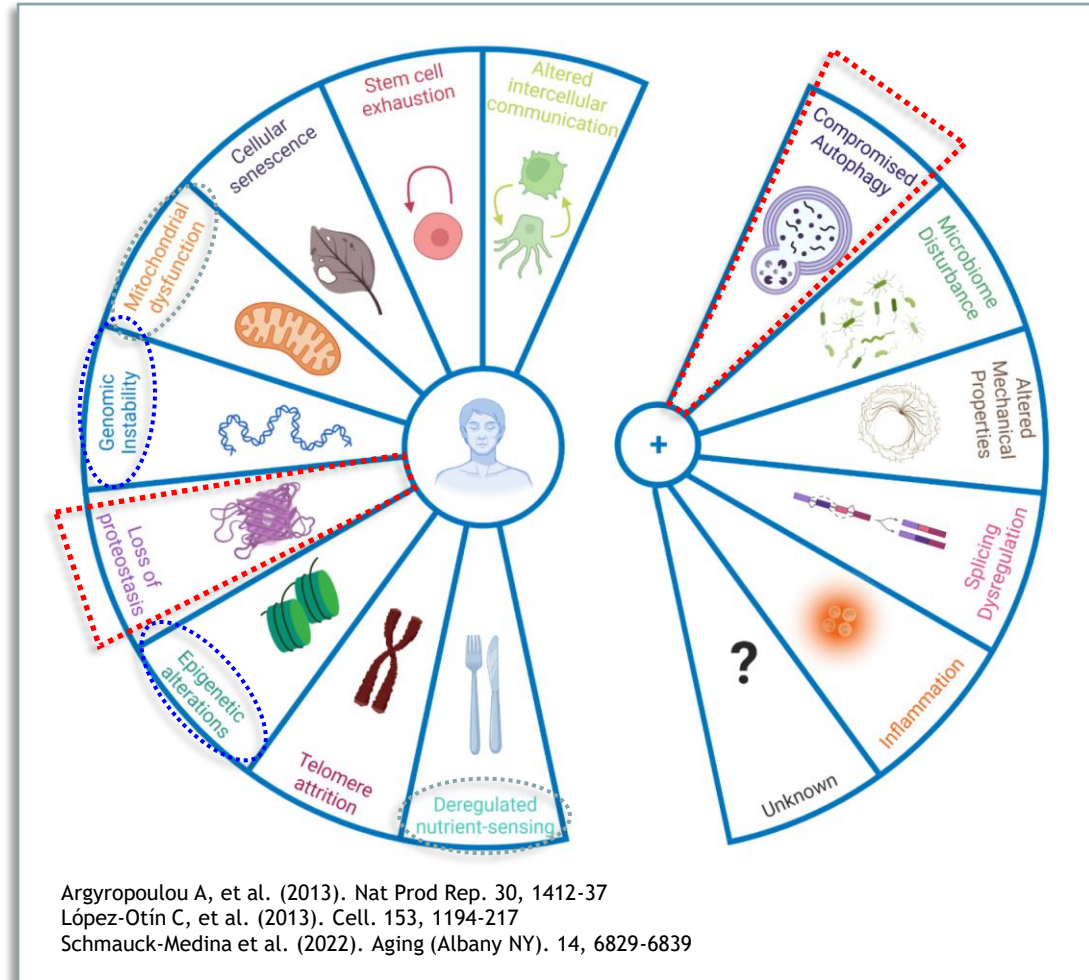
Ageing is an inevitable consequence of life for nearly all organisms

It mostly reflects the outcome of complicated interactions between genetic factors along with the accumulation of a variety of deleterious stochastic changes over time due to a progressive failure of homeostasis that promotes multiple biochemical, molecular, and cellular changes which lead to increased disability, morbidity, and inevitably to death.

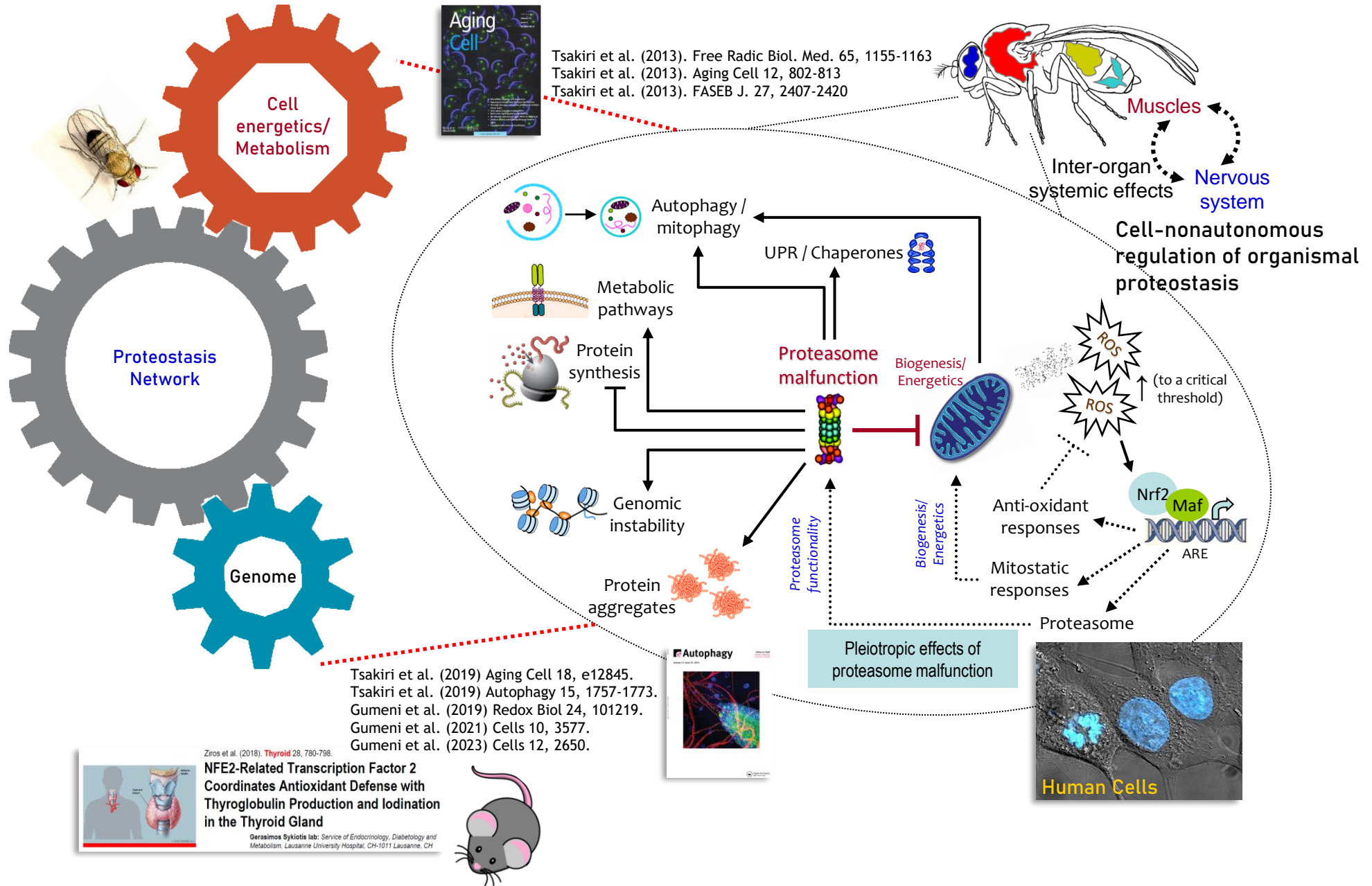




Hallmarks of Aging



Argyropoulou A, et al. (2013). Nat Prod Rep. 30, 1412-37
López-Otín C, et al. (2013). Cell. 153, 1194-217
Schmauck-Medina et al. (2022). Aging (Albany NY). 14, 6829-6839





(Neuro)-degenerative diseases

CDD *press* www.nature.com/cddis

ARTICLE OPEN Check for updates

Nrf2 activation induces mitophagy and reverses Parkin/Pink1 knock down-mediated neuronal and muscle degeneration phenotypes

Sentiljana Gumeni¹, Eleni-Dimitra Papanagnou¹, Maria S. Manola¹ and Ioannis P. Trougkos¹

Cell Death and Disease (2021)12:671 SPRINGER NATURE

Neurobiology of Aging 105 (2021) 137-147

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging.org

Amyloid toxicity in a *Drosophila* Alzheimer's model is ameliorated by autophagy activation

Eleni N. Tsakiri[#], Sentiljana Gumeni[#], Maria S. Manola, Ioannis P. Trougkos^{*}

Cardiopathies

Received: 4 April 2022 | Revised: 1 August 2022 | Accepted: 31 August 2022

DOI: 10.1111/accel.13715

Aging Cell **WILEY**

RESEARCH ARTICLE

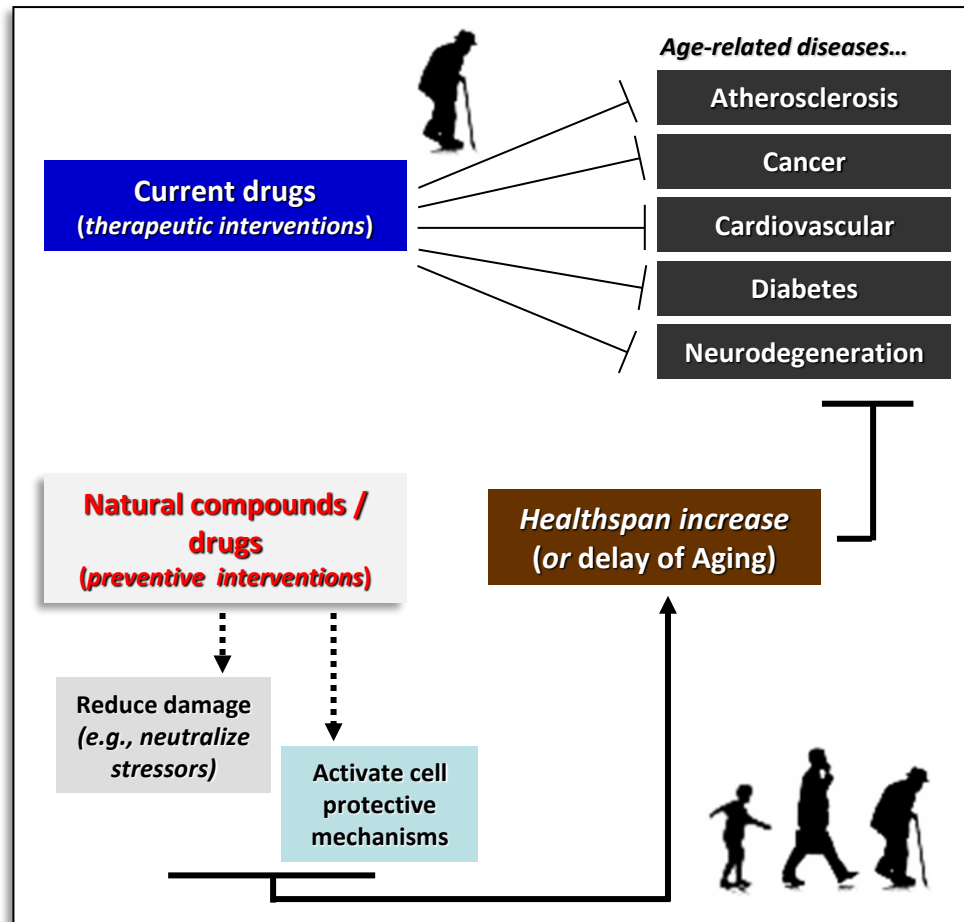
Autophagy activation can partially rescue proteasome dysfunction-mediated cardiac toxicity

Eleni-Dimitra Papanagnou¹ | Sentiljana Gumeni¹ | Aimilia D. Sklirou¹ |
 Alexandra Rafeletou¹ | Evangelos Terpos² | Kleoniki Keklikoglou^{3,4} |
 Efsthios Kastiris² | Kimon Stamatelopoulos² | Gerasimos P. Sykiotis⁵ |
 Meletios A. Dimopoulos² | Ioannis P. Trougkos¹



Can we decelerate the clock?

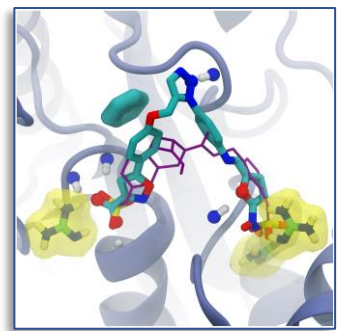
Anti-aging interventions as a systemic approach to also tackle age-related diseases



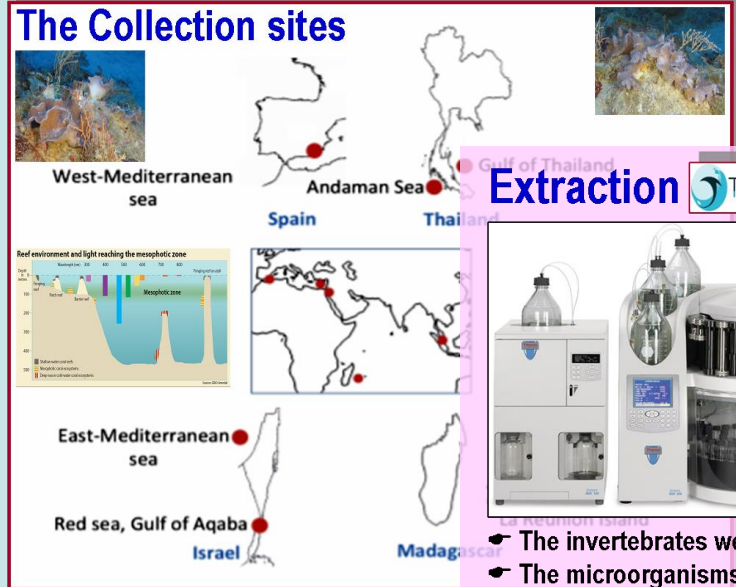
Natural products (*extracts or pure compounds*) exert a broad range of biological activities, and therefore, they constitute the ultimate inventory of seeking novel structures capable of diverse and sometimes extraordinary anti-aging effects



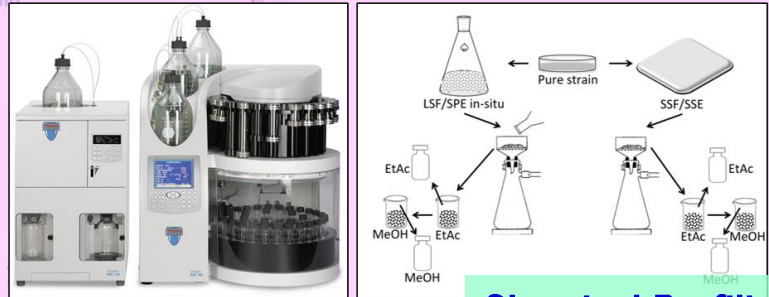
Small molecules for the modulation of age/age-related diseases-related therapeutic targets



Workflow pipeline

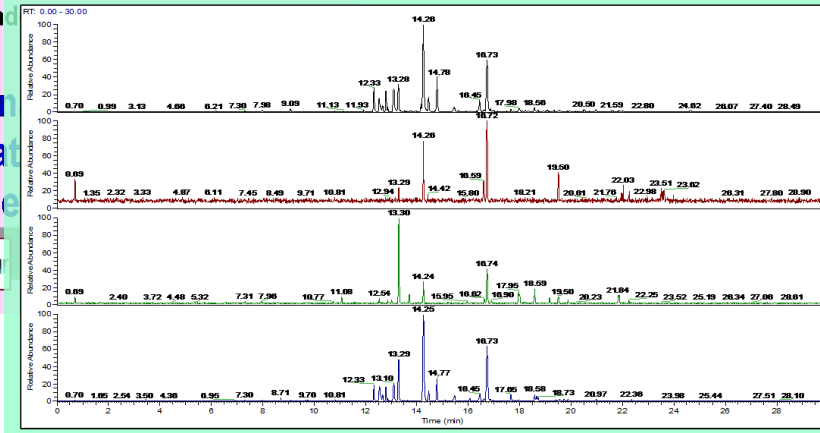


Extraction

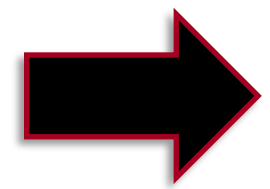


- The invertebrates were lyophilized and extracted
- The microorganisms were cultivated under

Chemical Profiling



• Extracts were submitted for LC-HRMS profiling for investigating their chemical content and for dereplication.



Fraction preparation for bio-e

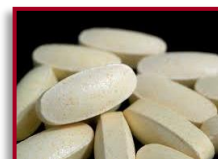




Bio-evaluation



Pharmaceuticals



Cosmeceuticals



Neutraceuticals



- Assay development
- Screening (cell-free, cell-based, or *in vivo*)





High-tech technological platforms - involvement in high throughput screening for the isolation of bioactive compounds from various sources of the biosphere

The screenshot displays three websites related to the research project:

- Tascmar:** A project website titled 'Tools And Strategies to access original bioactive compounds by Cultivating MARine invertebrates and associated symbionts'. It lists 70 researchers, 13 partners from 8 countries, 6.7 M€ EU funding, and a 4-year duration (2015-2019). It describes the project's goal to develop new tools and strategies to overcome bottlenecks in the discovery and application of marine-derived biomolecules.
- MICROCOSMETICS:** A website focused on the 'Exploitation of Microbial Biodiversity for the Discovery & Development of Novel Cosmeceutical Agents'. It outlines the consortium's goal to explore the global biodiversity of microorganisms for the discovery of novel anti-ageing active ingredients.
- MediHealth:** A website with the main goal of 'Novel natural products for healthy ageing from the Mediterranean diet and food plants from other global sources'. It describes the project's aim to introduce a novel approach for the discovery of active agents of food plants from the Mediterranean diet.

High throughput small molecules Discovery Platform

NPR RSCPublishing

REVIEW View Article Online View Journal

Natural compounds with anti-ageing activity

Aikaterini Argyropoulou,^a Nektarios Aligiannis,^a Ioannis P. Trougakos^{ab} and Alexios-Leandros Skaltsounis^{1a}

Cite this: DOI: 10.1039/c3np70031c



A feasible approach



Active and Healthy Ageing
For you & with you



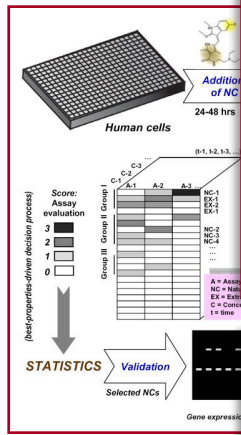
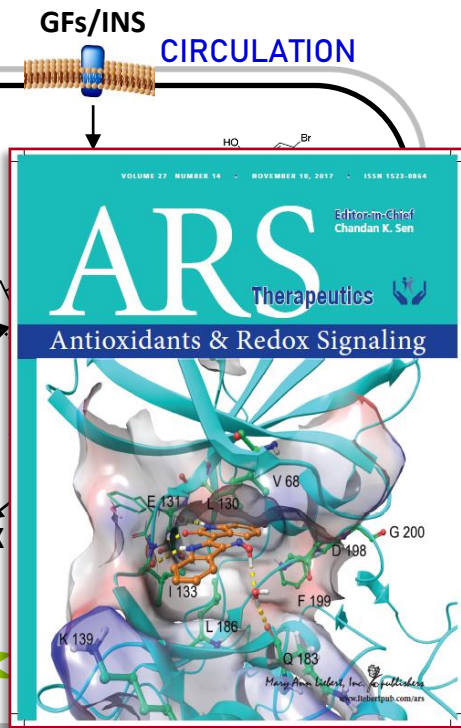
The indirubin derivative 6-Bromoindirubin-3'-oxime (6BIO) activates proteostatic modules, reprograms cellular bioenergetic pathways and exerts antiaging effects

ANTIOXIDANTS & REDOX SIGNALING
Volume 00, Number 00, 2017
© Mary Ann Liebert, Inc.
DOI: 10.1089/ars.2016.6910

ORIGINAL RESEARCH COMMUNICATION

The Indirubin Derivative 6-Bromoindirubin-3'-Oxime Activates Proteostatic Modules, Reprograms Cellular Bioenergetic Pathways, and Exerts Antiaging Effects

Eleni N. Tsakiri,¹ Nicolas Gaboriaud-Kolar,² Kalliopi K. Iliaki,¹ Job Tchoumtchoua,² Eleni-Dimitra Papanagnou,¹ Sofia Chatzigeorgiou,¹ Konstantinos D. Tallas,¹ Emmanuel Mikros,³ Maria Halabalaki,² Alexios-Leandros Skaltsounis,² and Ioannis P. Trougakos¹



6-bromoindirubin

SCIENTIFIC REPORTS

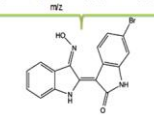
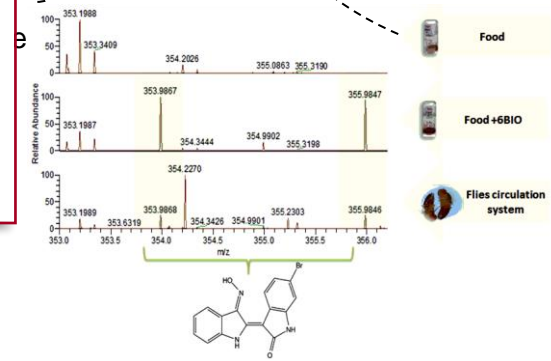
OPEN 6-bromo-indirubin-3'-oxime (6BIO), a Glycogen synthase kinase-3 β inhibitor, activates cytoprotective cellular modules and suppresses cellular senescence-mediated biomolecular damage in human fibroblasts

Received: 29 December 2016
Accepted: 25 August 2017
Published online: 15 September 2017

Aimilia D. Skirrou¹, Nicolas Gaboriaud-Kolar², Issidora Papassideri¹, Alexios-Leandros Skaltsounis² & Ioannis P. Trougakos¹



- Locomotor activity \uparrow
- Resistance to stressors \uparrow
- Glucose/Lipids \downarrow
- Healthspan/Lifespan \uparrow





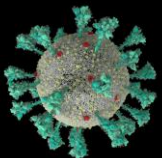
- A. Sklirou, PhD
- E. Papanagnou, PhD
- S. Gumeni, PhD
- Z. Evangelakou, PhD student
- M. Manola, PhD student
- D. Gianniou, PhD student
- E. Gkogkou, PhD student
- X. Louka, PhD student
- K. Theodosopoulou, MSc student
- V. Melingiotis, BSc student
- Th. Papadopoulou, BSc student
- M. Pentogenni, BSc student
- K. Zacharapoulou, BSc student
- M. Kostopoulou, BSc student

Happy to participate with colleagues from our COST projects or grant applications



The National and Kapodistrian University of Athens Trial:

COVID-19 patients, Vaccine recipients, omics analyses for Systems Vaccinology



SARS-CoV-2

Collaborators

- L. Alexopoulos (Nat. Tech. Univ. Athens, GR)
- I. Andreadou (Univ. Athens, GR)
- D. Bohmann (Univ. Rochester, US)
- A. Daga (Univ. Padova, IT)
- M. Dimopoulos (Univ. Athens, GR)
- N. Fokialakis (Univ. Athens, GR)
- V. Gorgoulis (Univ. Athens, GR)
- T. Grune (GIHN, DZD, DZHK, DE)
- M. Halabalaki (Univ. Athens, GR)
- S. Haralambous (Pasteur Inst, GR)
- G. Juhász (Hungarian Acad. Sci. HU)
- S. Kastritis (Univ. Athens, GR)
- E. Mikros (Univ. Athens, GR)
- J. Ouazzani (CNRS, FR)
- H. Overkleeft (Univ. Leiden, HL)
- A. Scorilas (Univ. Athens, GR)
- L. Scorrano (Univ. Padova, IT)
- A-L. Skaltsounis (Univ. Athens, GR)
- K. Stamatelopoulos (Univ. Athens, GR)
- H. Stuppner (Univ. Innsbruck, AU)
- G. Sykiotis (Lausanne Univ. Hospital, CH)
- E. Terpos (Univ. Athens, GR)
- O. Tsitsilonis (Univ. Athens, GR)
- S. Volarevic (Univ. Rijeka, HR)
- K. Vougas (BRFAA, GR)
- V. Zoumpourlis (NHRF, GR)



A TEAM APPROACH...
MORE OPTIONS & BETTER OUTCOMES

Funders €€€€

