

Human embryonic stem cells: an ideal model for the risk assessment of ionizing radiation during early embryo development *

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Diagnostic and/or therapeutic procedures that are based on ionizing radiation are being increasingly used. However, these procedures as well as the exposure to environmental radiation pose a threat to the early embryo possibly leading to prenatal death, growth retardation, organ malformation, mental retardation or childhood cancer [1]. Thus, a thorough risk assessment of radiation effects is mandatory in situations of inevitable or unintended exposure of the conceptus in utero. Data about the biological effects of a radiation exposure during the earliest stages of human development are scarce predominately stemming from atomic bomb survivors or observations made after fall-outs (e.g. Chernobyl). However, human embryonic stem (hES) cells that are derived from the inner cell mass of the blastocyst during embryo development present a valuable tool to examine the radiation effects on early embryogenesis. Apart from their indefinite self-renewing capacity, hES cells are pluripotent thereby being able to differentiate *in vitro* into all cell types of the body deriving from the three germ layers endoderm, ectoderm and mesoderm (Fig.1). Therefore, the effect of radiation on pluripotent embryonic cells and their respective progeny can be easily analyzed on a molecular level. This is basis of the BMBF funded project “In vitro Untersuchungen zur Wirkung von dicht und dünn ionisierender Strahlung auf die frühe pränatale Entwicklung”, which is performed in cooperation with the Universities of Applied Sciences Aschaffenburg and Albstadt-Sigmaringen.

In Germany, the work with hES cells requires ethical approval in accordance with the German Embryo Protection Act and the German Stem Cell Act and underlies certain restrictions regarding the choice of cell lines and the procedures used to study scientific questions. However, examining the effects of ionizing irradiation on early human development was regarded a top-ranking scientific goal and approval was granted to study the impact of ionizing irradiation. Yet, the initial GSI approval to use hES cells only comprised the analysis of cardiac differentiation with a limited number of hES cell lines. An amendment now allows us to use more sophisticated differentiation procedures, more suitable cell lines and not only cardiac differentiation protocols but also neuronal and endodermal ones to cover the entire developmental spectrum. Thus protocols for the generation of endoderm from human WA09 have been established (see GSI report S. Luft et al., 2013)

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as these cells later in development will give rise to lung, pancreas or liver. Likewise extra-embryonic endoderm differentiation is currently established as it provides signaling for cardiac differentiation, which has been shown to be impaired upon irradiation [2-3]. In summary, the hES cell based approach will provide insight into the impact of ionizing irradiation on human development and possibly cell regeneration.

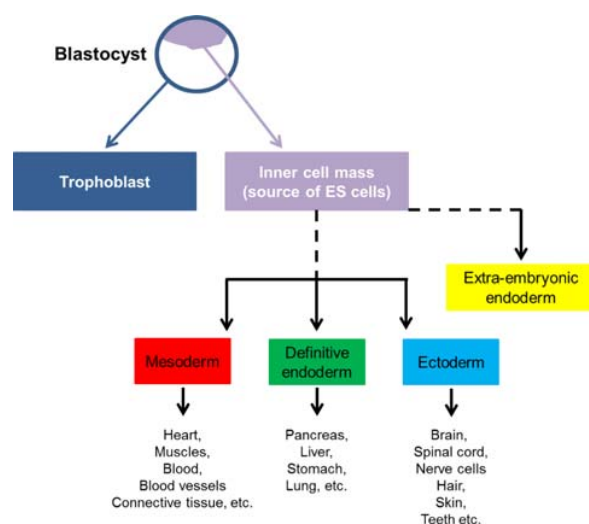


Figure 1: Human development can be mimicked by using human embryonic stem (hES) cells. hES cells can be differentiated *in vitro* into cells of the mesoderm, endoderm and ectoderm and their respective progeny. Likewise, they can form extra-embryonic tissue such as extra-embryonic endoderm, which gives rise to the yolk sac that provides early nourishment and serves as a circulatory system until the embryos internal circulation is established.

References

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