Progenitor Cells in Chromospheres: In Response to Arthur S. Tischler

Magda M. Santana, Monika Ehrhart-Bornstein, Cláudia Cavadas

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LETTERS TO THE EDITOR

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This is in response to the letter "What Happens in 'Chromospheres'?" by Arthur S. Tischler, commenting on our article titled "Isolation, Characterization, and Differentiation of Progenitor Cells From Human Adult Adrenal Medulla" [1]. We would like to acknowledge the comments, the interesting discussion, and potential other point of view on our results. We agree with Dr. Tischler about the fact that human chromaffin cells have the capacity to acquire a neuron-like phenotype in monolayer cultures without a "chromosphere" stage. We also observed this phenomenon in a previous study using human adrenal chromaffin cells in monolayer cultures [2]. Since the cell culture conditions of human chromaffin cells in monolayer cultures and suspension chromosphere cultures are different, careful investigation should be made before it is assumed that the same changes are occurring. Therefore, as suggested by Dr. Tischler, it will be important to compare the two cell culture types in terms of cell proliferation capacity, expression of progenitor cell markers, duration of cell culture, regulatory peptide expression, and catecholamine content. This new set of experiments will provide information on whether the mechanisms required for chromaffin cell transdifferentiation will involve a dedifferentiation or an unnatural intermediate step [3]. Even if we do not know the mechanism, and even if we did not directly evaluate the proliferation capacity, human chromospheres, like bovine chromospheres [4], express nine markers of progenitor cells (nestin, CD133, Notch1, nerve growth factor receptor, Snai2, Sox 9, Sox 10, Phox2b, and Ascl1), and more importantly, nestin-positive cells are present in human adult adrenal medulla, suggesting the presence of progenitor cells in human adult adrenal medulla. The possibility that a "priming" process, with an upregulation of genes required for transdifferentiation, also occurs during chromosphere culture cannot be discarded. Nevertheless, we think that this could also represent an advantage of the use of chromospheres as a source of cells for clinical purposes. The survival rate of chromosphere cells after grafting is currently being investigated in animal experiments. From data available on the transplantation of neural progenitor cells, we expect that the number of spheres isolated from one adrenal gland (27,000–280,000) should give rise to enough cells for grafting.

Moreover, one of the major problems of using embryonic stem cells and induced pluripotent stem cells still is their tumorigenicity. Therefore, if future data demonstrate that human chromospheres have a low cell proliferation capacity, this should emphasize the interest in their use for regenerative medicine.

MAGDA M. SANTANA
Center for Neuroscience and Cell Biology and Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal

MONIKA EHRHART-BORNSTEIN
Carl Gustav Carus University Medical School, Medical Clinic III, Dresden University of Technology, Dresden, Germany; contributed equally as a senior author.

CLÁUDIA CAVADAS
Center for Neuroscience and Cell Biology and Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal; contributed equally as a senior author.

Disclosures

The authors indicate no potential conflicts of interest.

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