Researchers reveal a master controller of development and aging

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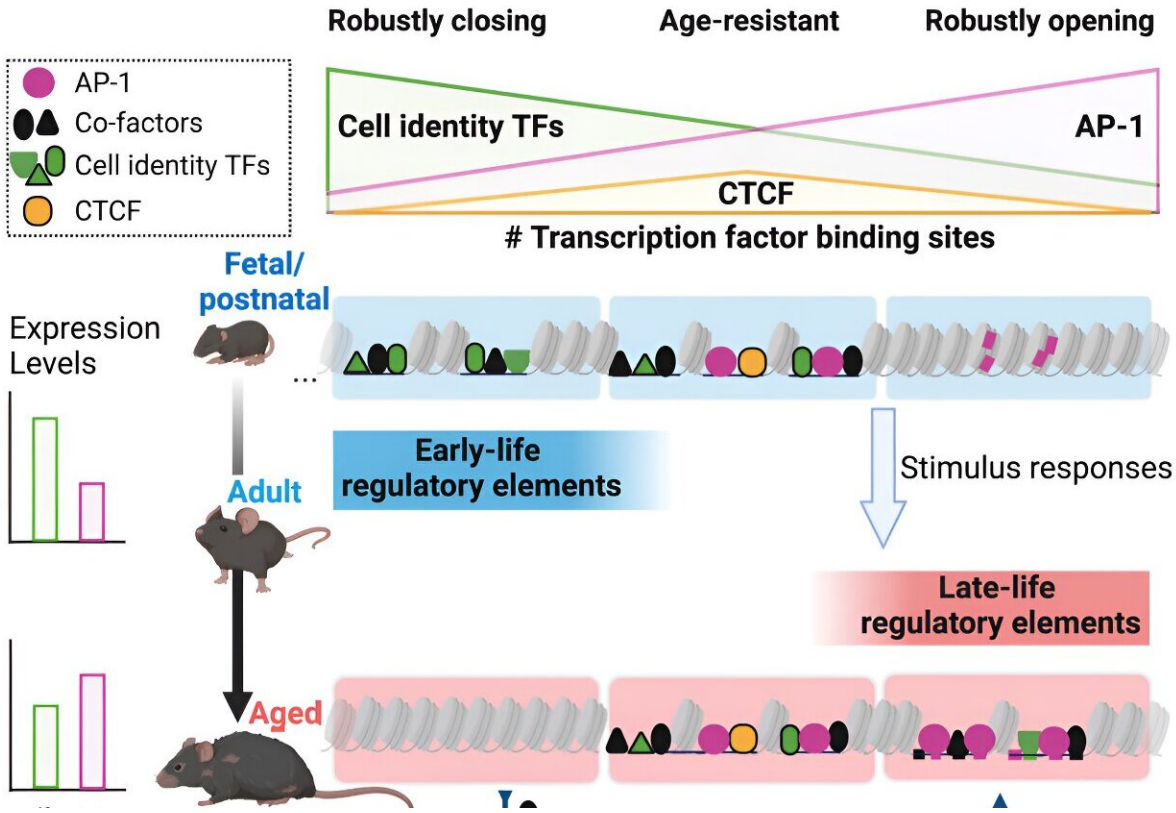

Credit: *Cell Metabolism* (2024). DOI: 10.1016/j.cmet.2024.06.006

University of Queensland researchers have unlocked crucial molecular secrets of aging in cells, potentially paving the way to improve quality of life as people age.

The study, published in *Cell Metabolism*, decoded the process by which genes regulate how people mature as they grow and age. It was led by Dr. Christian Nefzger from UQ's Institute for Molecular Bioscience with key contributions from Dr. Ralph Patrick and Dr. Marina Naval-Sanchez.

Dr. Nefzger said that until now the process of how genes change activity from birth to adulthood and into old age was largely unknown.

"By analyzing molecular datasets from both people and mice and then comparing different age groups over time, we investigated the activity of genes involved in both developmental and aging processes," Dr. Nefzger said.

"Master controller genes regulate which genes are turned on or off in each of our cells, making sure that each cell does its specific job, just as a conductor directs musicians to produce different sounds.

"We followed the activity of the master regulator Activator Protein 1 or AP-1 and found that it progressively activated adult genes, while the activity of 'early-life' genes involved in development were dialed down, and this process was shared across cell types."

Dr. Naval-Sanchez said the study found this process in our cells was predictable across the different life stages, as people mature.

"It was ongoing in adulthood, likely because AP-1 is also activated by a number of stress and inflammatory processes as well as by a protein in our blood that increases with age," Dr. Naval-Sanchez said.

"This further dampens genes most active early in life, which may drive many of the predictable changes of aging."

Dr. Patrick said to address the diseases associated with aging, like Alzheimer's disease, metabolic liver disorders and stroke, researchers must first understand the process causing bodies to age.

"By pinpointing AP-1 as a master controller linked to aging across cell types, we can now study the effects of drugs that reduce its activity to extend quality of life," Dr. Patrick said.

Dr. Nefzger said the goal is to prevent diseases of aging from escalating or occurring in the first place by targeting the underlying aging process to allow people to grow older in better health.

More information: Ralph Patrick et al, The activity of early-life gene regulatory elements is hijacked in aging through pervasive AP-1-linked chromatin opening, *Cell Metabolism* (2024). DOI: 10.1016/j.cmet.2024.06.006

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