The Use of Embryonic Stem Cells for Developmental Toxicity Testing

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Congenital abnormalities represent a severe medical and social problem, given that approximately 3% of all human newborns are affected. About 20% of these defects are associated with gene mutations and another 5% with chromosomal aberrations. Approximately 5 to 10% of the remaining abnormalities are known to be caused by teratogenic agents. It is thus mandatory in toxicological safety assessment of chemicals and drugs to evaluate adverse effects on reproduction and embryonic development according to OECD test guidelines or so-called segment studies encompassing three crucial periods of pre- and postnatal development and fertility (ICH, 1993). All of these test methods generally comprise time-consuming and expensive in vivo experiments mostly performed with mammalian species such as rats or rabbits.

In recent years, embryonic stem (ES) cells became available and shifted into focus. The ability to differentiate into a wide range of different cell types has made ES cells a very popular system to study developmental processes and gene function during cellular differentiation in vitro. More than 10 years ago scientists at ZEBET proposed a new in vitro assay - the so-called Embryonic Stem Cell Test (EST) – which makes use of this capacity to detect developmental toxicants during stem cell differentiation into cardiomyocytes. The EST has been scientifically validated by the European Centre for the Validation of Alternative Methods (ECVAM).

Currently the stem cell research group at ZEBET is committed to explore and develop additional stem cell based approaches, searching for novel predictive biomarkers of developmental toxicity and to extend the experimental approach to other cellular systems, like neurons and bone, in order to establish ES cell based tests for the prediction of developmental neuro- and osteotoxicity.