Review of: "Cell type-specific aging clocks to quantify aging and rejuvenation in regenerative regions of the brain"

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In the present manuscript, the authors used single-cell transcriptomic analysis to define an accurate chronological and biological aging clocks for different populations present in the neurogenic SVZ niche of mice at different ages. They also characterized how two rejuvenation interventions (parabiosis and exercise) are able to revert both the expression of specific genes and to stimulate age-associated compensatory pathways in certain cell populations within the SVZ.
In this review I will limit myself to analyzing the main aspects of the study not being able to evaluate in depth the technology of machine learning. In my opinion, this study is of primary interest as it highlights the predictive power of single cell analysis in determining specific genetic profiles characterizing cellular aging processes. And even more interesting is the authors' demonstration of how different populations within the neurogenic niche are characterized by differentially predictive gene expression profiles of aging processes, and respond differentially to cell rejuvenation interventions. Finally, the drafting of the text is very clear and fluent, in the face of a highly complex technology used, which makes reading the article accessible to a wide plethora of readers.
My comments are of a general nature and are intended to broaden the horizons of brilliantly obtained scientific results.
1) Why did the authors decide to study the neurogenic niche of SVZ instead of the hippocampal dentate gyrus? From a point of view of general interest it would have been much more impactful to quantify aging and rejuvenation processes in the hippocampal DG which represents a neurogenic niche present throughout life also in humans and is much more sensitive to the proneurogenic action of external interventions such as running. On the other hand, the neurogenic activity of human SVZ runs out during adolescence and therefore the translation value of the data obtained by the authors loses some value as it is not predictive in the field of neurogenic niche aging in humans.
2) In their results, the authors observe a small rejuvenation effect of running in only two of six cell types, oligodendrocytes and aNSCs-NPCs, with a greater implication for oligodendrocytes. These data lead to hypothesize a limited action of physical exercise in stimulating neurogenesis and anti-aging processes within the SVZ. Indeed, some works show that SVZ niche in mice is refractory to the proneurogenic stimulus provided by physical exercise (Bown J et al. 2003, Nicolis di Robilant et al. 2019). Did the authors verify from a cellular point of view an increase in subventricular neurogenesis correlated to their physical activity paradigms?