



Dutch Society for Research on Ageing

Newsletter

Number 1, 2016

The Dutch Society for Research on Ageing (DUSRA) promotes activities for scientists engaged in all areas of aging research. This includes studies in human and animal models, model systems and cellular models.

The society aims to:

- Gain a better understanding of the causes and consequences of the aging process.
 - The promotion of observational studies and experimental approaches in the biological and medical science, to get a better understanding of the ageing problem.
 - Provide a forum to discuss current ideas.
 - Discover new perspectives of interpretation, prevention and therapy of aging and age-related diseases.
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This newsletter is for members of the Society.

You can send your comments or contributions for the next newsletter to:

j.s.vriezen@lumc.nl

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FROM THE BOARD

Dear All,

Following the inspiring Kick-off meeting, thanks to you all, we have written a newsletter with some interesting information for you. First of all you will find included a summary of the Kick-off meeting. We also include a short summary of bullet points extracted from a Lorentz meeting that was held in January this year to discuss ways to stimulate translational science in ageing research. It will not surprise you that a major conclusion was that a large gap exists between basic and clinical science in ageing research and it became clear that both disciplines are eager to close that gap. With our DuSRA we intend to stimulate discussions in a thematic way to design, refine and jointly work on pipelines of research in which basic, biomedical and clinical groups work together. We do not have a lack of ideas but of navigators that can link fields of expertise in the light of a clinical endpoint.

With the DuSRA board we have used the conclusions of the Lorentz expert meeting to discuss the future of ageing research with ZoNMW, our major medical research council in The Netherlands. In addition we have taken the first steps to link our DuSRA with the Dutch Society for Internal Medicine to structure joint meetings concerning the themes and also with sister Societies on Ageing Research in the EU and the US. At a meeting in New York next year we will discuss collaborative efforts to generate more support for ageing research.

We hope you enjoy this Newsletter and wish you all a great summer.

Warm regards,

Eline Slagboom

On behalf of the DuSRA board



KICK-OFF MEETING- 'MEET THE DUTCH SOCIETY FOR RESEARCH ON AGEING'

On the 15th of April 2016, the Dutch Society for Research on Ageing (DuSRA) held its well-attended kick-off meeting in Leiden. In the historical setting of the Scheltema building about 90 participants from a variety of backgrounds met to interactively discuss the challenges and opportunities for ageing research. The mix of researchers, clinicians, health care professionals, policy makers and representatives from industry ensured an active exchange of ideas and a lively discussion.

The programme centred on eight oral presentations that aimed to highlight on the one hand the strength of the Dutch ageing research field, and on the other hand stressing the urgent need of tying together the research on the biology and molecular mechanisms of ageing with what is needed in the clinic and for immediate and long term health care and prevention for the elderly. These talks and Dutch ageing research in general were further supported and illustrated by poster presentations. The posters served as a means to make connections and meet up during a two hour dedicated time slot and during the lunch and the closing drinks. The potential impact of the meeting was illustrated by the active participation of the director of the National Institute of Aging (NIA) prof. dr. Luigi Ferrucci.

The meeting started with a welcome and introduction by prof. dr. Jan Hoeijmakers, one of the DuSRA board members. Prof. Hoeijmakers emphasised that fundamental knowledge on the biology of ageing is crucial not only to devise strategies to alleviate the negative effects of reaching old age, but is also likely to uncover common causes of non-communicable diseases. This would enable the development of strategies that cut across age-related



diseases such as dementia, cardiovascular diseases, and type 2 diabetes. Moreover, as was stressed in the presentation of the chair of DuSRA prof. dr. Eline Slagboom, the time is now to make the connection between more fundamental research on the biology of ageing and the pressing problems in the clinic and that are challenging the elderly and the health care providers alike. Prof. Slagboom underscored that

fundamental research (for instance though using animal models) should be much more put "at the service" of the scientific research questions associated with these problems. Prof. Slagboom therefore provided an exciting set of so-called research pipelines (s.a. muscle research, research into energy metabolism and metabolic health) along which the exchange of information, as well as integrated research projects, could be developed between research on the basic biology of ageing on the one and the needs of the clinic on the other hand.

During the presentations and the discussions there was largely agreement on the need of fundamental research on cellular and molecular mechanisms of ageing for which currently no direct relevance for the clinic could be foreseen. As ageing is such a ubiquitous phenomenon at all levels of biological organisation (from molecules, cells, tissues, to whole organisms), studying basic cellular processes can lead to unexpected yet crucial results. This



was very elegantly illustrated in the presentation of prof. dr. ir. Ellen Nollen. Prof. Nollen showed that her basic research on the cell biology of the nematode *Caenorhabditis elegans* has led to essential leads for understanding Alzheimer disease in humans. Her work illustrated that also non-vertebrate models have an essential role to play in ageing research. The use of a mouse model proved its value in the work presented by dr. Ingrid Meulenbelt. Her work on osteoarthritis uncovered a crucial link between developmental and ageing related processes. Key observations in human cohorts could be experimentally verified, among other using a mutant mouse model.

The value of well-characterised and longitudinally followed human cohorts was very nicely explained in the presentation of dr. Joyce van Meurs. The Rotterdam Study is a prospective cohort followed since 1990 and genetic and molecular data has been collected for many subjects since then. This data allows the identification of candidate genes and mechanisms underpinning a large variety of health related phenotypes. The increasingly well-organised national and international consortia in human genetics provide an exciting platform for validation and cross-checking of results.

What to do with all this basic knowledge in the human context? One realistic and sustainable way to influence the ageing and health care trajectory of humans is through nutrition. Research in models and humans alike has indicated that nutrition, both amount and composition, affects health parameters up until very late ages. The presentation of prof. dr. Lisette de Groot showed the potential of nutritional interventions. Focussing on the protein balance, her talk at the same time highlighted the need for nutritional studies specifically in the elderly as what is beneficial for young or middle-aged individuals may actually be detrimental at old age. A specific public health perspective was provided by prof. dr. Erik Buskens. Using the "Blue zones" (areas in the world for which exceptional longevity has been reported) as a starting point, prof. Buskens explored the possibilities of how to eradicate the large health and lifespan gaps that are observed between different regions in the Netherlands, sometimes over relatively short geographical distances. One of the major challenges and focal points of DuSRA is to connect the knowledge on genetics, molecular mechanisms, and (nutritional) life style to these disparate life expectancies.



The DuSRA kick-off meeting did not only provide a Dutch perspective as it is realised that we should use the potential of international cooperation as many, if not all, of the discussed issues and major health and ageing challenges should be tackled in, and have a global context. Therefore, the board of DuSRA was especially pleased with the presence of a delegation from the Brazilian scientific community in Sao Paulo and prof. dr. Luigi Ferrucci. Prof. Ferrucci in his presentation provided valuable insights into how he has and is shaping the research agenda of the NIA and what the specific challenges are that are associated with

bridging the very broad range of research approaches and topics in the ageing field. Currently, the NIA is focussing on how energy budgets relate to the ageing process and whether changes with age in these budgets could be both drivers of ageing as well as a means to influence its course.

For more information on the programme and the (abstracts of) the posters, mail us and ask for the booklet of the meeting (J.S.Vriezen@lumc.nl).



LORENTZ MEETING 6-8 January 2016

'TRANSLATIONAL AGING RESEARCH. *Challenges and opportunities*'

SUGGESTIONS TO IMPROVE TRANSLATIONAL EFFORTS OF AGEING RESEARCH

Why examining the ageing process?

Age is a common risk factor for all major chronic diseases we are faced with today (perhaps with the exception of depression). Lifestyle factors apparently interact with physical changes occurring in the course of life to disrupt normal physiology. Therefore, it is of critical importance for our understanding of the pathogenesis of all chronic disorders to map the aging process *per se* and find ways to beneficially modulate it. So far, this has been done with great success primarily in laboratory animal models. The time has come to shift focus to the aging process in humans.



The Lorentz meeting advised on five major points of improvement to stimulate translational research.

1. Improving communication and joint programs for basic and clinical sciences.
2. Improving the understanding and modulation of human ageing.
3. Improving research in the human biomedical and medical domain.
4. Improving accessibility of human big data and biological material.
5. Support for future focus.

Read the whole article (volgende gedeelte link naar website met stuk)

Improving communication and joint programs for basic and clinical sciences.

Problem: The lack of contact between basic, biomedical, and clinical research hampers exploration of the translational potential of results. These disciplines need to understand, and eventually share, each other's language, ideas, jargon, and methods.

- **Solution a:**
Stimulate clinical parties to join DuSRA, make integrated meeting programs and working groups.
- **Solution b:**
Define and structure working programs as research pipelines with the goal to improve the health of specific systems. For example, the musculoskeletal system, the brain-heart axis (neuro-cardio-vascular degeneration), and neuroendocrine systems. as they affect multiple diseases. Draw pipelines of subsequent steps in joint research of clinicians and basic scientists based on improvement of specific systems, defined by surrogate and clinical endpoints (see also point 2-4).

- **Solution c:**

Training programs for 'Navigators'. The Max Planck Institute in Cologne created special jobs for 'navigators', dedicated to translational science which combined in their training program sufficient knowledge of basic sciences and clinical research to connect these disciplines.

Improving the understanding and modulation of human ageing.

Problem: Suboptimal alignment between ageing research in animal models and humans.

- Central ageing mechanisms in animals include energy metabolism and homeostasis (brain/muscle/cell driven), damage control (immune response, DNA repair, proteasome), and developmental programs (stem cell maintenance, epigenetic maintenance of differentiation). Many of these pathways have to be more systematically investigated for their relevance to human ageing.
- Research in animal studies is providing leads by which such mechanisms can be modulated during the life course. These need to be followed up in physiological studies of humans and animals simultaneously. International experts at the Lorentz meeting indicated that The Netherlands is in a fantastic position to reach such complementarity.
- Animal studies should focus on providing novel biomarkers monitoring the modulation of physiological ageing in specific functional systems (1b) and that can be used in humans. Focus for biomarker studies on longitudinal human and animal cohort studies.

Improving research in the human biomedical and medical domain.

Problem: Medical interventions in elderly fail if drugs were not tested in heterogeneous elderly populations. For age-related diseases, drugs are often developed for surrogate endpoints (improvement of clinical endpoint takes too long). In trials they tend to fail because of unexpected (pleiotropic) negative effects on clinical outcomes. Likewise, preventive intervention studies are usually too small to test what treatment works best for which group of elderly.

- More research into the effect of drugs in elderly individuals including testing drugs and the molecular pathways they affect in aged cells and tissues (of animals and humans).
- Larger scale physiological (challenged) studies in elderly humans. Larger and longer intervention studies focused on testing resilience and modulation of healthy ageing.
- Increase coherence of human biomarker research. Come to agreement on reliable maximally informative biomarker sets that establish individual physiological/biological age to be used as outcome measures in intervention studies

and in population-level surveys. Maximally informative means predictive of morbidity/mortality at different age strata.

- Better classification of elderly patient groups (for personalized medicine) requires collection of hospital-based elderly patient cohorts (in addition to population based cohorts).
- Formation of collaborations around deeply phenotyped human cohorts with high definition and multilevel genomics data to produce reliable and reproducible (genomic) markers for disease and healthy ageing.
- More attention for ongoing life course studies (currently in the longest study individuals were followed from birth to 70 years). Focus on familial risk (better control treatment of hypertension in middle aged offspring of dementia patients). Focus on diversity in the population (gender, origin) and include studies in developing countries of which the ageing population will grow even faster than ours.

Improving accessibility of human big data and biological material.

Problem: Only about 15% of stored biosamples are being used in research, knowledge on repositories of human biosamples, human data and data analysis tools is not sufficiently distributed.

- Organize datawarehouses of patient material, biological samples in cohorts and in animal studies.
- Improve trainings for basic animal and clinical scientists to work with these and human web based data and promote collaboration between computational biologists and clinical scientists to improve methods of data analysis.

Support for future focus.

- Focus research programs on translational research eventually applicable in clinical practice. Balanced reviewing panels of clinical and basic scientists for projects on ageing research to improve funding for translational research. 'Ageing' has often been a priority in funding programs without experts in reviewing panels.
- Focus on influencing central mechanisms driving ageing where clinical, basic human and animal studies jointly explore functional systems; to help in designing the pipelines, attract professionals trained in translational research for disease.
- Focus on increasing awareness of content and value of ageing research in industry in order to gain support for including ageing research in large funded programs. It is noteworthy that a company such as Calico has recruited many prominent scientists with distinguished track records in basic research. Calico, as DuSRA, strongly believes that more funding for basic research is essential for combating ageing and associated diseases.

QUOTES **From interviews taken by Rebecca Miller at the Lorentz meeting**

Andrzej Bartke, Professor Geriatric Medicine, Southern Illinois University School of Medicine, Director of Southern Illinois University's Aging and Longevity Research Laboratory, Carbondale, USA:

"Not that long ago ageing was simply considered unavoidable. Now we know we can manipulate ageing. There is no question about it. And it would be a shame not to take benefit of that knowledge..."

"Rather than tackling cancer, or dementia, or cardiovascular disease, we should focus on slowing or reversing the single most prominent risk factor associated with all those diseases: AGE..."