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Stellingen

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Viral vector-mediated gene transfer in fundamental and applied cardiovascular research

Besides transductional and transcriptional targeting, other targeting principles may be required to achieve truly myocardial scar fibroblast-specific transgene expression in myocardial scar fibroblasts. (This thesis)

Selective inhibition of connexin 43 expression in myocardial fibroblasts can act anti-arrhythmically by reducing the depolarizing effect of myocardial fibroblasts on cardiomyocytes. (This thesis)

The incorporation of target sequences of microRNAs whose expression is downregulated upon injury or disease into a transgene would limit its expression to diseased cells lacking those microRNAs. (This thesis)

As integrin stimulation appears to induce physiological hypertrophy via AKT, it could provide a novel way to treat patients suffering from pathological cardiac hypertrophy. (This thesis)

The ability to regenerate adult heart tissue from endogenous cells may face fewer obstacles to clinical translation than other approaches to cardiac repair, like the introduction of exogenous stem-cells or pluripotent stem cell-derived cardiomyocytes. (Qian L, *et al.* Nature. 2012; 485:593-598)

Engineering new adeno-associated virus vector pseudotypes by shuffling of cap DNA sequences has proven valuable not only for changing their cell tropism but also for altering their immunological properties. (Hinkel R, *et al.* Expert Opin Biol Ther. 2011; 11:723-37)

miRNAs play crucial and specific roles in human cardiac differentiation. (Fu J-D, *et al.* PLoS ONE. 2011; 6:e27417)

Efforts to develop modified AAV capsids specifically adapted not only for cellular entry but also for post-entry processing in particular cell types and under certain conditions are likely to produce more useful vectors for gene transfer than AAV vectors adapted for cellular entry alone. (Ward P and Walsh CE. Virology. 2009; 386:237-48)

Conscious thought processes in the brain, the processes that constitute the experiences of free will, are realized in a neurobiological system that is totally deterministic. (Searle JR. Free will as a problem in neurobiology. 2001)

The observation that transient membrane disruptions in cells of contracting tissues allow access of high-molecular weight compounds into these cells deserves more attention as this phenomenon may be utilized for therapeutic purposes.

The restricted capacity of the human brain to comprehend the almost infinite complexity of the human body is a major limitation for the development of novel therapeutics.

Jim Swildens

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