HINTERGRUND

The generation of cardiomyocytes (CMs) from pluripotent stem cells (PSCs) holds great promise for cardiac regenerative medicine. Of particular interest are CMs derived from induced pluripotent stem cells (iPSCs) because they can be obtained by converting autologous somatic cells into an early embryonic PSC-like state, thus circumventing ethical concerns related to the use of embryonic stem cells (ESCs).

PROBLEMSTELLUNG

However, a fundamental obstacle in the use of induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) are contaminating undifferentiated PSCs that remain in the population of differentiated cells which carry the risk of tumour formation. This problem is due to an incomplete in vitro differentiation of PSCs to CMs. While genetic manipulations are effective in removal of contaminating PSCs they raise safety concerns. PSC ablation by immunologic targeting is safe but less efficient because single-cell dissociation is required.

LÖSUNG

In this regard, the most promising strategy is the selective chemical ablation of undifferentiated cells in PSC-derived populations using small molecules which are not toxic to differentiated cells of interest.

The diamines of the general formula (see figure), particularly salicylic diamines, are capable of selectively eliminating PSCs from their differentiated derivatives.
Generation of pure CMs by effective iPSC elimination upon treatment with small molecule agents ("SM").

**VORTEILE**

- Compounds toxic against PSCs but not against differentiated derivatives
- Compounds readily available
- New route to cardiomyocytes
- Useable in tissue repair
- First in vitro results

**ANWENDUNGSBEREICHE**

The diamines exhibited high cytotoxicity to murine and human PSCs but not to CMs derived from these.

They are suitable for the elimination of PSCs from differentiating derivatives that contain CMs, either in unpurified or pre-purified form.

A further advantage of the diamines is that the compounds are readily available and show significantly higher PSC-specific cytotoxic activity in comparison to
known small molecules.

SERVICE

First in vitro results with murine and human cells are available. On behalf of the University of Cologne, PROvendis offers access to rights for commercial use as well as the opportunity for further co-development.