Tumour suppressors are genes that can prevent the development of cancer. All our cells have a functional set of these genes, but they can become defective over time. The affected cells thus become partially unprotected and, combined with additional mutations in other genes, can give rise to cancer. Understanding how tumour suppressor genes work may help us to design drugs that block cancer. Tumour suppressor genes are now known to control many aspects of cell biology and organismal physiology, such as cellular pluripotency, cell senescence, and metabolism. We aim to achieve an integrated understanding of cancer protection.

Our goals are to:

- Understand the mechanisms of tumour suppression and identify new tumour suppressor regulators.
- Study the interplay between tumour suppression and ageing.
- Analyse the involvement of tumour suppressors in the regulation of metabolism and protection from metabolic damage.
- Characterise cellular senescence as a tumour suppression mechanism.
- Investigate cellular pluripotency and the involvement of tumour suppressors in the process of reprogramming to induced pluripotent stem (iPS) cells.
- Explore the role of cell plasticity in cancer, tissue regeneration, and ageing.
- Search for new frontiers in cell plasticity.

“We have found that damaged cells secrete factors that promote reparative activities in the surrounding cells, including loss of differentiation and plasticity. This could be beneficial to repair the damaged tissues, but it could also favour the expansion of dormant cancer cells.”
New tumour markers for the prognosis of head and neck cancer

Head and neck cancers include a heterogeneous group of tumours located in the oral cavity, pharynx and larynx. The survival rate of patients with this pathology has hardly improved over the last decade. Stratification of patients has been limited, until now, to a clinical classification and not a molecular one. Analysis of patients’ biopsies showed that about half of them possess high levels of the p21 protein as well as mTOR activation. We have unravelled the molecular mechanisms by which p21 levels are linked to the activity of oxidative damage with ageing is undisputed, the large majority of attempts to prove that oxidative damage is relevant for ageing have failed. All these attempts, however, have manipulated only one component of the complex network of antioxidant defences. In contrast to these previous attempts, we have approached this issue by increasing the levels of NADPH, a simple co-factor required for almost all antioxidant reactions and whose levels are known to determine the global antioxidant capacity of cells. To achieve this, we generated transgenic mice with an increased expression throughout their bodies of glucose-6-phosphate dehydrogenase (G6PD), one of the most important enzymes for the production of NADPH. We found that G6PD transgenic mice have overall higher levels of NADPH and, consequently, a better protection against oxidative damages. Importantly, these mice are not predisposed to cancer and, indeed, have a modest increase in longevity. These observations point to novel strategy to delay ageing-related diseases, including cancer.

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Antioxidant defences delay ageing and age-related diseases

Accumulation of cell damage plays an important role in ageing. There is no clear answer about which types of cellular damage...