



Characterizing the gut microbiota as a way to reduce the group size in rodent studies

Hansen, Axel Jacob Kornerup; Hansen, Camilla Hartmann Friis; Krych, Lukasz; Buschard, Karsten Stig; Lundberg, Randi; Ellekilde, Merete; Nielsen, Dennis Sandris

Publication date:
2014

Citation for published version (APA):
Hansen, A. J. K., Hansen, C. H. F., Krych, L., Buschard, K. S., Lundberg, R., Ellekilde, M., & Nielsen, D. S. (2014). *Characterizing the gut microbiota as a way to reduce the group size in rodent studies*. Abstract from 9th World Congress on Alternatives and Animal Use in the Life Sciences, Prag, Czech Republic.



Session V-2: Disease models *in vivo*

Co-chairs

Nicolas Dudoignon, Sanofi R&D, France

Tobias Schnitzer, Roche Diagnostics, Germany – IQ consortium

Session V-2: Oral presentations

V-2-077

The effect of additional rodent enrichment on local and systemic bacterial infection models, hematology, clinical chemistry, and serum cortisol

J. Fernandez¹, C. McLahan², K. R. Sharp³, A. M. Queenan¹, W. Shang⁴, J. Hastings⁵, L. Smith⁵, L. Varacallo⁵, A. Barron⁶, G. van den Dobbelsteen⁷ and A. S. Lynch⁴

¹Infectious Diseases & Vaccines, Janssen R&D, a Johnson & Johnson Company, Springhouse, USA; ²Laboratory Animal Medicine, Janssen R&D, a Johnson & Johnson Company, Springhouse, USA; ³Laboratory Animal Medicine, Janssen R&D, a Johnson & Johnson Company, LaJolla, USA; ⁴Infectious Diseases & Vaccines, Janssen R&D, a Johnson & Johnson Company, Raritan, USA; ⁵Preclinical Development and Safety, Janssen R&D, a Johnson & Johnson Company, Springhouse, USA; ⁶Nonclinical Statistics & Computing, Janssen R&D, a Johnson & Johnson Company, Raritan, USA; ⁷Bacterial Vaccines, Janssen R&D, a Johnson & Johnson Company, Leiden, The Netherlands
jfern5@its.jnj.com

Objectives: To determine the effects of foraging enrichment added to standard enrichment (SE) in a mouse skin (MS) (Fernandez et al., 2011) infection or rat endocarditis (RE) (Fernandez et al., 2012) model. Effects on hematology (H), clinical chemistry (CC) and serum cortisol (SC) were examined.

Methods: Animals were group housed into SE (mice, Nestlets™; rats, acrylic tubes) and additional enrichment (AE)(SE with autoclaved hamster food (mice) or sunflower seeds (rats)) groups. After 28 days, a group of mice or rats were euthanized and blood was collected for H, CC, and SC (rats). The remaining animals participated in a *S. aureus* MS or RE model. In both infection models, untreated animals were compared to vancomycin-treated animals.

Results: Additional foraging material had no apparent effect in either infection model with respect to bacterial load at the infection site or the efficacy of vancomycin. Additionally, H and CC values were similar for each group. SC in rats was lower in the AE group ($p < 0.03$), suggesting that the animals did not experience additional stress from the added enrichment, and may have benefited.

Conclusion: Animals could benefit from the additional foraging enrichment to enable natural behavior. Clinical chemistry and hematology should be evaluated prior to implementing in a research program.

References

Fernandez, J. et al. (2011). *Antimicrob Agents Chemother* 55, 5522.
Fernandez, J. et al. (2012). *Antimicrob Agents Chemother* 56, 1476.

V-2-246

Characterizing the gut microbiota as a way to reduce the group size in rodent studies

A. K. Hansen¹, C. H. F. Hansen¹, L. Krych², K. Buschard³, R. Lundberg^{1,4}, M. Ellekilde¹ and D. S. Nielsen²

¹Department of Veterinary Disease Biology, University of Copenhagen, Frederiksberg, Denmark; ²Department of Food Science, University of Copenhagen, Frederiksberg, Denmark; ³Bartholin Institute, Rigshospitalet (National University Hospital), Copenhagen, Denmark; ⁴Scientific Research & Development, Taconic, L. Skensved, Denmark

akh@sund.ku.dk

The gut microbiota of animal models has a substantial impact on the expression of and the variation in the models (Bleich and Hansen, 2012). E.g., in models of type 2 diabetes the correlation between essential parameters and the gut microbiota composition is 30-40% (Ellekilde et al., 2014), while it in the oxazolone model of atopic dermatitis is more than 80% (Lundberg et al., 2012). Today, high throughput sequencing enables a full characterization of the microbiota based upon a non-invasive fecal sample. In animal experiments group size is calculated as $2 \times Z\text{-values (Significance + power)} / (\text{Average effect level} / \text{Uncontrolled variation})$ (Ellekilde et al., 2014). Therefore, it is possible to characterize the microbiota composition of individual animals in sensitive studies and thereafter turn the “uncontrolled” variation into “controlled variation” by incorporating the characterization in the data evaluation model. Alternatively, only mice with a gut microbiota coding for a strong expression of the disease could be used. We have previously shown that mice might be inoculated with tailor-made microbiota around weaning to achieve the immunological phenotype induced by the early life colonization (Hansen et al., 2012). A third approach might be to feed the mothers a microbiota-modulating diet that will induce a specific phenotype in their offspring (Hansen et al., 2014).

References

Bleich, A. and Hansen, A. K (2012). *Comp Immunol Microbiol Infect Dis* 35, 81-92.
Ellekilde, M., Krych, L., Hansen, C. H. et al. (2014). *Res Vet Sci* 96, 241-250.
Hansen, C. H. F., Nielsen, D. S., Kverka, M. et al. (2012). *Plos One* 7, e34043.
Hansen, C. H., Krych, L., Buschard, K. et al. (2014). A maternal gluten-free diet reduces inflammation and diabetes incidence in the offspring of NOD mice. *Diabetes*, in press.
Lundberg, R., Clausen, S. K., Pang, W. et al. (2012). *Comparative Medicine* 62, 371-380.



ALTEX

Proceedings

Dagmar Jírová and
Horst Spielmann:
Welcome

Keynote lectures:
M. Vácha

**Animals: biomechanisms or
evolving organisms on the
way to a reflexive thought?**

M. Goldman

**The rational use of animals
in drug development:
contribution of the Innovative
Medicines Initiative**

R. Mokry

**European strategy for 3Rs
and replacement
of animal experiments**

U. Marx

**Human-on-a-chip –
a paradigm shift
from animal testing**

N. Gillett

**Industrial perspectives on
the 3Rs and animal welfare**

R. Kolar

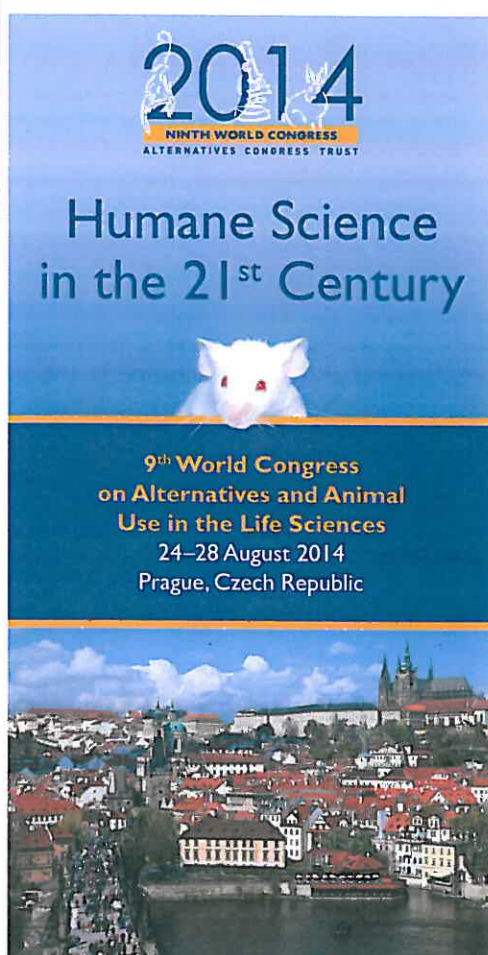
**How long must they suffer?
Success and failure of
our efforts to end the animal
tragedy in laboratories**

H. Zhengming

**Future perspectives
for alternatives to animal
testing in China**

R. Kavlock

**Lessons learned from ToxCast
and prospects for the future**



Theme I
New Technologies

Theme II
Predictive Toxicology

Theme III
**3Rs in Academia and
Education**

Theme IV
**Communication,
Dissemination and Data
Sharing**

Theme V
**Efficacy and Safety
Testing of Drugs
and Biologicals**

Theme VI
Human Relevance

Theme VII
Ethics

Theme VIII
Refinement and Welfare

Theme IX
**Global Cooperation,
Regulatory Acceptance
and Standardization**

Theme X
Additional Sessions

