Analysis of the Effects of Age in Biological Systems

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Stem cells of various origins (hematopoietic, neural, mesenchymal, etc.) obtained from younger donors seem to be superior to the same stem cells harvested from older donors [1]. Why? No one really seems to know. Some investigators have reported declining stem cell numbers with age, while others have shown no change, or even an increase in number with donor age. Almost all investigators agree however, that stem cells lose potency with increasing donor age, for unknown reasons [2-8]. Similar observations have been made concerning stem cells obtained from donors displaying chronic health conditions, particularly chronic inflammatory diseases, such as heart failure and autoimmune diseases. Again, it is unclear why these underlying conditions results in changes in stem cell potency.

Some time ago, looking at stem cell use in hematopoietic transplantation, my colleagues and I demonstrated that children transplanted with newborn cord blood stem cells had significantly longer telomeres in cells isolated from their blood than comparable children transplanted with adult stem cells [9]. Thus, recipients of young stem cell transplants would be less likely to undergo premature cellular aging than those receiving older cells, which would be particularly important in pediatric patients who might live for decades after transplantation. These results implied that the telomerase enzyme might be in part involved in maintaining stem cell function.

Similarly, numerous studies (including our own unpublished data) have indicated that MSCs isolated from older donors, as well as from patients with chronic disease conditions, are neither as prevalent (in terms of the number of cells in the sample), nor as potent as those isolated from younger, healthier donors [2-8]. MSCs collected from older or disease-afflicted donors seem less able to differentiate into different cell types, and more prone to dying during culture. Finally, similar observations have been made for neural stem cells [3].

If stem cell quality declines with donor age, then there should be concern when using adult stem cells for cell-based therapies, either in regenerative medicine of for tissue engineering. The ability of older stem cells to respond to injury and disease may be compromised during aging, and could contribute to inferior tissue repair. A possible explanation for these observations is the accumulation of endogenous DNA damage, which is known to occur in a variety of cell types, and would be expected to limit the utility of aged stem cells; although no one really knows why.

Thus, it seems that the purveyors and utilizers of biochips and tissue chips would be ideally situated to uncover the reasons for these effects of aging. It should be possible using single cell and mixed cell/tissue populations to determine if the effects are cell intrinsic or extrinsic, due to changes at the transcriptional or translational level, or a result of secreted factors. Rapid, high-throughput analyses should be used to identify possible culprits in these processes, and then test the hypotheses for validity. Proper implementation of these tools should allow for more rapid, more economical, and more precise identification of druggable targets to counteract the effects of aging on our stem cells.

References

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