





## IHU HealthAge 1st SAB

### September 5-7, 2024

Identifying exerkinases as new tools against sarcopenia: the exemple of apelin

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RESTORE










## Considering exerkinases as new marker of healthy aging

An **exerkine** is a bioactive molecule or signaling factor that is produced and released by tissues in response to physical exercise. These molecules can include proteins, peptides, metabolites, and hormones. Exerkinases play a crucial role in mediating the beneficial effects of exercise on various organs and tissues, influencing processes such as metabolism, inflammation, tissue repair, and overall health.



### Exercise-Induced Myokines With Therapeutic Potential for Muscle Wasting

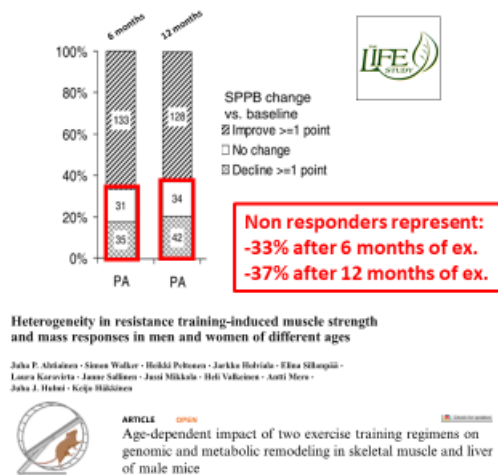
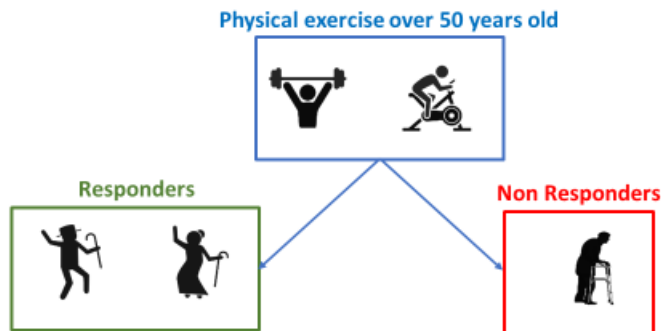
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- ↑ IGF-1 (McCall et al., 2003)
- ↓ Myostatin (Walker et al., 2004)
- ↑ Decorin (Kanzleiter et al., 2014)
- ↑ IL-15 (Bazgir et al., 2015)
- ↑ Irisin (Kim et al., 2015)
- ↑ BMP7 (Kim et al., 2016)
- ↑ Angiopoietinlike 4 or ANGPL4 (Laker et al., 2017)
- ↑ FGF21 (He et al., 2018)

- ↑ IL-6 (Ostrowski et al., 1998)
- ↑ LIF (Broholm et al., 2008)
- ↑ VEGF (Arany et al., 2008)
- ↓ Myostatin (Hittel et al., 2010)
- ↑ Irisin (Boström et al., 2012)
- ↑ Myonectin (Sobidin et al., 2012)
- ↑ SPARC (Aoi et al., 2013)
- ↑ Apelin (Besse-Patin et al., 2014)
- ↑ CCL2 or MCP-1 (Catoire et al., 2014)
- ↑ CX3CL1 or fractalkine or FKN (Catoire et al., 2014)
- ↑ IL-15 (Shin et al., 2015)
- ↑ Musclin (Subbotina et al., 2015)
- ↑ SDF1 (Puchert et al., 2016)
- ↑ FGF21 (Tanimura et al., 2016)
- ↓ CCL5/RANTES (Ishiiuchi et al., 2018)

# Physical exercise responsiveness in aged people: identifying new exerkinetics to propose new strategies.

**Context:** Physical exercise favours healthy aging. However, increasing data demonstrate a physical responsiveness over 50 in human and in mouse model of natural aging.



# Physical exercise responsiveness in aged people: identifying new exerkinetics to propose new strategies.

**Work plan:** 1) Identifying new exerkinetics in mouse 2) validating their potential interest in fish 3) Translational to human

## 1) Identifying new exerkinetics in natural aged mice



Forced daily chronic training (8weeks)

-Battery of physical tests to evaluate the response to training



-Histologic and molecular marker of muscle hyper/atrophy  
 -Blood and urine collection every 2 weeks for proteomic and metabolomic analysis

## 2) Validation of potential targets



Validation of the selected targets on Killifish (gain or loss of function)

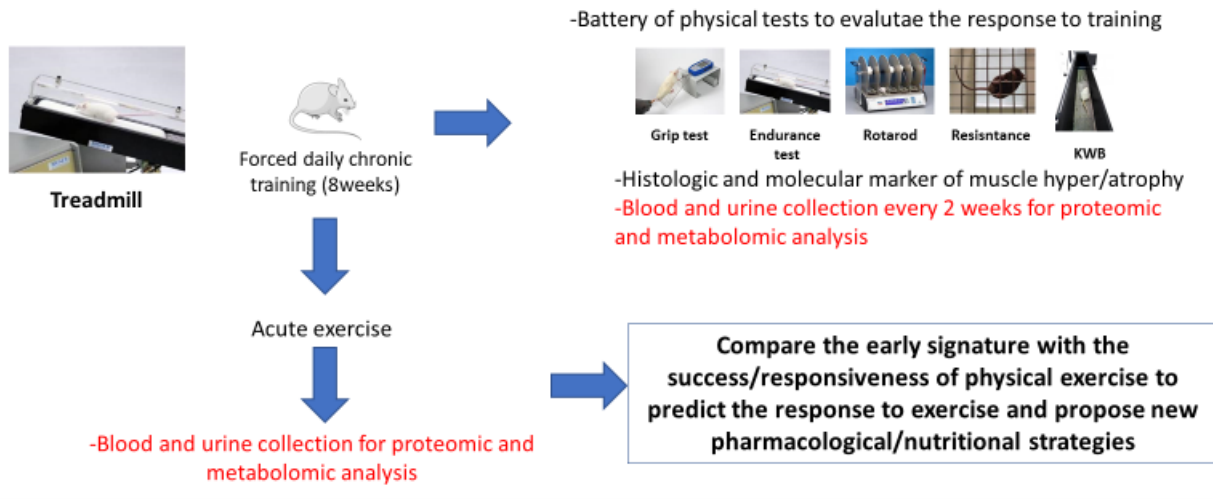
Signature of exercise response/New candidates or targets

3) Translational validation of the signature to humans



# Physical exercise responsiveness in aged people: identifying new exerkinetics to propose new strategies.

**Ultimate ambition of the project:** Identify a very early signature able to predict the success or the responsiveness of a physical exercise in human



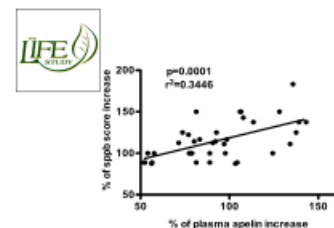
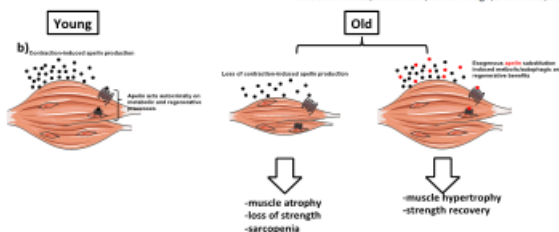
# Apelin's project: towards a better understanding of exercise-induced muscle apelin production to fight against age-related frailty

## The Background

**nature medicine** ARTICLES  
<https://doi.org/10.1038/s41591-018-0212-4>

### The exerkinetic apelin reverses age-associated sarcopenia

Clara Virel<sup>1</sup>, Laura Lukjanenko<sup>2</sup>, Annika Batai<sup>1</sup>, Simon Delanyello<sup>1</sup>, Jean-Philippe Pradier<sup>1</sup>, Sophie La Gerdaie<sup>1</sup>, Alaine Durigues<sup>1</sup>, Nancy Guethel<sup>1</sup>, Ophelia Penrice<sup>1</sup>, Sonia Karaz<sup>1</sup>, Uwe Lue<sup>1</sup>, Mylène Camus<sup>1</sup>, Karina Chava<sup>1</sup>, Estienne Maudou<sup>1</sup>, Anne Bigot<sup>1</sup>, Vincent Mouly<sup>1</sup>, Mathieu Vignaux<sup>1</sup>, Allan F. Pagano<sup>1</sup>, Angèle Chepar<sup>1</sup>, Fabien Pillard<sup>1</sup>, Sophie Guyonnet<sup>1</sup>, Matteo Cesari<sup>1</sup>, Odile Barlet-Schütz<sup>1</sup>, Marco Pahor<sup>1</sup>, Jerome N. Feige<sup>1</sup>, Bruno Vellas<sup>1</sup>, Philippe Valet<sup>1\*</sup> and Cedric Dray<sup>1\*</sup>



Relationship between the capacity to produce apelin and the response to physical exercise

**PATENT: C. DRAY, C. KNAUF, O. KUNDUZOVA, I. CASTAN-LAURELL, P. VALET. Method and pharmaceutical composition for use in the treatment of dysfunction associated with aging. EP N° 2785 365**

BIOAGE

BioAge Announces Positive Topline Results for BGE-105 in Phase 1b Clinical Trial Evaluating Muscle Atrophy in Older Volunteers at Bed Rest

Apelin agonist BGE-105 resulted in statistically significant improvement vs. placebo in muscle size, quality, and protein synthesis in volunteers ≥65 years old during 10 days of bed rest, with no serious adverse effects

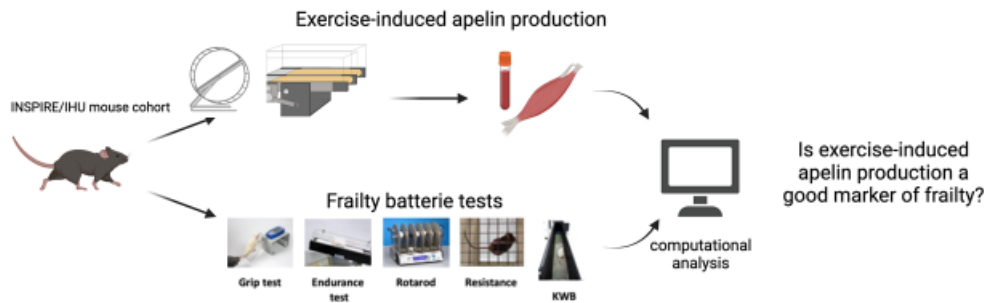
Results support advancement to Phase 2 study of BGE-105 to prevent adverse muscle atrophy-related outcomes for older patients in the ICU

December 08, 2022 09:00 AM Eastern Standard Time

## Apelin's project WP1: apelin in plasma as marker of exercise

- The Project: Is exercise-induced muscle apelin production a good marker to prevent frailty?

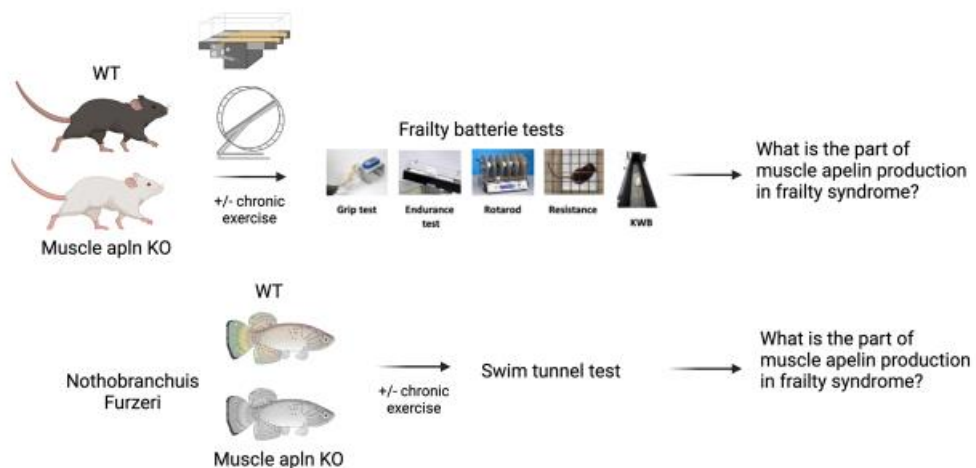
### WP1



## Apelin's project WP2: identify the precise role of muscle apelin during exercise

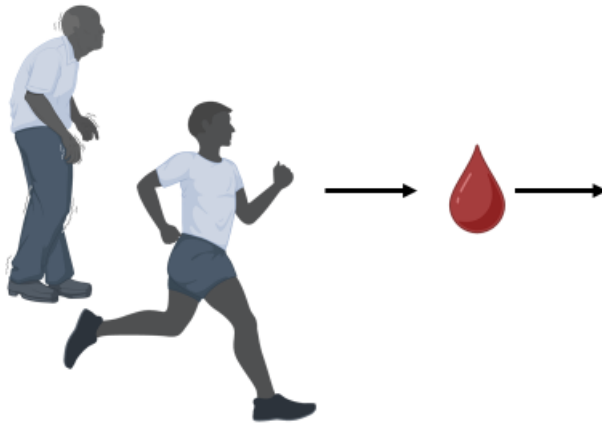
- The Project: Is exercise-induced muscle apelin production a good marker to prevent frailty?

### WP2



## WP3: Translational potential of measuring plasma/urine exerkines

Life's Cohort/DoHealth's Cohort



-Physical fitness characteristics

-Blood exerkines before and after training

-Considering exerkine as predictive factors of exercise success?