

K-MEDI hub

Pioneering preclinical research

A state-of-the-art research and development centre in Daegu, Korea – K-MEDI hub – is creating a medical industry ecosystem for the research and development of new drugs and medical devices. At its Preclinical Research Centre, one strong research focus is evaluating the impact of stress on the welfare of laboratory animals in the context of preclinical research. The aim is to improve international standards and guidelines for experimental conditions in the future, improving both the welfare of laboratory animals and the quality of research results.

During animal studies, laboratory animals are often limited to a confined space for the entire experimentation period. This can cause unnecessary stress to the animals and has significant implications regarding animal welfare. New methods for alleviating the stress of laboratory animals are required to improve welfare and the quality of animal studies.

The Institutional Animal Care and Use Committee (IACUC) is currently making efforts to promote the welfare of laboratory animals as a principle of humane animal study. In addition, the South Korean Ministry of Agriculture, Food, and Rural Affairs (MAFRA) has announced a five-year plan for animal welfare that will raise public awareness and enhance animal laboratory ethics by supporting the functions of IACUC.

With these goals in mind, K-MEDI hub, a rising medical facility in Korea, is pioneering preclinical research to evaluate and improve the welfare of laboratory animals during animal studies. This research will be vital for providing and implementing improved guidelines for conducting preclinical animal studies in the future.

THE K-MEDI HUB
Located in Sinseo Innovation City, Daegu, the K-MEDI hub is a public institution under the Ministry of Health and Welfare of Korea. It is a research and development centre composed of four core research facilities: New Drug Development Centre, Medical Device Development Centre, Preclinical Research Centre, and Clinical Drug Manufacturing Centre, all working towards supporting the unmet needs of the medical industry and medical research. In particular, K-MEDI hub was developed to create a medical industry ecosystem for the research and development of new drugs and medical devices.

The Preclinical Research Centre (PRC) is certified to provide high-quality veterinary care in a wide variety of laboratory animal species including rodents, rabbits, dogs, pigs, and non-human primates. One of the main goals of the PRC is to establish a cutting-edge animal experimentation system that will support K-MEDI hub's overall objective of developing new drugs and medical devices. In addition, the centre designs and implements various strategies to provide customised support for animal studies. With the work carried out at the PRC, new methods



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can be devised to improve the welfare of laboratory animals, the end goal being for these methods to be adopted globally.

The K-MEDI hub PRC was certified by the Ministry of Food and Drug Safety in 2016 and awarded full accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC-i) in 2020. As a result, it is recognised as a nonclinical study institution that encourages the humane treatment of animals in science and maintains a high level for the care and use of laboratory animals. The PRC constitutes animal testing systems for the development of chemically synthesised pharmaceutical products and medical devices. One research area of interest at the centre aims to evaluate the level of stress induced by experimentation environments on laboratory animals.

STRESS IN LABORATORY ANIMALS
Laboratory animals are often subjected to a lot of stress due to their constrained environment. Stress response hormones include cortisol and corticosterone, both of which are frequently found to be elevated in laboratory animals that are exposed to the experimental conditions currently accepted as standard practice. For example, increased corticosterone in

the blood is widely known to be a reliable indicator of stress in laboratory mice.

Stress in laboratory animals can change the subject's physiological indicators, which affects the results of the studies being conducted and could have a

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significant impact on the accuracy, reliability, and reproducibility of animal studies. Stress can also affect an animal's physical and psychological wellbeing. In turn, this impacts their ability to cope with difficult situations, which, again, could possibly skew the results of animal

studies, as stressed animals are unlikely to give natural responses.

Under common experimental conditions, cage tilting, damp substrate, alarming noises, placing the animal in an empty cage, changing the timing and amount of light received each day, and being moved between cages are all capable of inducing increased depression-like symptoms in laboratory animals. To limit the impact that stress has on both the animal welfare and the experimental outcome, change is needed across all fields and in all countries in the way animal studies are conducted, bringing new methods and standards into practice.

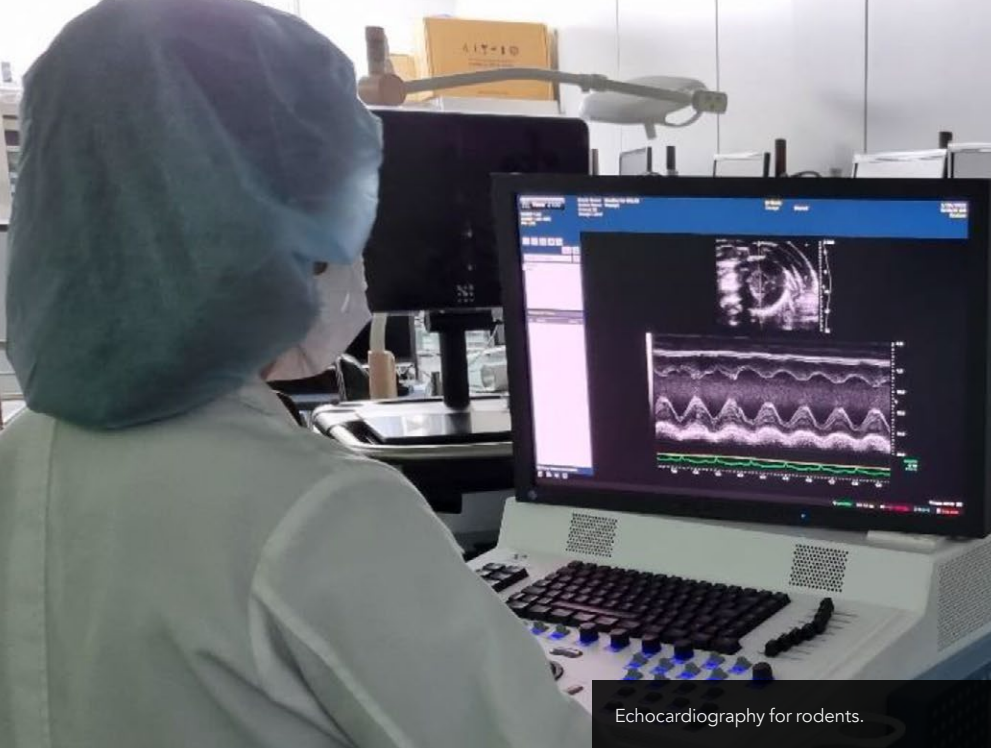
EVALUATING STRESS UNDER EXPERIMENTAL CONDITIONS
Providing a proper breeding environment and environmental enrichment for laboratory animals in order to reduce stress is a solid basis for animal studies. Improving the overall welfare and, in turn, reducing the stress of experimental animals could be as simple as providing shelters, soft flooring, toys for enrichment, and social housing, as well as other

factors that could improve conditions for laboratory animals during an experiment and limit stress exposure.

In one study at K-MEDI hub PRC, stress levels were evaluated in relation to the breeding environment of mice. Six different environmental conditions were provided by combining individually ventilated or individually isolated cages with a single breeding or group breeding environment, as well as providing



Stress in laboratory animals can significantly impact the accuracy, reliability, and reproducibility of animal studies.



Echocardiography for rodents.

enrichment materials in the form of a platformed shelter and a diamond twist that could be gnawed to make a nest, or withholding such enrichment. The study aimed to evaluate changes in the mice's body weight and serum corticosterone concentration as stress indicators in response to the various experimental conditions. The assumption was that animals exposed to stress would have raised corticosterone concentrations and would decrease their rate of body weight gain.

The researchers found lower corticosterone concentrations in the serum, as well as a higher body weight, in the animals kept in individually ventilated cages that were provided with enrichment, thus indicating lower stress levels. In contrast, mice that were kept in individually isolated cages and not provided with enrichment showed higher stress indicators. This confirms that isolation and environmental enrichment have fundamental effects on mouse behaviour and should be taken into account in the design of experiments with stress-related animal models and in animal welfare assessment.

FUTURE IMPLICATIONS

By improving animal welfare during research, the design of high-quality animal studies can be better facilitated. Director of the PRC, Dr KilSoo Kim explains, 'the study conducted at

the PRC is important for providing appropriate guidelines for both the management and operation of laboratory animal breeding and the welfare of laboratory animals on a wider scale'. Dr Kim continues: 'The findings of the researchers at K-MEDI hub PRC

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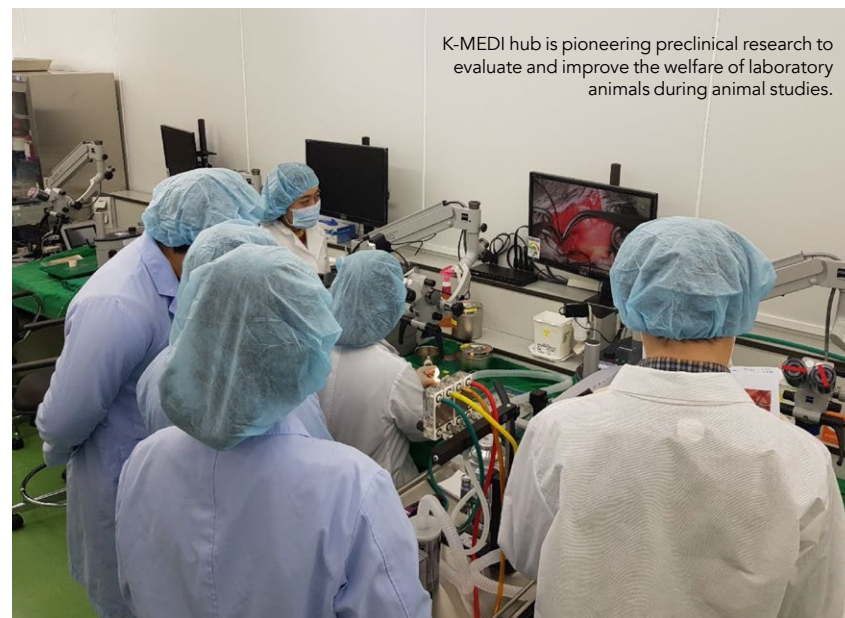
will be used to provide appropriate guidelines for the management and operation of laboratory animal breeding and improve the welfare of animals used in experimentation across all fields'. In particular, their results will be used to

enhance environmental conditions for laboratory animals and improve animal welfare by reducing unnecessary stress on laboratory animals over the whole experimentation period.

By improving the welfare of laboratory animals and reducing stress, the accuracy, reliability, and repeatability of animal studies will be significantly increased. This will strengthen the credibility of the results and conclusions drawn from studies using animal experimentation in the future. At K-MEDI hub PRC, in addition to studying ways that stress can be reduced in rodents during experimentation, the scientists are further expanding this research to evaluate the impacts of stress on the welfare of pigs and dogs. The results will have an influence on the methods used for implementing animal welfare, not only for laboratory animals, but also for industrial and companion animals further down the line.

The PRC at K-MEDI hub is currently devising and continuing to develop ways to promote animal

welfare during preclinical research. This could improve international standards for experimental conditions in the future, improving both the welfare of laboratory animals and the quality of research results.



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Behind the Research



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Research Objectives

K-MEDI hub was developed to create a medical industry ecosystem for the research and development of new drugs and medical devices.

Detail

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Bio

Jin-Young Yang, PhD

Dr Jin-Young Yang is a president of K-MEDI hub. He manages all the work and develops the K-MEDI hub into the world's best R&D hub in the advanced healthcare sector and as a cornerstone of the health industry.

KilSoo Kim, DVM, PhD

Dr KilSoo Kim is a director of Preclinical Research Centre at K-MEDI hub and a

professor of toxicology at the college of veterinary medicine at Kyungpook National University. He manages all the work for Preclinical Research Centre at K-MEDI hub. He is increasing the success rate of commercialization in the international medical industry by supporting preclinical animal studies of new drugs and medical devices.

Woori Jo, DVM, PhD

Dr Woori Jo is a senior researcher in Preclinical Research Centre at K-MEDI hub and an adjunct professor at Kyungpook National University. She conducts efficacy evaluation for new drug or new medical device development by surgically induced

disease model. Her research focuses on efficacy tests in cardiovascular disease model using echocardiography.

Gwang-Hoon Lee, DVM, MS

Gwang-Hoon Lee is a researcher and an attending veterinarian of Preclinical Research Centre at K-MEDI hub. He tests new drugs or new medical devices using laboratory animal including non-human primates and strives to promote welfare of all species of animals including laboratory animals.

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References

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Personal Response

In what ways could the research findings of K-MEDI hub be implemented elsewhere?

Animal welfare is a growing concern for all animals, not just laboratory animals. There are many voices calling for improvement of animal welfare and this animal welfare will be improved based on the scientifically proven experimental results that housing environment affects the stress of animals. We hope that it will be a guideline for IACUC in particular which is responsible for animal welfare even in laboratory animals. In the field of non-clinical testing, we will do our best to provide accurate animal studies that take into account the animal welfare.