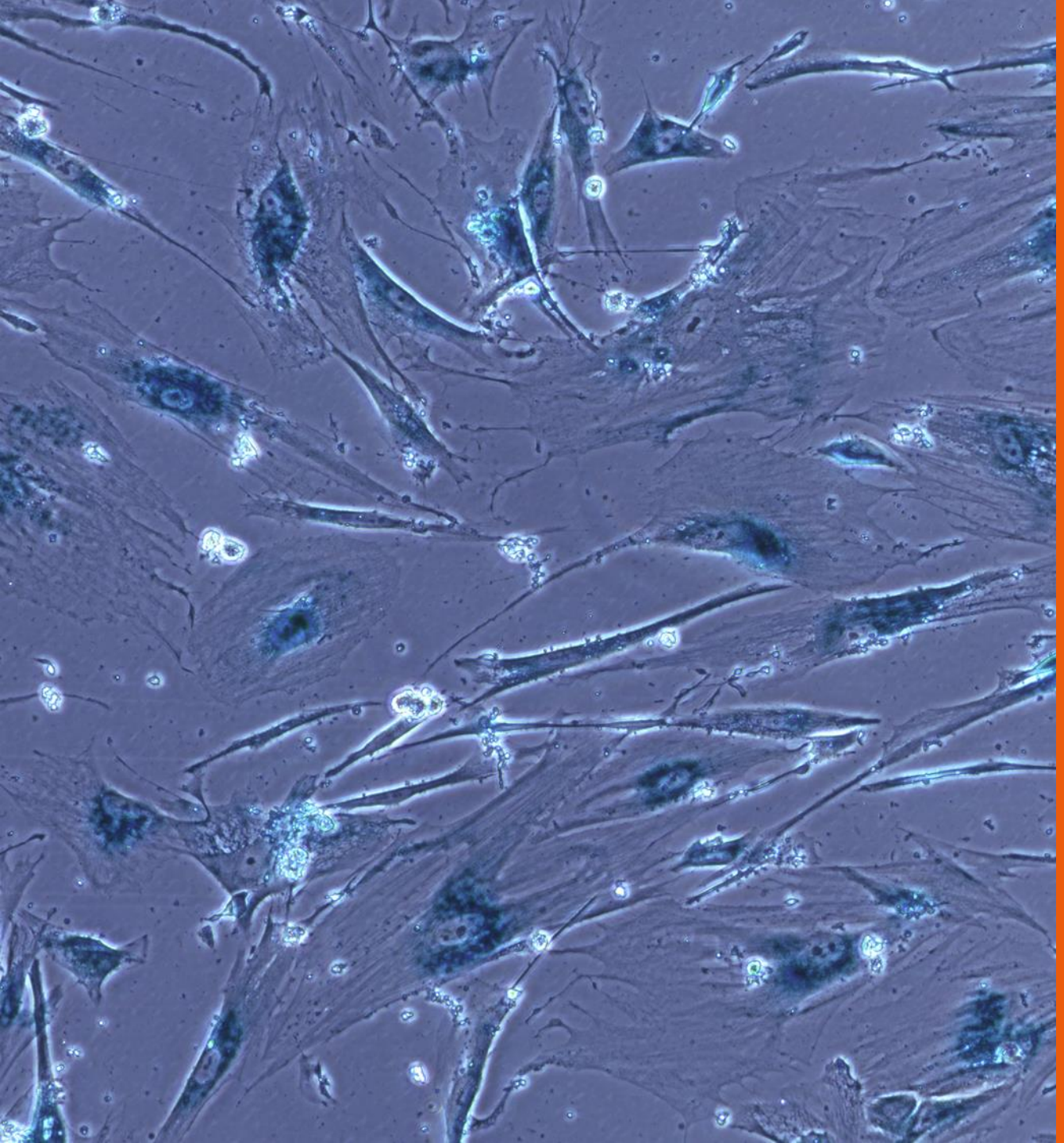


StarkAge Therapeutics

Immunotherapy Against Senescence

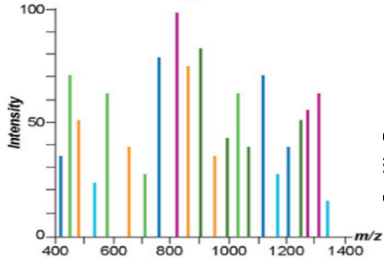
Corporate Presentation
02-Aug-2022

STARKAGE THERAPEUTICS

StarkAge Therapeutics: Highlights

STARKAGE THERAPEUTICS

Marker identification and quantification



Computational analysis

ExoCise™: *(platform)* ▶ **Senescence biomarkers**

- ✓ Privately-held biotech company, founded by Dr Thierry Mathieu, located at the Institut Pasteur of Lille, France
- ✓ Focus : **to delay or halt disease progression and improve quality of life** of patients with age-related diseases associated with senescent cells accumulation
- ✓ Innovation : combining cell surface marker from proprietary discovery platform **ExoCise™**, with immunotherapy to eliminate senescent cells
- ✓ Lead indications: Idiopathic Pulmonary Fibrosis shortly followed by liver fibrosis associated with *metabolic disorder(s) (e.g. NASH/NAFLD)*
- ✓ Other indications in oncology or cardiology are under evaluation
- ✓ First data presented at international scientific congresses

ExoCise™ Platform: StarkAge Therapeutics core technology to generate needed validated targets

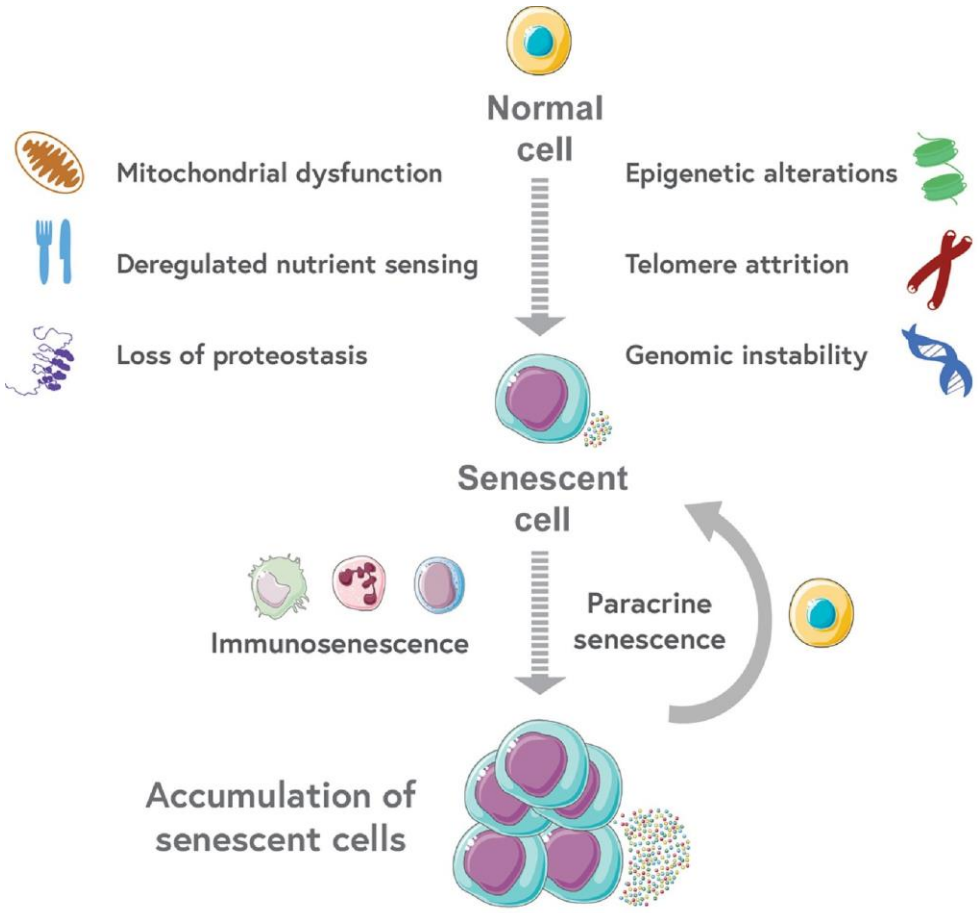
STARKAGE THERAPEUTICS

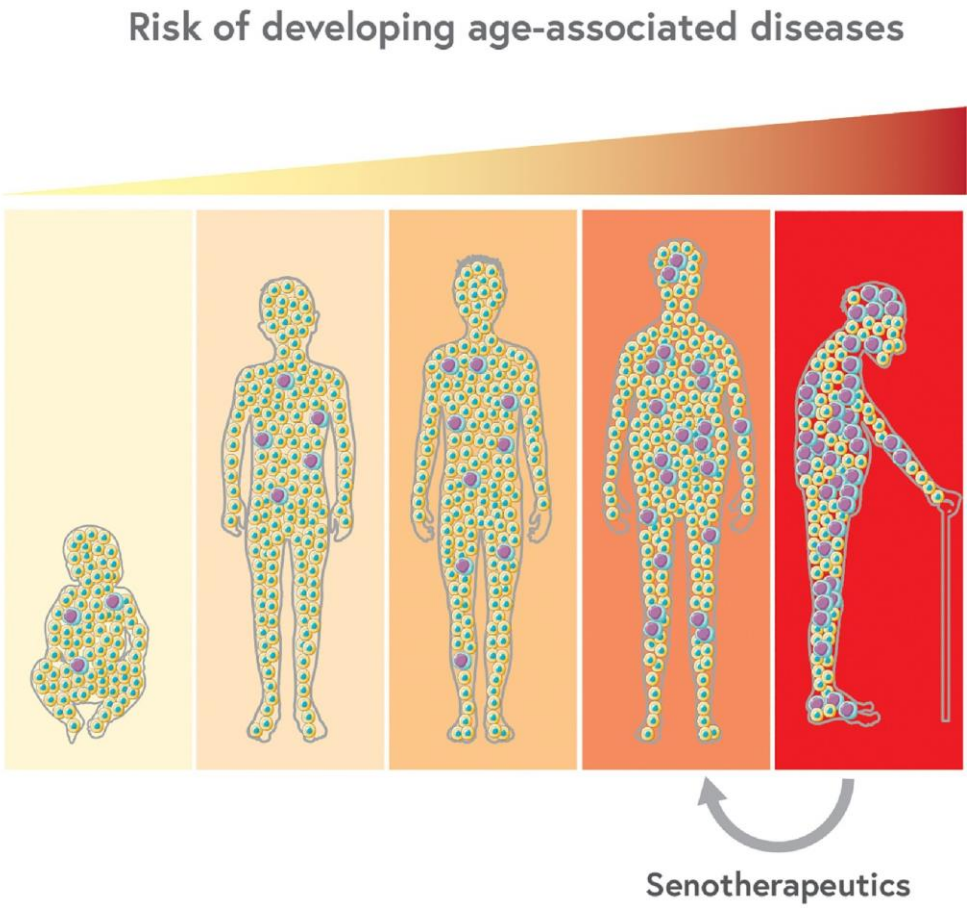
- **Identification of validated targets for considered diseases**
  - **Specific** to each age-related disease
  - **Predictive** of each disease state and progresses

→ ***Targeted Immunotherapy***

→ ***Diagnostics***

Hallmarks of aging induce normal cells to become senescent …





Borghesan M, Trends Cell Biol, 2020

… however senescent cells are not always detrimental – understanding context is key for success

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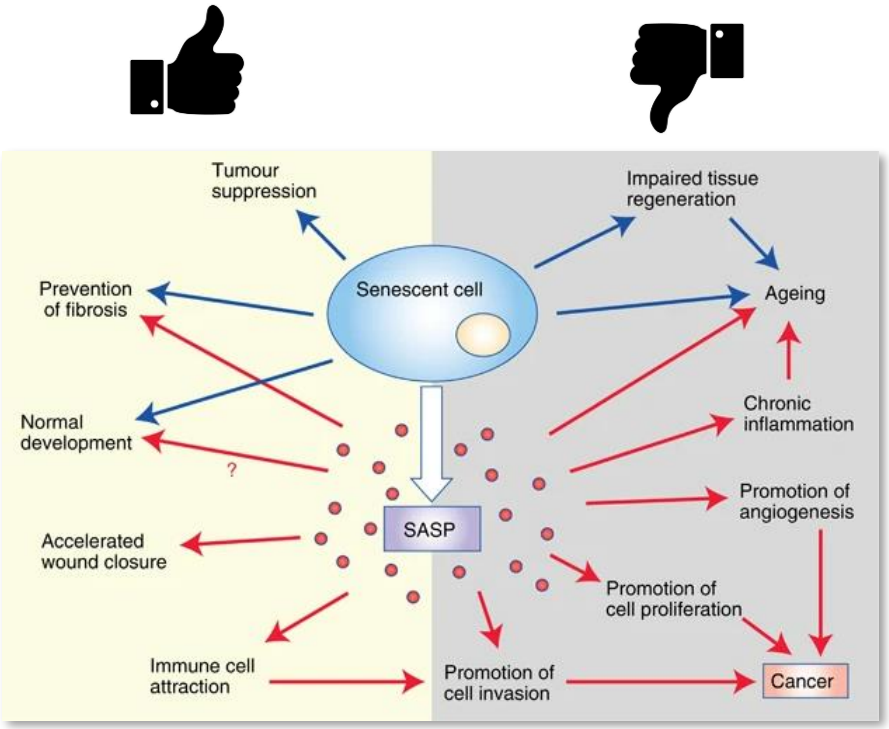
Beneficial



Detrimental

Age-related diseases

"It is clear that the manifestation of each senescence hallmark is context-dependent and varies according to factors such as the stress trigger, the cell or tissue type […]."

Paramos-de-Carvalho D *et al.*, eLife, 2021

Detrimental senescent cells offer multiple potential targets opportunities for specific therapies

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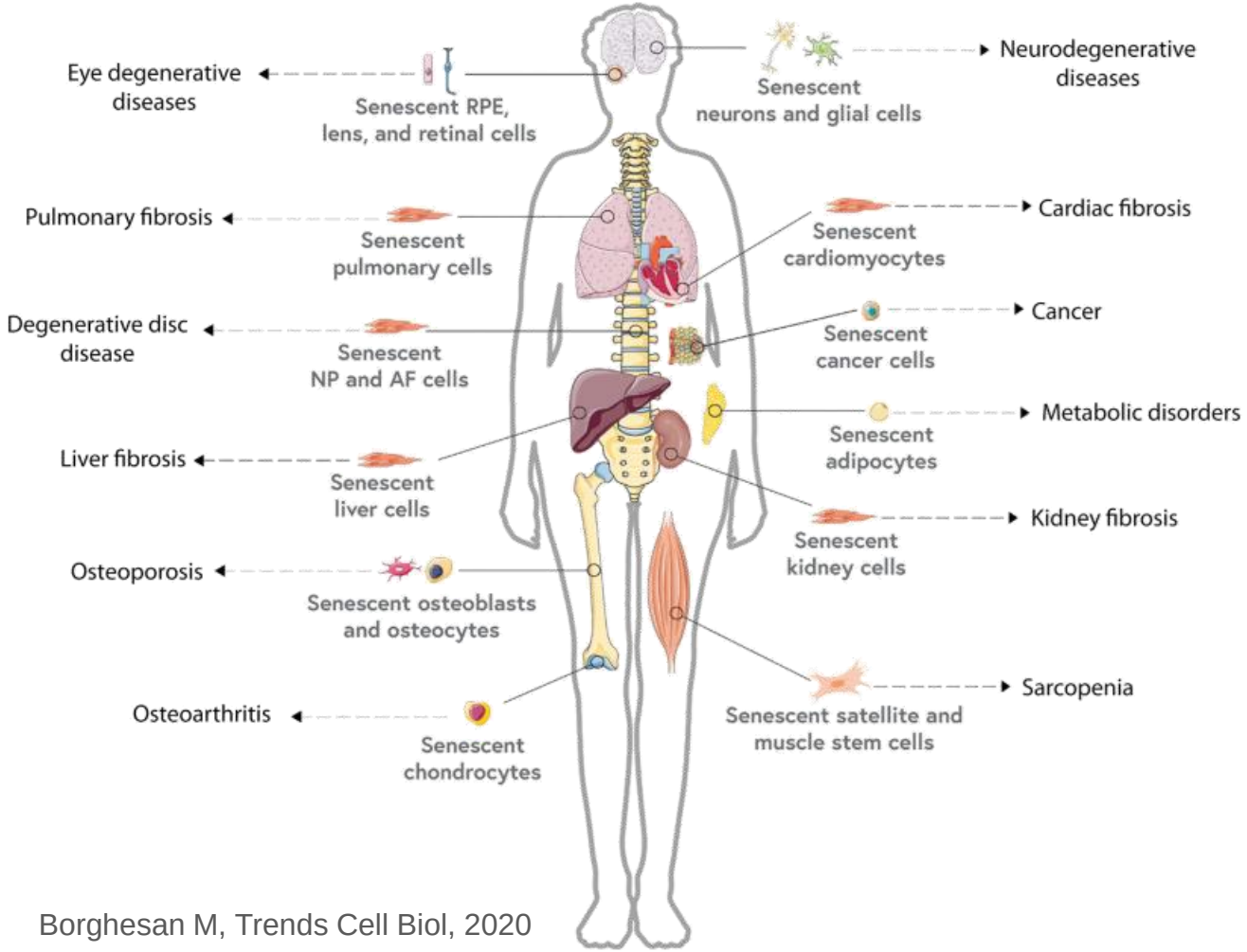


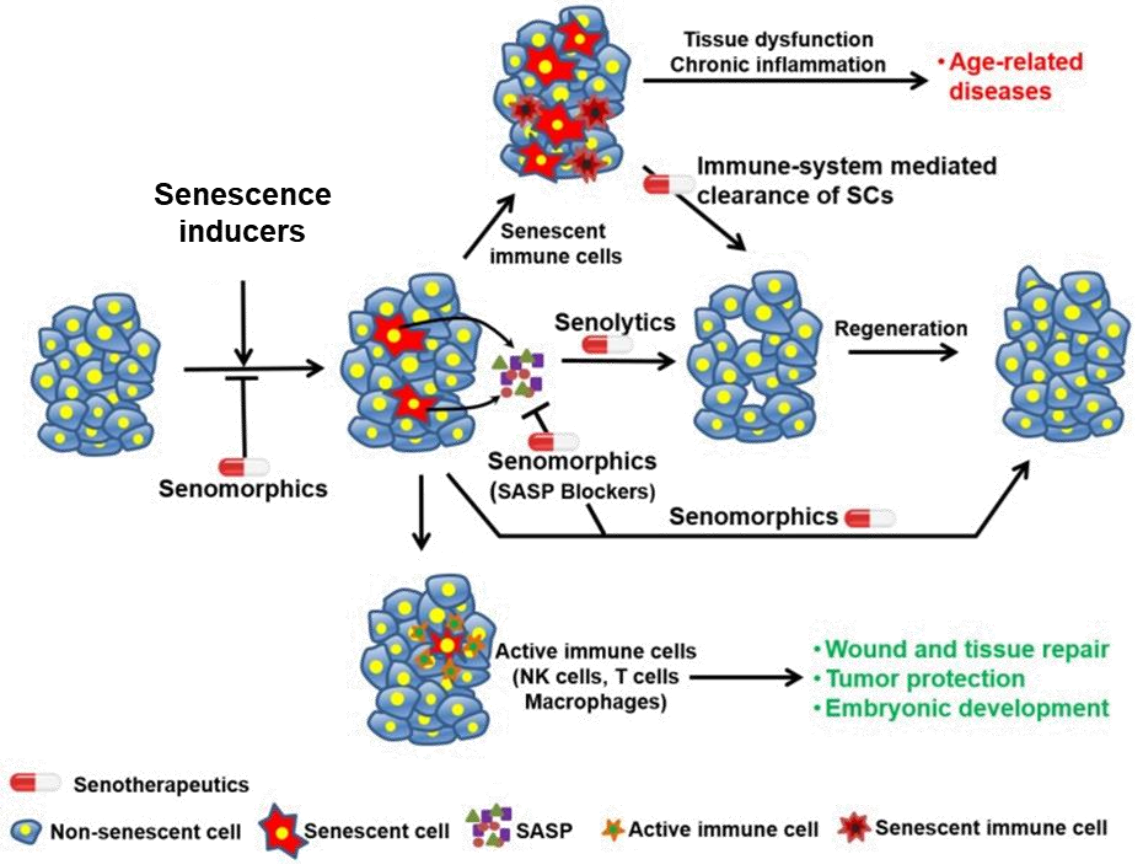
Borghesan M, Trends Cell Biol, 2020

Senescent cells play a role in age-associated diseases

- ✓ Numerous senescence-associated diseases
- ✓ The manifestation of each senescence hallmark is tissue and physiopathological context-dependent

A precise characterization of senescent cells in specific pathological context is necessary to develop specific therapy

StarkAge has chosen the "senolytic" approach
Many limitations exist



Kim EC et al, BMB rep., 2019

Current therapeutic approaches targeting cellular senescence: Senotherapeutics is comprised of 3 main classes:

- ✓ ***Senolytics*** which kill senescent cells +/- selectively
- ✓ ***Senomorphics*** which modulate or even reverse the phenotypes of senescent cells to those of young cells by interfering with triggers of cellular senescence, targeting senescent cells directly, or blocking SASP
- ✓ ***Mediators of the immune-system clearance of senescent cells***

These current therapeutic approaches have several limitations

Currently tested senolytics and senomorphics have serious limitations calling for specific senotherapeutics

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UNIVERSATILITY	SELECTIVITY	TOXICITY	RESISTANCE
✓ Variable efficacy and variable potency across different senescence models ✓ Inconsistency between in vitro and in vivo effects	✓ Lack of sparing effect on physiologically beneficial senescent cells	✓ Versatile agent-dependent systemic toxicities	✓ Pharmacological resistance and proliferative recovery of senescent cell subpopulations following senolysis

Adapted from Carpenter VJ, Cancers, 2021
doi.org/10.3390/cancers13040723

StarkAge Therapeutics approach : IMMUNOTHERAPY

StarkAge Therapeutics will address these limitations by combining several techniques …

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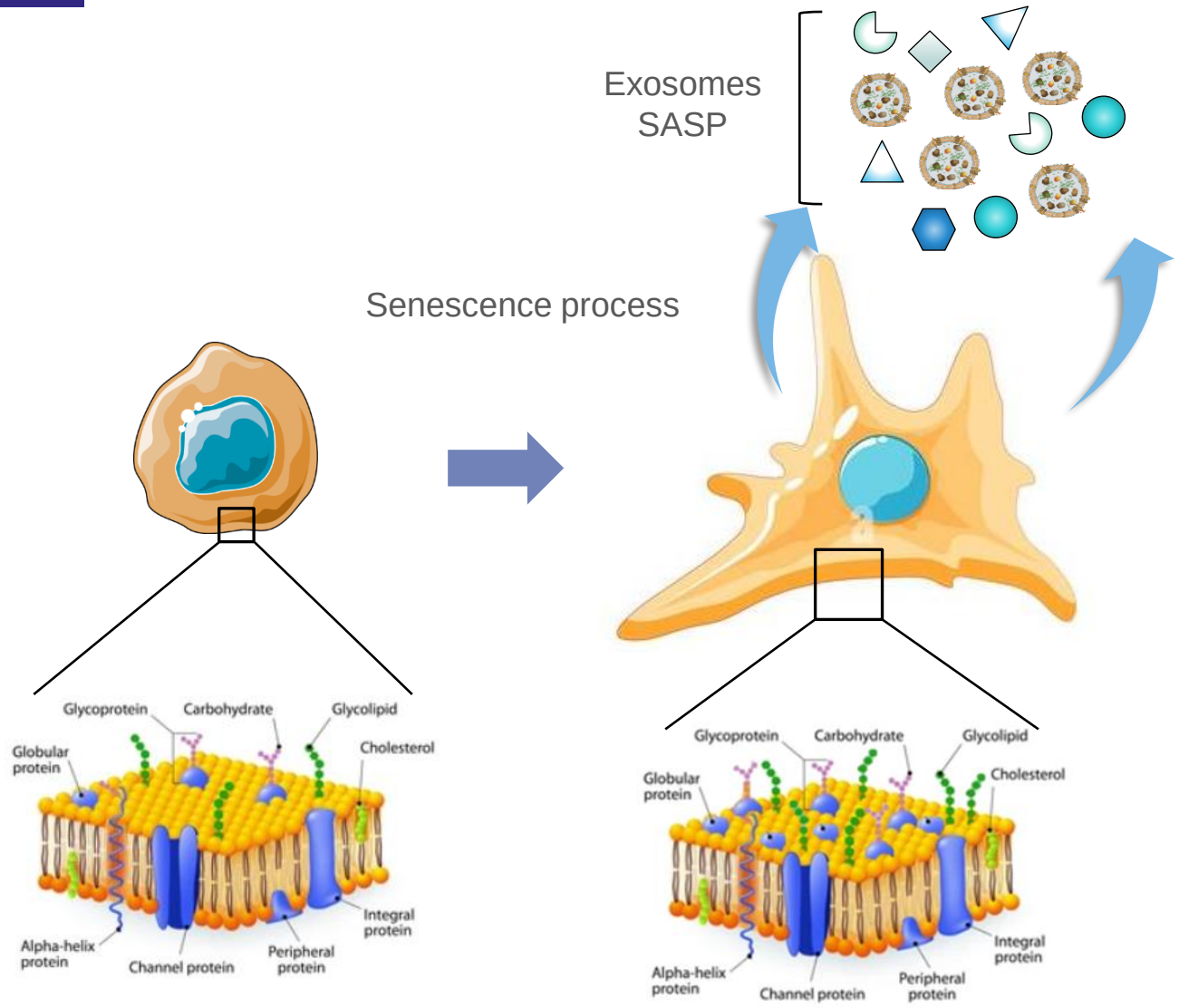
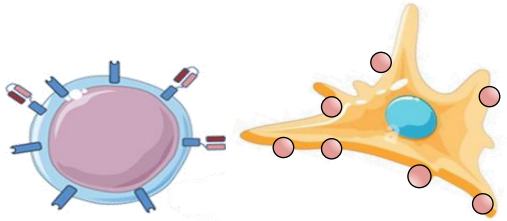


Diagnostic based on characteristics of exosomes from senescent cells

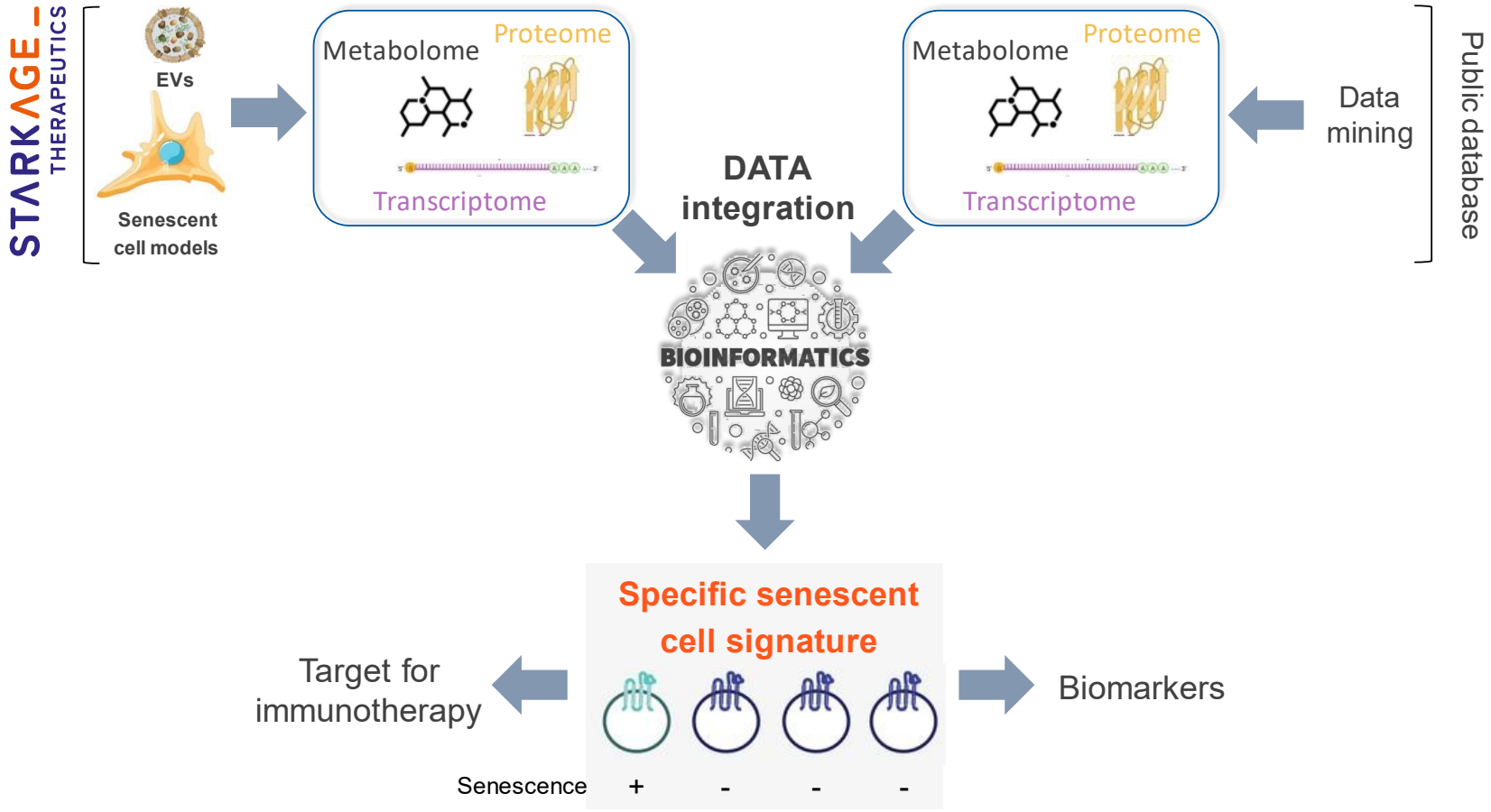
New age-related disease management



Immunotherapy targeting novel specific senescent cells surface markers (via surfaceome)

… including core multi-omics validation …

From the concept of unique surface marker to the concept of complex surface signature:
multi-omics approach to precisely define specific senescent cells surface targets for immunotherapy



"This type of comprehensive analysis is fundamental to define biomarker candidates with greater selectivity to specific pathological contexts, but information is still lacking and more studies are needed, especially in vivo."
Paramos-de-Carvalho D *et al.*, eLife, 2021

… in a carefully evaluated sequence of experiments to de-risk discovery strategy and target selection in human

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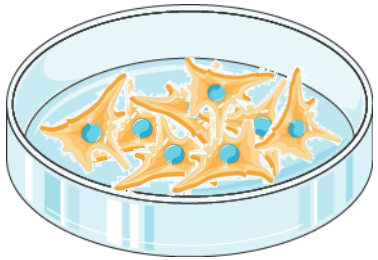
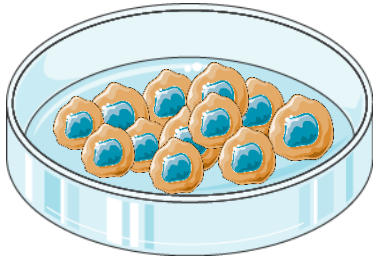
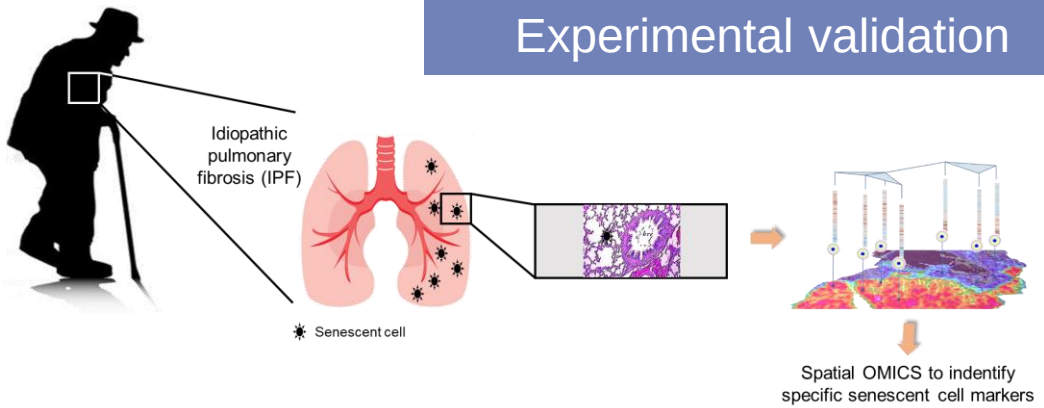
ILLUSTRATIVE – IPF





Multi-omics
&
Experimental validation



Multi-omics
&
Experimental validation

In summary: ExoCise™ Platform is StarkAge Therapeutics core technology to generate needed validated targets

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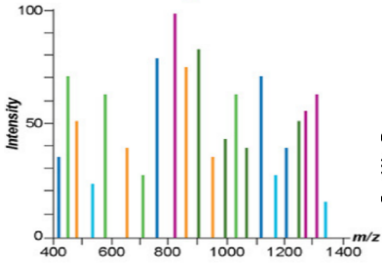
Marker identification and quantification



Computational analysis

- **Identification of validated targets for considered diseases**
  - **Specific** to each age-related disease
  - **Predictive** of each disease state and progresses
  - → ***Targeted Immunotherapy***
  - → ***Diagnostics***

- **Some key competencies required**
  - Multi-omics capabilities: collaboration with academia
  - Exosome extraction / analysis: internal ✓
  - Internal core Bioinformatics: *strategic – to be recruited*
  - Initial CAR-T expertise to be built

Our #1 priority will be Idiopathic Pulmonary Fibrosis followed by NASH / NAFLD, both linked to fibrosis

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Evolution over time

Lead Programme	Respiratory	**IPF ✓**	*(COPD – COVID-19 t.b.d)*
Fast Follower	Metabolic	**Liver fibrosis (incl. NASH / NAFLD)**	
Under Evaluation	Oncology	Fibrosis post chemotherapy or radiotherapy	
	Cardiology	Heart fibrosis	

StarkAge Therapeutics lead by a team with multiple experiences to navigate the early stage of the company …

STARKAGE THERAPEUTICS

Dr. Thierry Mathieu
Président, founder

MD, specialized in immunology, Dr. Mathieu participated in the creation, management and transfer of the ***Synlab Biology*** Group (formerly known as ***Labco***), of which he was Scientific Director. He has created several start-ups in the bio-technology and innovation sector.

SYNLAB

Dr. Pierre-Michel Bringer
CEO

Pierre-Michel has over 35 years of Pharmaceutical Industry experience in multiple countries, spanning M&A / licensing, communication, strategic planning, marketing & sales with ***Sanofi***. Most recently he served 13 years as Investor Relations Officer with ***Novartis***. Pierre-Michel holds a Doctorate of Pharmacy.

NOVARTIS sanofi

Dr. Benjamin Le Calvé
CSO

Benjamin obtained his PhD in 2011 at the Free University of Brussels, followed by several positions in various research centers in Canada, France and Belgium to develop competences in the oncology and senescence fields. Recently, he was a member of the research and development department at **Celyad Oncology**.

Celyad Oncology

Hussain Sheikh
CFO

Hussain is an entrepreneur serving entrepreneurs. For the past 10 years he has supported the leaders of startups and SMEs in their development, fundraising and financial management. Very familiar with the innovation ecosystem, he helps leaders develop their growth strategy, business model and organizations.

LINK eurasanté Entreprendre et Réussir

Jennifer Campbell
Administration Director

An expert in international communications, philanthropy, and marketing, Jennifer created and led global private-public partnerships and programs for ***Disney*** for 12 years. As Director of Philanthropy at ***L'Oréal***, she helped create and launch the ***L'Oréal Foundation*** where she served as Secretary-General and led the signature "For Women in Science" partnership with ***UNESCO***, among others.

L'ORÉAL Disney

… and guided by an international Scientific Advisory Board

STARKAGE THERAPEUTICS

Chief Scientific Officer

Senescence Expertise

Ana O'Loghlen, PhD
Senescence and aging incl. exosomes

Blizard Institute of the Queen Mary University of London (UK)

David Bernard, PhD
Age-related diseases incl. fibrosis and inflammation

Cancer Research Center of Lyon (CRCL) (France)

Fabrizio d'Adda di Fagagna, PhD
Senescence and aging incl. telomeres

IFOM in Milan and CNR in Pavia (Italy)

Clinical Expertise

Vincent Cottin, MD
IPF and other lung fibrosis

Louis Pradel Hospital and Claude Bernard University in Lyon (France)

Pascal Pfister, MD
Drug development – medical affairs

Ex-Novartis and ex-Nicox

More details on members of the SAB: https://starkagetx.com/wp-content/uploads/2022/02/StarkAge-Tx-SAB-Announcement-FINAL.pdf

Since its inception, StarkAge Therapeutics has setup its own lab at *Institut Pasteur Lille* and built a research team

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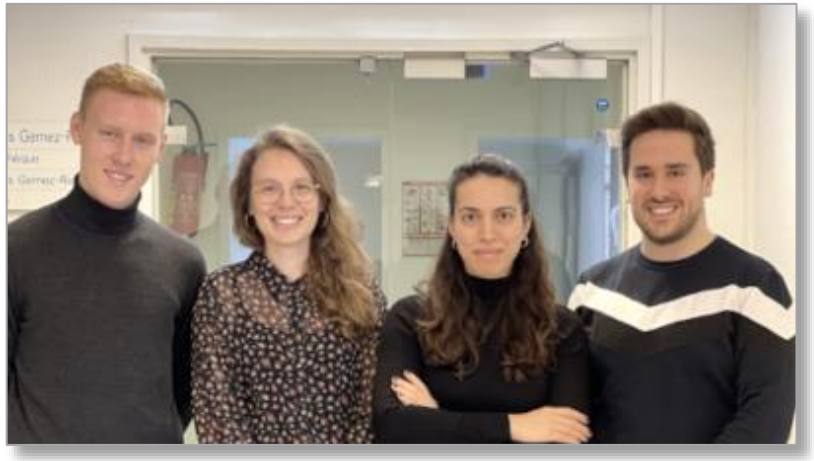
Ultracentrifuge



Team of researchers specialized in senescence, immunology and molecular biology

Cell culture equipment

Molecular biology devices

Flow cytometer Miltenyi

New data were recently presented at an international scientific congress[1], more expected at ICSA[2] 2022

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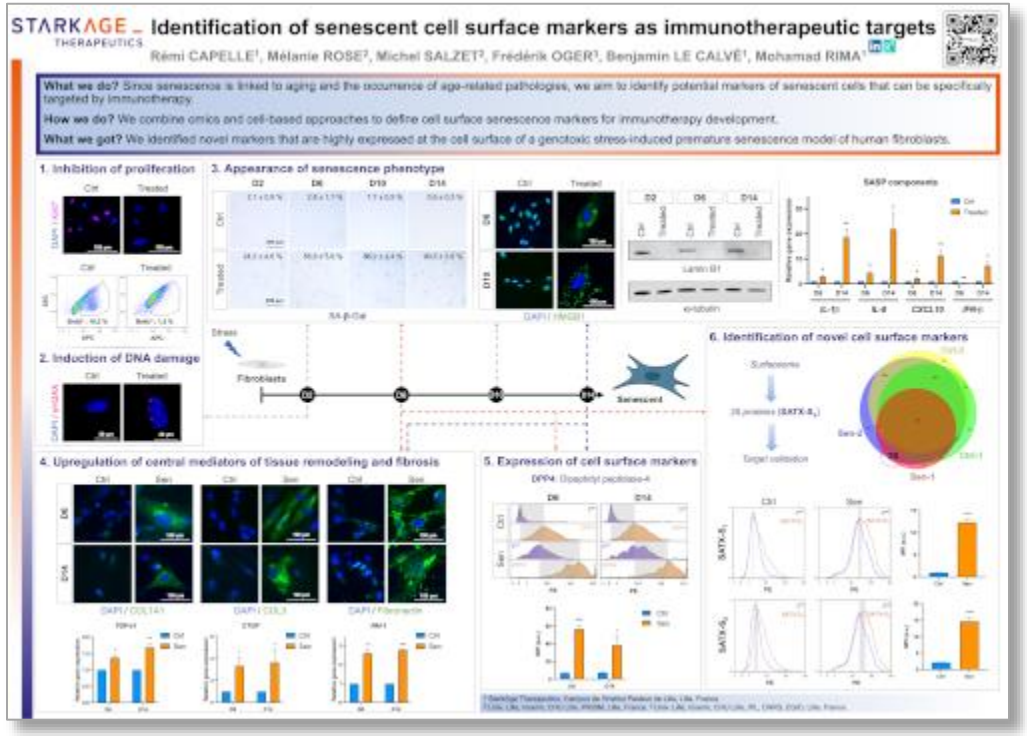

Abstract:

"Identification of senescent cell surface markers as immunotherapeutic targets".

Besides its role in healing and regeneration, senescence is linked to aging and the occurrence of age-related pathologies. To develop immunotherapies aiming to eliminate senescent cells in a pathological context, it is important to identify targets that are highly specific to these senescent cells. Herein, we combine Omics and cell-based approaches to define cell surface senescence markers that can be targeted via immunotherapy. We started by developing and dissecting a genotoxic stress-induced premature senescence model of human fibroblasts in vitro. After the complete characterization of its senescent phenotype, we investigated the expression of potential senescence markers in this model. Interestingly, using Omics approaches, we identified novel cell surface markers that are exclusively expressed in senescent cells, which makes them of interest for immunotherapies. In addition, whereas some senescence markers were upregulated at early and late senescence states, others were downregulated, emphasizing the role of the stress used to induce senescence in defining the appropriate molecular response. Together, our findings pave the road towards defining the cellular signature of senescent cells in a specific physio pathological context and describe new targetable senescent cell surface proteins.

Download Poster as PDF

1: CAMS 2022 (Cellular Aging and Metabolism Symposium) – A Coruña, Spain, July 18-20 2022
2: ICSA 2022 (International Cell Senescence Association) – Groningen, The Netherlands, Sept. 29 – Oct, 1 2022

STRATEGY 3-5 years:
Translating discovery into clinical candidates

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❑ FLAWLESS EXECUTION WILL DRIVE SUCCESS

- ✓ Advance lead program(s) and select de-risked signature(s) in human
- ✓ Build teams and develop expertise internally and with external academic or industrial partners
- ✓ Leverage value creation guidance from external collaborations incl. SAB
- ✓ Establish StarkAgeTherapeutics as a leader in senescence – build credibility
- ✓ Generate more data

Conclusion

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- Harness immunotherapy to selectively eliminate senescent cells can limit of age-related diseases impact
- ExoCise™ cell surface marker platform can be applied to many age-related diseases involving senescence, particularly fibrosis
- IPF is the lead indication followed by NASH/NAFLD
- StarkAge Tx has been granted €2M funding (2021-2024) from BPI France (DeepTech)
- Key next steps
  - present further data and prepare publications
  - accelerate transition from cell culture to human / ex-vivo tissues, particularly for IPF
  - build bioinformatics capabilities
  - build liver fibrosis disease group
  - initiate internal CAR-T expertise

Contacts

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