Understanding the biological mechanisms of ageing at the fundamental and applied levels: this is the primary ambition of IRCAN, the French and European leader in this emerging field associated with many chronic diseases and cancers. IRCAN's research work is structured into five main areas: cellular senescence, (epi)genomics, regeneration, the extracellular environment and the environment (including the study of the impact of climate change on ageing).

Cellular senescence and senotherapy

IRCAN is particularly active in the field of cellular senescence, based on a long-standing American discovery: the organism first ages by accumulating senescent cells following various forms of damage. It is therefore a question of preventing cells from going into senescence or eliminating them in a preventive or curative manner. This is what **senotherapy** is all about.

Dr Dmitry Bulavin's team at the IRCAN recently threw a spanner in the works by publishing their findings in the journal *Cell Metabolism* in 2020: using a mouse model, they demonstrated that senescent cells that are killed are not replaced, thus forming holes in the organs concerned. Senotherapy must therefore be rethought to neutralise senescent cells by means of senomorphic drugs or to kill them by replacing them at the same time by mobilising stem cells.

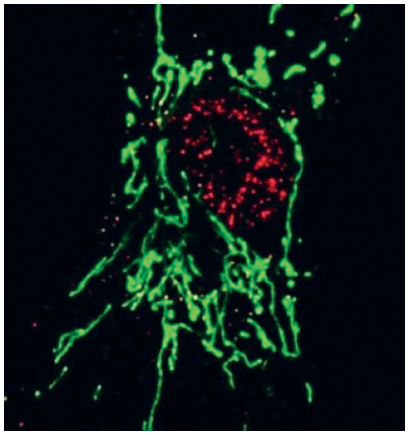
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Other discoveries on the senescent cell can be attributed to Dr Julien Cherfils-Vicini's team: the study of the immunosuppressive properties of the senescent cell has made it possible to identify a target (since patented) with production of antibodies to block this mechanism. This immunotherapy approach is at the preclinical model stage where its effectiveness is being tested on lung fibrosis for example.



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Telomere research: the ageing clock

Research on **telomeres** is also very present at IRCAN, involving four of its teams. It is vital to better understand the functioning of this ageing clock programmed during development – a clock that can run out of control in the event of stress. The challenge is a major one: to discover the telomeric factors that contribute to ageing but not to cancer!

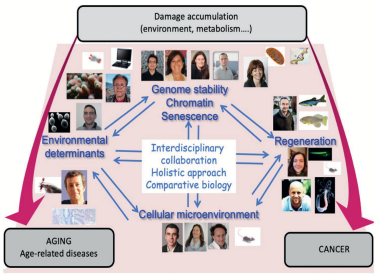
To do this, IRCAN researchers are developing organisms with extreme longevity and regeneration characteristics, such as marine invertebrates considered to be ‘quasi-immortal’, such as corals and other sea anemones: promising avenues studied by the teams of Dr Eric Röttinger and Prof. Eric Gilson, who are trying to understand how the telomeres of these organisms react to contrasting environments and what the molecular mechanisms are.

National and international programmes

With a view to taking action on both prevention and cure, Prof. Éric Gilson has been responsible for the scientific coordination of Inserm’s major transverse programme **“AgeMed”** (2017-2023). The participation of some twenty French teams has enabled the consolidation of an interdisciplinary research community at national level. The successor to “AgeMed”, the Thematic Cooperation Programme **“InterAging”** runs from 2021-2025 and aims to broaden the scope of

collaborations under the leadership of Inserm, with teams from Germany (Cologne), Singapore, the UK (London) and China (Shanghai).

The IRCAN is therefore ideally placed to provide clinicians with useful markers for assessing a person's state of frailty or anticipating the response to an immunotherapy treatment. This is the case, for example, of an ambitious programme of the ARC Foundation on "Cancer and Ageing" in which the IRCAN is a partner: the study of cohorts of patients suffering from age-related cancer will make it possible to aggregate these different parameters. The ultimate goal is to improve patient care.



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