Kick off meeting Focus group "DIO mouse model and diet composition"

Berlin 2013, Jan 16th, 10:00-16:00

Helmholtz Gemeinschaft Geschäftsstelle
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Minutes

Participants: Dr. Petra Wiedmer, MDC Berlin
Dr. Mauricio Berriel Diaz, DKFZ Heidelberg
Dr. Johannes Beckers, HMGU
Dr. Jan Rozman, German Mouse Clinic
Dr. Carola Meyer, HMGU
Dr. Juliane Kampe (organizer), HMGU

Topic 1: Introduction and Direction

J. Kampe welcomed the participants to the kick-off meeting of the ICEMED Focus group "DIO mouse models" and briefly outlined the background of the focus group within the ICEMED Alliance. The demand for such a focus group was expressed at the ICEMED kick-off meeting in Munich in October 2012 where all partners of the alliance got together for the first time since approval of the grant. The ask for a focus group arose during data presentation at the initial kick off meeting and the use of different high fat diets, different mouse strains in all partner labs studying diabetes and obesity lead to discussions about comparability of data sets. The ICEMED coordinator Prof Matthias Tschöp initiated the founding of the focus group "DIO mouse models" including representatives from labs that use animal models for their research. The representatives of the focus group come from the following institutes:

- Max Delbrück Center for Molecular Medicine Berlin-Buch (MDC)
- Deutsches Krebs Forschungszentrum (DKFZ)
- Helmholtz Zentrum München (HMGU)
- German Mouse Clinic

To start the kick off meeting the overall goal of the focus group was discussed with the long-term aim to publish the work/results/generated data in a high impact journal. The details of the content of the paper were argued and discussed by all participants:

- what data set of which animal cohorts does already exist in different labs of icemed partners,
- what data is already published on high fat diets and diet-induced obese (DIO) mouse models),
- what does the focus group want to concentrate on in the paper,
- how can the focus group develop a platform that can be accessed by all icemed partners,
- there is a need to define parameters that focus group will concentrate on (to not get lost in the overwhelming number of variables in this type of research).

It was concluded that the number of possible factors/variables in diabetes and obesity research regarding research diets and animal models are endless. The two main factors that the focus group will concentrate on are research diets and mouse strains. The unified view was that a recommendation should be formulated for the use of all available research diets that are in use in Germany and worldwide for specific disease model endpoints (obese, diabetic,…) and placed on a platform that can be utilized by ICEMED partners (ie intranet on the ICEMED website). Another factor would be the type and strain of mouse model. It was agreed on that the

platform should function as a forum at the same time for people to discuss and communicate various results/data/experience. In the long term it would be applicable to create an "ICEMED – standard" for the use of mouse models and research diets for diabetes and obesity research.

Topic 2: Diet

It was agreed to dissect all the different types of research diets that are available in Germany and which diets are the most commonly used diets in studies that are published in high impact journals. The most important variables affecting outcome when using high caloric diets are:

- Definition of diet source (detailed reference of supplier, modification, treatment)
- Type of diet (pellet, non-pellet, consistency, taste, smell, replacement frequency)
- General information on diet composition (protein, carbohydrates, lipids)
- Additives/substances (ie selene, butyrate)
- Age of experimental animals at onset of diet
- Duration of diet treatment
- Type of control diet (chow, low fat diet,…) very critical
- Grade of diet (purified, semi-purified)
- Treatment of diet (irradiation, autoclavation)

The most common used suppliers of research diets are Altromin, ssniff, Research Diets. One critical aspect that was discussed is the available data on diet composition provided by the suppliers: how precise are the data sets, in which animals was data generated (mostly pigs), how consistent is the quality of the diet according to the supplier? It was suggested that caloric data should be requested from the diet supplier that was measured in mice. Another aspect to consider is the comparability to the "big+famous" US-labs and their choice of research diet.
It was decided to not include the microbiota aspect in this analysis to avoid more complexity.

Topic 3: Mouse model

In respect to the mouse model it will be critical to consider the following variables:

- mouse strain (genetic background)
- supplier of strain (in house bred, bought from supplier)
- mice house-keeping parameters

- type of cage (size, IVC ...)
- single housing versus group housing
- light-dark cycle timing
- room temperature and humidity of facilities

The experience with different mouse models that have been used to date in various research facilities was discussed amongst attendees. Questions that came up included: "myths surrounding Bl6 mice": are there different outcomes when put on HFD on bodyweight and food intake, are there obesity-prone/resistant Bl6 mice?, differences between Bl6 mice from Denmark vs USA?
Petra Wiedmer presented data on different diets and their effect on body weight distribution, food intake, glucose homeostasis. The data presentation was followed by a long, detailed discussion on the use of different animal strains in research and their outcomes. It was stated that it is extremely important to define the outcome/endpoint that is important to the researcher. The question is: what experimental animal do I want? Obese, diabetic, both…The answer has or can have a huge impact on the choice of the mouse model. Everybody agreed that it would be ideal/beneficial/helpful to have some agreement within the icemed allicance to have standard mouse models for standard endpoints that all partner researchers could access.

Topic 4: Definition of endpoints/read-outs

In order to evaluate the effect of diets and/or mouse models on endpoints that will be measured the following parameters need to be considered:

- group size
- gender differences for all parameters below:
  lean versus fat mass
  distribution of fat (subcutaneous, abdominal; NMR, DEXA)
  body weight, food intake
  fasting glucose (how often, time of day, duration of fasting)
  GTT (how is glucose measured?, duration of fasting, normalised to BW, Lean body mass, fat mass…?
  blood insulin levels
  other phenotype data???
- Which read-outs are used: (ie clamps for leptin resistence)?
- Which disease model is required: which diet is best to achieve that: 60% vs 40% HFD?

Topic 5: Milestones

Short term:
Establish inventory of current DIO mouse models of icemed partners (possibly non-icemed partners?)
Establish intranet platform+forum on icemed website (excel sheets, data sets, linked to icemed partners, interactive)
Define research goal for focus group publication (to provide information on relevant parameters before starting the experiment? What is already out there in the literature?
Organise 2nd focus group meeting mid may in Munich

Mid term:
Plan possible experiments (ie test different diets in one lab under similar research/laboratory conditions)

Long term:
Publication
Maintain/possibly extend icemed platform and forum on website

Topic 6: To do list

The following to-do-list was agreed on:

J Kampe – search/scan recent literature on current research diet/mouse model data of the last 12 months worldwide, check whether to include non-icemed scientists to the analysis

C Meyer – create excel table/template for inventarisierung/Meta analysis to send out to all icemed partners to fill in with existing data sets

P Wiedmer – information on intranet platform for icemed website (what is focus group?,…)

J Rozman – search/list available diet options to make animals obese/diabetic (what high caloric diets are available and used in germany?, make a list of different high fat diets)

J Beckers – coordinate list of most commonly used research diets, include cafeteria diet (high fat, high sucrose diet), which control diets?

M Berriel Diaz – mouse models (genetic background, sub-strain, supplier)

H Brönnecke – collect/analyse/coordinate existing data

All – establish platform within icemed alliance for standard protocols for research diets/mouse models, publish in high impact journal

The next meeting for the focus group is scheduled for the 13th May 2013 to evaluate literature search and data files from meta analysis.

Topic 7: Outcome: What are the questions/tasks for the focus group?

What is the gold standard for the "perfect" mouse model for diabetes research with respect to diet and strain?

Most current models in the literature and clinical studies are performed in male animals (tricky to get females diabetic). How can the data be translated to female models?

Create and establish "ICEMED standard" and make visible/accessible on PLATFORM+FORUM on icemed website through intranet (important to keep it internal).

Internal recommendations on icemed website for research diets, mouse strains for specific endpoints and disease paramters.

Establish an inventory among icemed partners with respect to animal models (diet, age, mouse strain, supplier,…) and specific endpoint in animal research (obese, diabetic mousemodels)

Forum is essential: somebody needs to oversee information, update, define (ie which strain, supplier,…)

Draft questionnaire for all icemed partners for diet, mouse model to fill in:

- Mouse strain (Jackson, …)
- Diet (Research diets, …)