Published in final edited form as:

Exp Gerontol. 2008 July ; 43(7): 603–604. doi:10.1016/j.exger.2008.05.009.

Tissue Ageing: Do insights into molecular mechanisms of ageing lead to new therapeutic strategies?

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In most industrialized countries, people are living longer. Both the absolute number and proportion of elderly individuals in these societies is increasing dramatically as a result of reductions in mortality, lower fertility rates, and baby boom cohorts entering old age. Therefore, clinicians are now faced with increasing numbers of diseased elderly, and the majority of medical problems are ones for which age is a significant risk factor. Unfortunately, evidence based medicine as the highest standard has not been able to provide data for the management of diseases of the elderly largely due to the fact that, for many years, people older than 70 were excluded from clinical trials. Given the significant increases in disease incidence with age, the likelihood of concurrent medical conditions, and changes in pharmacokinetics and responses to medications in the elderly, clinical studies specifically focused on aging individuals are necessary.

Advances in the treatment of diseases of the elderly will require a dialogue between clinicians and researchers. The medical specialty of Geriatrics tends to focus on the symptoms of diseases of old age whereas biogerontologists tend to focus on the biological basis for ageing with less emphasis on the mechanisms and treatments of diseases. A crosstalk is therefore needed to bridge the gap between these groups and to translate scientific advances into progress in the diagnostics and therapeutics. The workshop “Tissue Ageing: from Molecular Biology to Clinical Perspectives” held in Halle/Saale, Germany, in 2007 was the third in a series of meetings to stimulate such an exchange of ideas. Reviews and original research reports of attendees of this meeting are the basis of this special issue.

The spectrum of reports included range from molecular studies of genes and proteins to clinical studies, with many reports focusing mechanisms of DNA and cellular damage. The role of the Poly (ADP-ribose) polymerase (PARP) as a major enzyme involved in the DNA repair response is described by Beneke et al., whereas Ang et al. concentrate on apolipoprotein E (ApoE) and its role in the ageing process highlighted by studies of a knockout mouse model. The group of Mueller et al. describe the tissue-specific appearance of cellular markers of ageing. They report that patients with emphysema show increased levels of senescence-associated beta galactosidase in fibroblasts in the lung compared with those in the skin. These results suggest that the induction of a senescent phenotype by cigarette smoke, as observed in emphysema, primarily occurs in the lung. Another exogenous source of cellular damage is

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radiation from sun exposure, producing mostly oxidative stress in the skin. Interestingly, Schroeder et al. describe that beside UV, infrared light is a major source in photoaging of the skin. Argenitono et al. further concentrate on this issue and show the effects on matrix metalloproteases as well as collagen regulation after UV-A, UV-B and infrared radiation of dermal fibroblasts. Oxidative stress as a major cause of cellular aging is often analysed within cells by fluorescent probes. The pitfalls of such measurements are described by Broemme et al. A major source of reactive oxygen species (ROS) leading to oxidative stress is the respiratory chain of the mitochondria. Interestingly, Meissner et al. identified a specific pattern of a mitochondrial DNA deletion among different tissues. Targeting ROS can be important for the treatment of patients as well. A therapeutic approach for patients undergoing cardiac surgery is summarized by Pepe et al. The positive effect of low stress as an adaptive response to the ageing process is called hormesis and described on the cellular level by Berge et al. In combination with carbohydrates, ROS can induce the formation of advanced glycation endproducts (AGEs). AGEs measured in the skin are related to chronological age and the body mass index of healthy subjects, as shown by Corstjens et al. Sarcopenia is an important consequence of aging and a major cause of disability and mortality. Studies of approaches to prevent sarcopenia in an animal model are presented by Arora et al., and Bauer et al. present an overview of sarcopenia in humans. The use of stem cells to prevent or reverse tissue structural and functional changes in aged tissues holds great promise. Whether cardiac cell therapy in its present form is a realistic concept for elderly patients is discussed by Stamm et al. In line with a possible consequence of tissue ageing, Simm et al show that the drug Cariporide may protect young human myocardium but not old myocardium against ischemia reperfusion injury. Different approaches to avoid or modulate aging are described by Aspinall et al. for the immune system or by Niemann et al. for the cardiovascular system. In summary, the proceedings of this workshop illustrate how understanding basic mechanisms of ageing may lead to better treatment of patients in the near future.

Fruitful discussions during the meeting made it quite apparent that an interdisciplinary platform is needed for a productive exchange of knowledge between basic and clinical scientists. We look forward to an acceleration of translational research emerging from these interactions.