Centre universitaire de santé McGill
Institut de recherche

McGill University Health Centre
Research Institute

CONFERENCE CAHR 2021 VIRTUAL
May 5-7, 2021

CONGRÈS DE L'ACRV 2021 VIRTUEL
5 au 7 mai 2021

GDF-15 as a biomarker of HIV reservoir size in ART-treated PLWH

Stéphane Isnard, PhD

FRQ-S CIHR/CTN Post Doctoral fellow
Dr Jean-Pierre Routy's lab
Montréal, Canada

No conflict of interest

Background

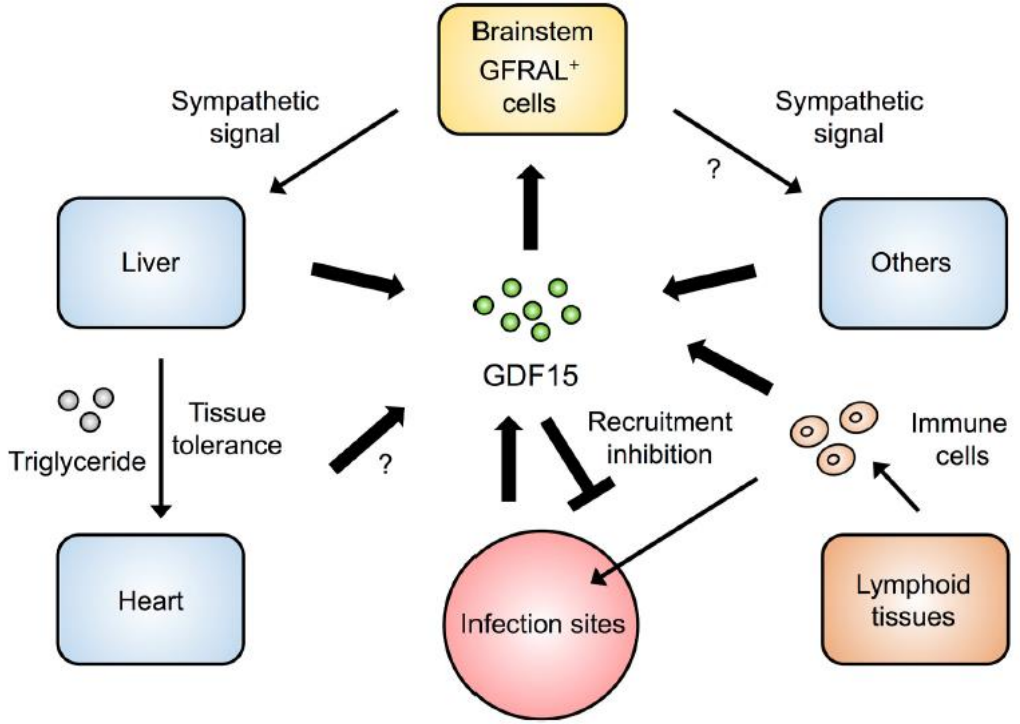
GDF-15 = Growth Differentiation Factor 15

Atypical member of the TGF-β family

- **Regulates bodyweight** through a peripheral – brain axis: speci
  receptor GFRAL in the brainstem.

- Also a marker of **mitochondrial stress** induced by hypoxia,
  mitochondrial DNA damage, reticulum endoplasmic stress, et

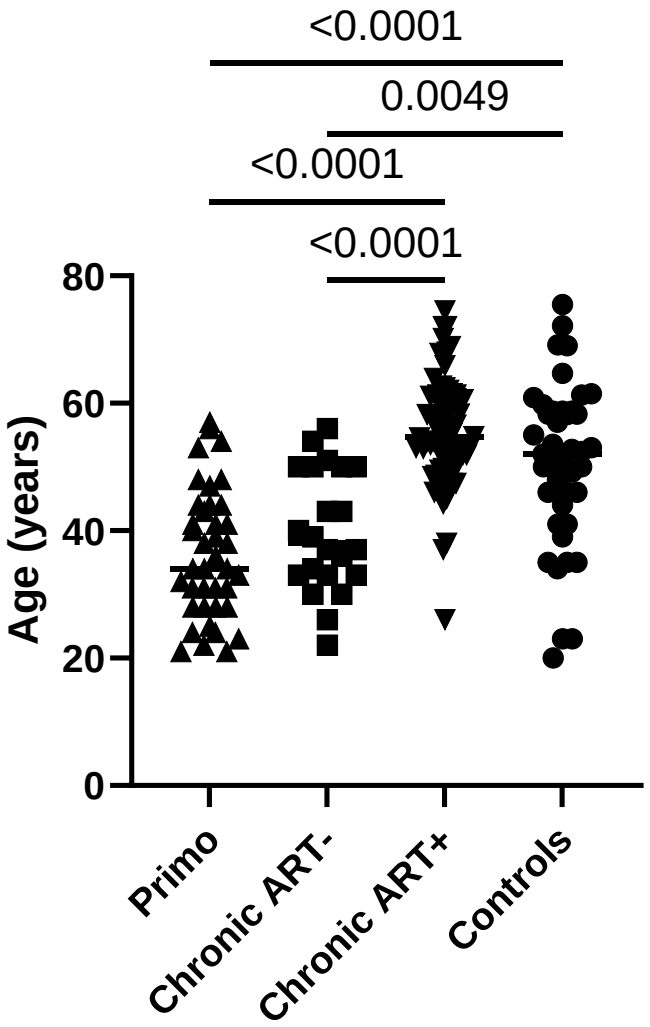
- **Circulating levels of GDF-15** are elevated in people with:
  - → **Aging**
  - → Cardiovascular diseases
  - → Sepsis
  - → Cancer
  - → Asthma
  - → Severe COVID-19

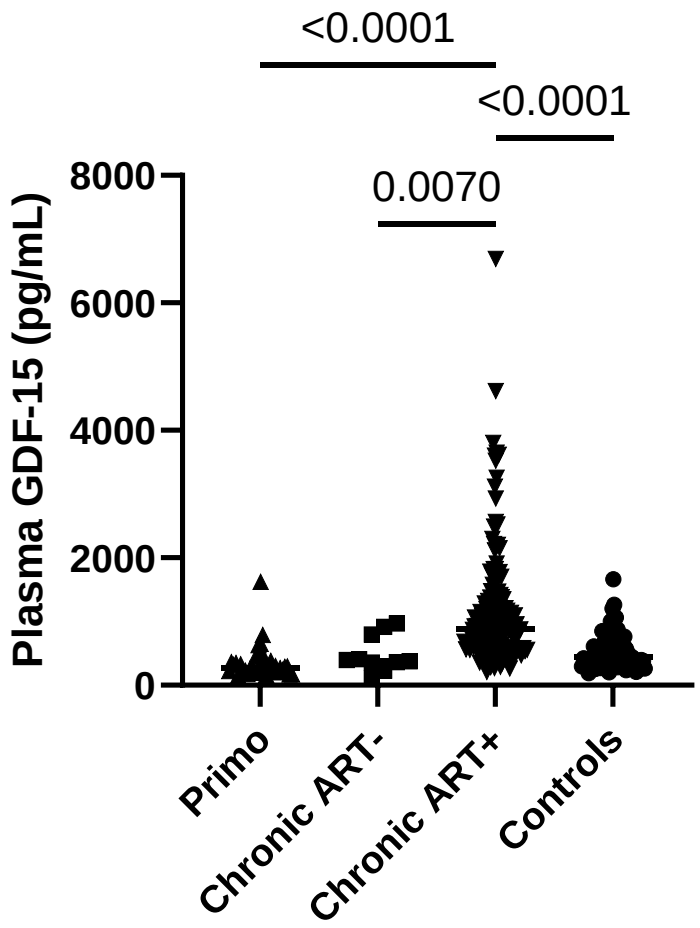


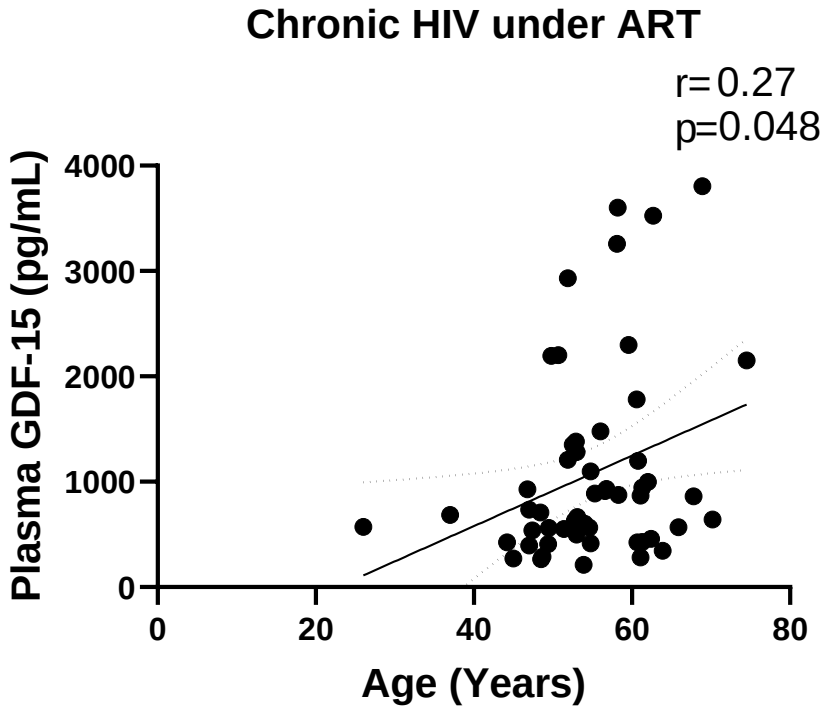
Fujita, Arch Biochem Biophys2020

Objectives: Are circulating GDF-15 levels different in People living with HIV compared to uninfected controls?
What mechanisms influence GDF-15 levels in PLWH ?

Plasma levels of GDF-15 in PLWH are linked with age in ART-treated PLWH



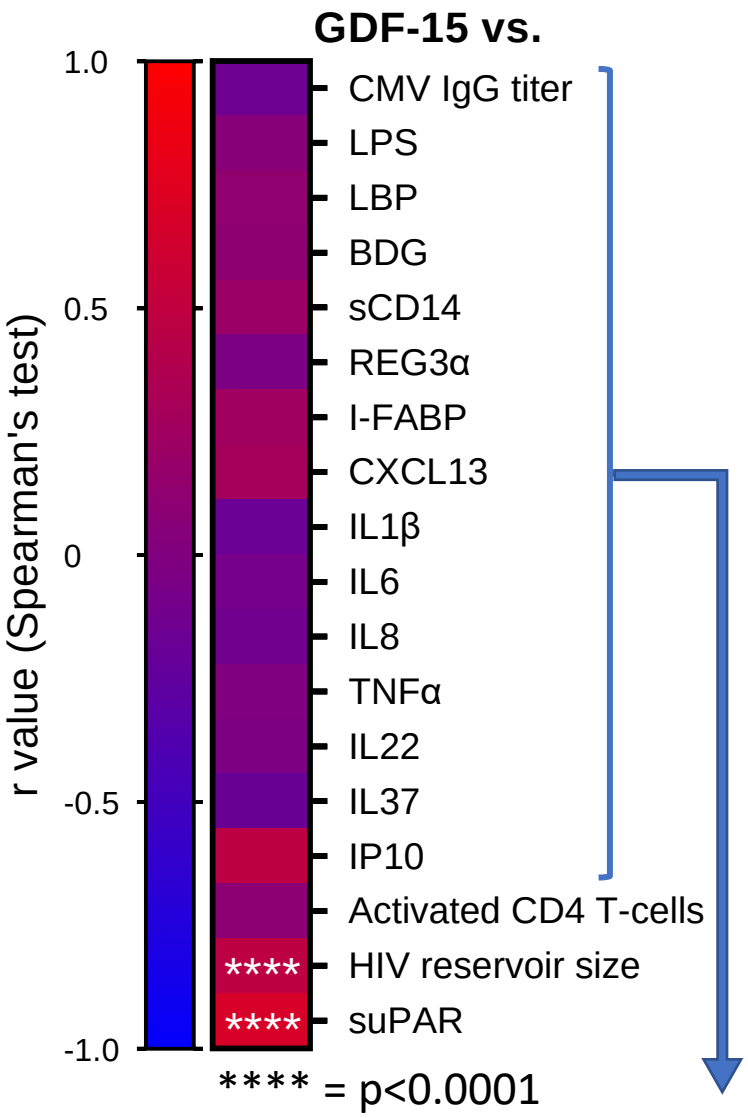




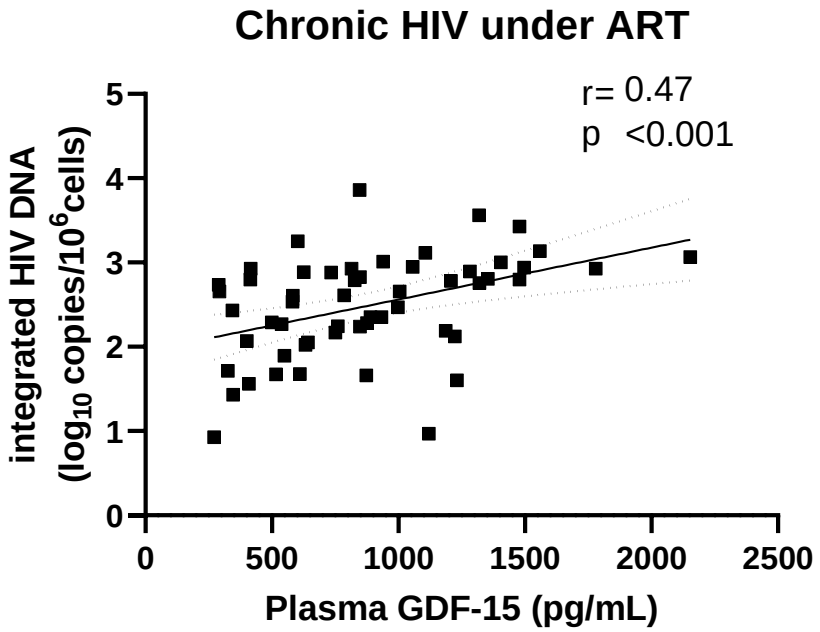
Plasma GDF-15 levels were **higher in ART-treated PLWH** compared to uninfected controls.
GDF-15 levels were associated with **age**. Sex and type or class of ART had no influence on GDF-15 levels.

GDF-15 levels are associated with reservoir size and risk of comorbidities, independently of inflammation

In ART-treated PLWH:

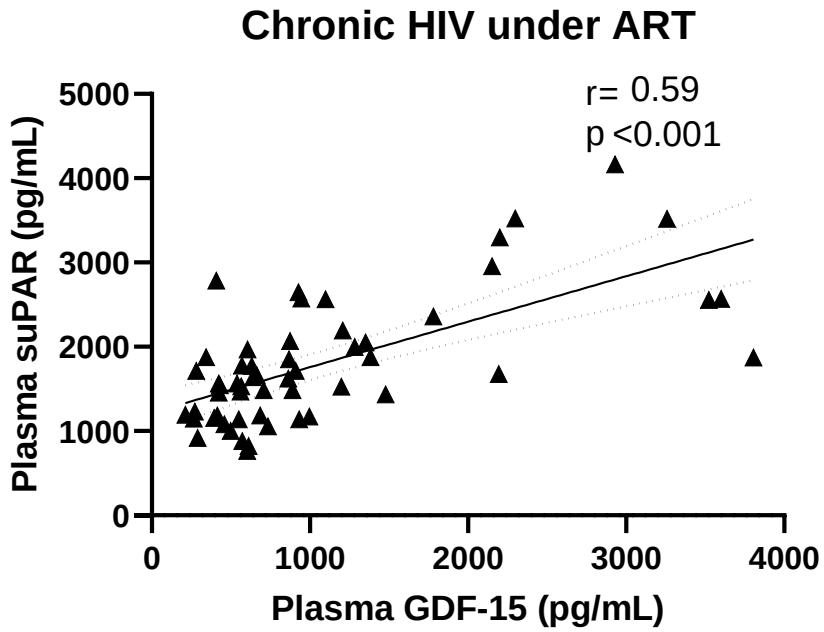


Reservoir



Association with HIV reservoir size, independently of age, sex, and class or type of ART

Comorbidities



Association with the marker of non-AIDS comorbidities suPAR (soluble urokinase plasminogen activator receptor)
(see Hoenigl et al. *CID* 2019)
independently of sex and class of ART

No association between GDF-15 levels and **inflammation** markers including inflammatory cytokines, gut damage and microbial translocation markers.

Conclusion: Circulating GDF-15 levels were associated with **HIV reservoir size** and **non-AIDS comorbidity** marker suPAR, independently of age, sex, and inflammation markers.

In vitro stimulation experiment confirmed that inflammatory stimuli do not induce GDF-15 in blood samples (data not shown).

Future directions: Molecular mechanism and confirmation of the role of GDF-15 in non-AIDS comorbidities
Is GDF-15 a marker of accelerated aging in ART-treated PLWH?

Acknowledgment

Team Jean-Pierre Routy
Dr Jean-Pierre Routy
Dr Léna Royston
John Lin
Brandon Fombuena
Dr Franck P Dupuy
Dr Jing Ouyang
Dr Xiaorong Peng
Simeng Bu

Rayoun Ramendra
Josée Girouard
Angie Massicotte
Cezar Iovi

CVIS
Drs C Costiniuk,
B Lebouché, A de
Pokomandy, J Szabo,
M Teltscher, J Cox,
E Beauchamp, LP Haraoui,
M Klein, Nurses and staff

Team Dr P Ancuta
Team Dr N Chomont
Team Dr C Tremblay
Team Dr M Durand,
Dr C Chartrand-Lefebvre

All study participants

Stephane.isnard@mail.mcgill.ca

Montreal Primary HIV-infection cohort
Canadian HIV and Aging Cohort