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The Origin of a New Progenitor Stem Cell Group in Human Development

An Immunohistochemical-, Light- and Electronmicroscopical Analysis

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230
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Preface

Since studies on human stem cells are legally restricted in Germany (Wiedemann et al. 2004), the use of the stem cells in this study needs some introductory explanations. The applied human embryos and fetal tissues have been obtained in the years 1968 (Vossmeyer 1971 and Holstein et al. 1971) and 1985 (Wartenberg 1985, 1989 a, b): we got them from legal interruptions in local hospitals in Hamburg and in the University Hospital Bonn, Germany. The material was taken from male and female embryos and fetuses ranging from 21 to140 mm crown-rump length (CRL). They derived from medical abortions which were provided for pathological examinations. In each case, the consent of the heads of the clinical institution (in Bonn: Prof. Dr. Krebs, head of the Gynaecologic Clinic, University of Bonn, Germany) and that of the physicians who performed the medical treatment were obtained. When the present studies on stem cells were started, the embedded tissues could still be used and gave excellent results even after several decades of storage. In all cases, the stem cells have been obtained long before the current legislation restricted the studies on human stem cells. The restrictions presented in the Delphi study already mentioned (Wiedemann et al. 2004) were merely retrospective. Whatever the legal obligations are about the use of human stem cells, the results presented here offer a very important view on stem cell biology. The human embryonic and fetal material used for Chromogranin A-immunohistochemistry was based on the specimens already described (Møllgård et al. 2010 and Mamsen et al. 2012). In short, they were obtained in connection with legal abortions carried out in Copenhagen, Denmark. Oral and written information was given and informed consent was obtained from all contributing women, according to and approved by the Regional Committee on Biomedical Research Ethics Copenhagen and Frederiksberg Counties (KF (01) 258206).

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Abstract

In light and electron microscopic sections of plastic-embedded human embryonal and fetal organs, the origin of a new group of progenitor stem cells has been found which are dealt with in the present studies. The distribution of these cells can result in a large quantity of ectopic stem cells. The observation of these ectopic stem cells leads us to postulate the existence of a basic wave of stem cell progenitors. This process proceeds earlier and independently from germ cell migration. This first wave of progenitor stem cell migration initially reaches the peri-aortal AMG region (**A**ortal-**M**esonephric-**G**onadal region). From here, some of these progenitor cells enter the aorta, are distributed through the vascular system, and become the embryonal stem cells (reserve cells) in many peripheral tissues. A second part delivers progenitor cells for the adrenal "anlage." Within the peripheral Zona definitiva of the adrenal cortex, the progenitor cells multiply and subsequently leave the adrenal cortex through a gate of the capsule. The progenitor cells arrive at the pre-aortal sympathetic plexus ("second brain"). Within the plexus ganglia they form new organ-like clusters, the paraganglia. In a second process, the progenitor cells (chromaffin cells) enter sympathetic nerve bundles. Here an "axonal migration" starts, which guides the progenitor cells to several peripheral organs. During this migration process, the stem cells develop into their final state. In the adrenal cortex, the ingrowing nerves guide the stem cells to the adrenal medulla. In the pancreas, the ingrowing nerve fibers guide the stem cells to the islets.

Keywords Human · Progenitor stem cells · AMG region · Adrenal · Zona definitiva · Para-aortal plexus · Paraganglia · Autonomic nervous system · Guided axonal migration · Pancreas · Gonadal and Intestine stem cells · Stem cells II · APUD system · Teratoma