19 LUGLIO

at 4.30 p.m.

Room A204, *Povo 1*

UNIVERSITÀ DI TRENTO
Dipartimento di
Biologia Cellulare, Computazionale e Integrata - CIBIO

CIBIO EXTERNAL seminar

CGAS-STING IS REQUIRED FOR SENESCENCE AND AGING IN TELOMERASE DEFICIENT ZEBRAFISH

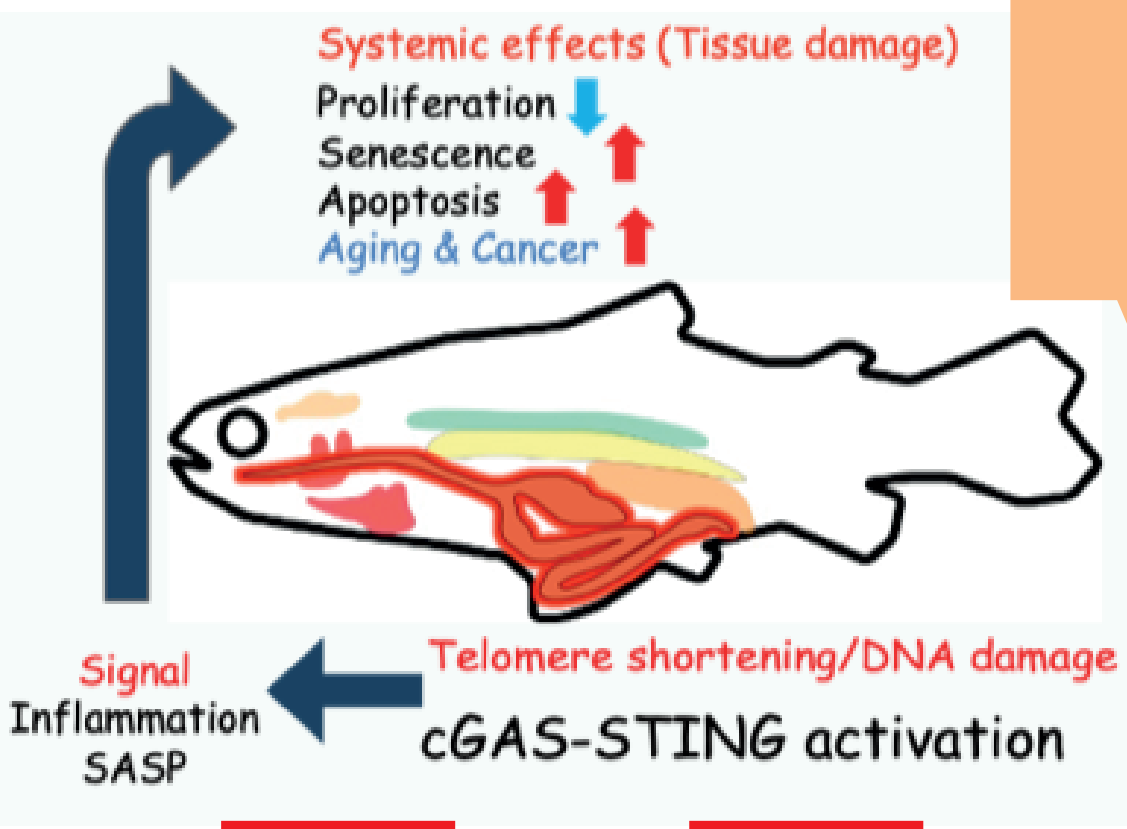
Miguel Godinho Ferreira

IRCAN - Institute for Research on Cancer and Aging of Nice

Telomere shortening occurs in multiple tissues during human aging. As telomeres become critically short, they are sensed as DNA damage and activate p53, resulting in apoptosis or replicative senescence. Consequently, short telomeres reduce tissue cell proliferation, leading to loss of homeostasis and aging. The cGAS-STING pathway senses short and dysfunctional telomeres. This pathway is part of the innate immune system, signalling inflammation upon viral infection and was shown to modulate cell senescence.

We study the consequences of telomere shortening in zebrafish at the organism level. Like humans, zebrafish telomeres shorten to critical length during normal aging. Telomerase deficient zebrafish (tert) die prematurely while recapitulating aging phenotypes, such as reduced fertility, cachexia, increased inflammation, and age-associated diseases, such as cancer.

We show that STING is responsible for tert zebrafish premature aging. We generated sting tert double mutants and observed reduced cell senescence and interferon responses when compared to tert single mutants. Consistently, sting tert double mutants had low p53 levels and increased cell proliferation. At the organism level, we observed that inactivation of STING rescues infertility, fewer spontaneous cancers, while increasing the lifespan of tert mutants by 40%. Thus, telomere shortening activates cGAS-STING, resulting in type I interferon inflammation and premature aging of tert mutants.



Contacts
Department of Cellular, Computational and Integrative Biology - CIBIO
Via Sommarive, 9
38123 - POVO (TN)
comunicazione.cibio@unitn.it