Humanise basic research in cardiology from here!

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If you are not active in basic research on a daily basis, you may wonder what the idea is behind this title and how important this issue really is. It is for sure not meant to indicate that current basic research in cardiology is against our ethical principles. That is not the issue. In the Netherlands there is ongoing debate on the use of laboratory animals for cardiovascular research. There is even a political party active with chosen representatives in parliament, requesting continuous attention for the subject. The debate is useful and important to keep researchers sharp and to force them to minimise the use of animals. The strategy works extremely well in the Netherlands. It is impossible to convince the medical ethics committee of a hospital to include any patients in a trial. At the University Medical Center Utrecht a term of three to four months is the rule with some exceptions going up to 12 months. In reality the situation in animal research is comparable. The main difference is that investigators will give up their efforts if the proposal does not pass in the first six months. The laboratory animal is treated as a patient with respect to post surgical care and pain relief, independent of whether it concerns a mouse or pig.

This situation will be hard to improve. What could be improved is the use of human cell lines to make models for cardiac disease and for basic studies. Cardiovascular research has a longstanding and logical drawback compared with oncology. Neoplastic cells have a tendency to proliferate and are already dedifferentiated. Therefore, there are unlimited numbers of cells available for research. In contrast the cardiovascular system depends mostly on non-proliferating and highly differentiated cells. This is true for cardiomyocytes but also relevant for endothelial cells.

Some recent developments in molecular cardiology are gradually and step by step changing this situation. An important development was the finding that ventricular cardiomyocytes can be grown from human embryonic stem cells.[1] These cells have a limited value for therapeutic applications, but are a major breakthrough for understanding cardiac development and cellular biology. Spectacular was the finding of human cardiomyocyte progenitor cells also reported in this journal and awarded the Einthoven award for best pre-clinical paper in 2008.[2,3] Pushed by the Bush administration, investigators were able to convert human skin fibroblasts to embryonic-like stem cells, the so-called induced pluripotent stem cells (iPS).[4] According to the editors of *Science* the most important development in 2008. All these cell lines now make it feasible to study the role of genes, RNA and proteins in human cells and differentiated cardiomyocytes. Genetic defects can be studied in the ideal genetic background instead of transgenic mouse models. Early steps of cardiomyocyte disease including failure and hypertrophy can be analysed in the culture dish. Here is the new boost to cellular electrophysiology and hopefully also to the clinical EP laboratory. Drugs can be screened and interference with RNA can be studied on the functional level. Using human cardiomyocytes and endothelial cells will shorten the path to potential therapeutic applications. In the past we have experienced only too often that all animal species are different from man at the end of the day. Maybe not so much on the DNA level, but certainly in lifestyle. A healthy laboratory animal is essentially distinct from our patients.

These developments on the molecular and cellular level are very exciting. In the Netherlands we are in the fortunate situation of having ample funding through large initiatives supported by the ministry of economic affairs, such as TI Pharma, Smart Mix, CTMM and BMM. In conclusion, the Netherlands is in good shape to move basic research in cardiology forward. The field could benefit from a better integration of research efforts and should look ahead to keep funding at a high level. For this purpose it could be worthwhile to professionalise the fundraising efforts on the national level. ■

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