Pharmacogenomics and Therapeutic Target Validation of Cardiovascular Disease Models

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Pharmacogenomics Network Analysis of Therapeutic Genes

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Rat Cerebral Vasospasm Model

HE staining (x 100)


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HSP72 Protein after SAH

Saline

N Day 1 Day 2

SAH

Day 1 Day 2


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HSP72 Protein after SAH and Antisense

Saline  SAH  Antisense  Sense


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Effect of Antisense HSP72 ODN on Cerebral Vasospasm

![Graph showing the effect of Antisense HSP72 ODN on cerebral vasospasm over time. The graph compares the arterial diameter (%) between different treatment groups: 0.3ml SAH, 0.3ml SAH + Antisense HSP72 ODN, and 0.3ml SAH + Sense HSP72 ODN. The graph includes error bars indicating variability.](image-url)


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Effect of GGA on HSP72 Gene Expression


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Pharmacogenomics network analysis in treatment of cerebral vasospasm by GGA

Effect of Antisense HO-1 ODN on Angiographic Vasospasm in Rat SAH Model

% Change in Vessel Diameter

Pharmacogenomics network analysis in treatment of cerebral vasospasm by AVS (nicaraven)

Comparative Genomics of Disease Models

Human (2003)

Low Throughput  High Throughput
Advantages of Zebrafish as Disease Model Animal

1. Short reproductive cycle.
2. Large number of offspring per mating.
3. Embryos are transparent allowing internal organs and neurons to be visualised.
4. Strong correlation between human genetics, anatomy and disease.
5. Rapid layout of body plan, allowing study of disease at early stages of embryonic development.
6. Ethically preferred in the drive to reduce, refine and replace.
7. Cost effective.
Zebrafish Heart Failure Models

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Control Zebrafish Heart
Zebrafish Heart Failure Model
Carvedilol Treatment of Heart Failure Model
Carvedilol Therapeutic Gene Discovery

Detection of therapeutic target genes by DNA Micro Array

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Laser-Captured Microdissection

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Therapeutic Gene Validation with Calvedilol

Gene Expression

Control  HF  HF

siRNA cocktail / Morpholino Antisense法

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赤: Up by PECI kd
緑: Down by PECI kd