

An international effort to cure premature ageing

Richard Faragher¹, Makoto Goto²

Key Words: Aging/Ageing, senescence, Werner syndrome, research network

Human civilizations are remarkably diverse. However, their citizens share a common cliché that the only certainties in life are death and taxes. Now, in the developed world there is a third virtual certainty; which is that death will come as a consequence of old age. This population ageing is the central demographic fact of the 21st century. By 2030 anywhere from 25% to 40% of first world citizens will be over 65. Living this long is a testament to medical progress.

Unfortunately, ageing is associated with an increased chance of death or the development of long-term morbidity. UK morbidity costs (in 1995) were estimated to be anywhere between £14 to £45 billion and are predicted to rise to somewhere in the region of £30 to £65 billion by the year 2030. These costs reflect a tremendous burden of human misery arising from poverty and poor quality of life. Improving healthy life for older people is thus the key challenge faced by biomedicine today.

Ageing is the unprogrammed consequences of mutations or processes favouring early life fecundity. It is innately complex and multifactorial rendering it a difficult area of research in which to apply post-genomic technologies. This has led to a need for more tractable model systems which recapitulate some, but not all aspects, of the normal ageing process. Perhaps the most famous of these is Werner's syndrome; an autosomal recessive genetic disorder in which



Figure 1. Meeting participants in front of Keio Plaza Hotel, Shinjyuku, Tokyo.

Table 1. Werner Syndrome Consortium Meeting Programme

Day 1

- Opening Remarks. *Makoto Goto, MD. Toin University of Yokohama, Japan*
- British ageing research: an overview of collaborative opportunities. *Richard Faragher, PhD. Brighton University, UK*
- Werner syndrome updated. *Makoto Goto, MD.*
- Clinical features of Werner syndrome: from a metabolic point of view. *Koutaro Yokote, MD. Chiba University, Japan*
- Stress, immunity and ageing. *Janet Lord, PhD. Birmingham University, UK*
- The role of stress kinases in the replicative lifespan of Werner's syndrome cells. *Terry Davis, PhD. University of Cardiff, UK*
- Homologous recombination and the Werner syndrome protein. *Kiyoshi Miyagawa, MD. University of Tokyo, Japan*

Day 2

- Chemical synthesis in the study of accelerated aging. *Mark Bagley, PhD. University of Cardiff, UK*
- Searching for hints of drug discovery from the study of Werner syndrome. *Yasuhiro Furuichi, PhD. GeneCare Institute, Japan*
- Biomarker discovery for Werner syndrome, using proteomic serum profiling. *Naohisa Tomosugi, MD. Kanazawa Medical University, Japan*
- Alteration of IgG oligosaccharide structure during normal and accelerated ageing. *Munehiro Nakata, PhD. Tokai University, Japan*
- What has replicative senescence got to do with organismal ageing? *Richard Faragher, PhD.*

Day 3

- Transcriptomic analysis of replicative senescence. *David Kipling, PhD. University of Cardiff, UK*
- Gene expression profiling in Werner syndrome family. *Yuichi Ishikawa, MD. Japan Cancer Institute, Japan*
- Modelling wrn function using *Drosophila melanogaster*. *Robert Saunders, PhD. The Open University, UK*
- Dermatological features and collagen metabolism in Werner syndrome. *Atsushi Hatamochi, MD. Dokkyo University, Japan*
- DNA microarray analysis of Werner and Werner-like syndrome. *Yasuhito Ishigaki, PhD. Osamu Nikaido, MD. Kanazawa Medical University, Japan*

individuals prematurely display many, but not all, of the features of normal human ageing. Although the identification of the mutation causing Werner's syndrome took place in America, this was underpinned by the outstanding work of the Japanese clinical community, which identified more than three quarters of all the world's Werner's syndrome patients. In the United Kingdom, research into the fundamental biology of the disease has provided a mechanistic understanding of how the disease operates at the cell and tissue level. These developments set the scene for the first meeting of the Anglo-Japanese Werner's syndrome consortium in Tokyo earlier this year. This consortium is funded by the Biotechnology & Biological Sciences Research Council of the United Kingdom with the goal of sharing resources and expertise. Space precludes a full description of the science presented however we have listed the subject areas covered in Table 1 so that readers can source key literature references independently.

The central scientific points of the meeting were (i) that existing drugs and improved care regimes now have the potential to considerably increase the life expectancy of Werner syndrome patients (ii) that the most likely cause of primary pathology in the disease

is premature cellular senescence (with concomitant activation of p38 map kinase signaling); raising the possibility that inhibitors of this pathway currently in clinical trials may be realistic future therapies for the disease and (iii) that an intact Werner's syndrome helicase is a key molecular requirement for the development of many different types of cancer. On a more general note, the meeting showed that real advantages can be gained by providing research funding which allows chemists, biologists and clinicians to collaborate across national boundaries on a single biomedical problem. Werner's syndrome research in particular is now shifting towards the type of multi-national, multi-disciplinary mode of research which inspired the Editors to found *Bioscience Trends*. It is hoped that we will have significant biomedical progress to report in the years to come.

(¹SPARC Programme Director, School of Pharmacy & Biomolecular Science, University of Brighton, Brighton UK; ²Division of Anti-Ageing & Longevity Sciences, Department of Clinical Engineering, Faculty of Medical Engineering, Toin University of Yokohama, Yokohama, Kanagawa, Japan.)